



Neurodegeneration-related genes influence *C. elegans* pharyngeal activity

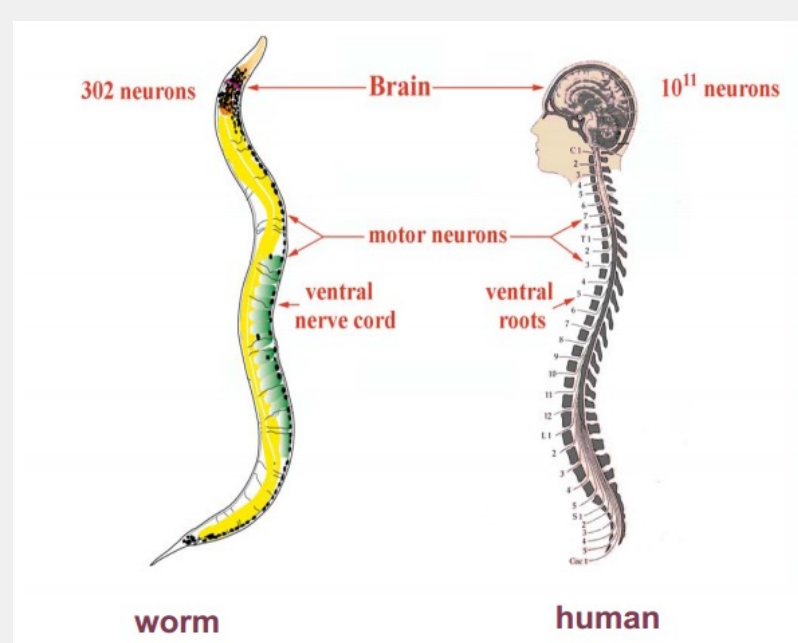
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Abstract

Pharyngeal pumping and its reduction following mechanical insult are well-studied *C. elegans* behaviors. Here, we assessed new applications of pharyngeal pumping assays in the study of neurodegenerative disease and psychiatric illness. We examined five genes implicated in two forms of neurodegeneration, Hereditary Spastic Paraplegia (HSPs) and Alzheimer's Disease (AD), for both baseline pharyngeal pumping and the depressive response after touch stimulus. All five mutants showed reduced baseline pumping rate, suggesting a potential utility of this assay to study neurodegenerative disease on a broad scale. However, regarding the induced pumping response, which has been linked to schizophrenia, only specific genes, the HSP-related *atln-1*/Atlasin and the AD-related *ptl-1*/tau, showed defects. Together, we highlight two pharyngeal pumping behaviors as genetically distinct, potentially informative settings for understanding the functions of genes linked to neurodegeneration.

Background

- C. elegans* are a useful model system to study the behavior of neurodegenerative disease and possible links with psychiatric diseases
 - Similar number of genes ~ 20K
 - ~ 40% of genes implicated in human **disease** have equivalents in worms



- Psychiatric illnesses have observable behaviors called endophenotypes.
- Proto-phenotypes are endophenotypes that have been conserved during evolution
- Endophenotype in schizophrenic patients is an excessive startle/arousal
- Proto-phenotype in *C. elegans* WT is inhibition of pharyngeal pumping that normally occurs at a high rate.
- Depression in pumping rate following mechanical stimulation has been linked to both neurodegeneration and psychiatric disease

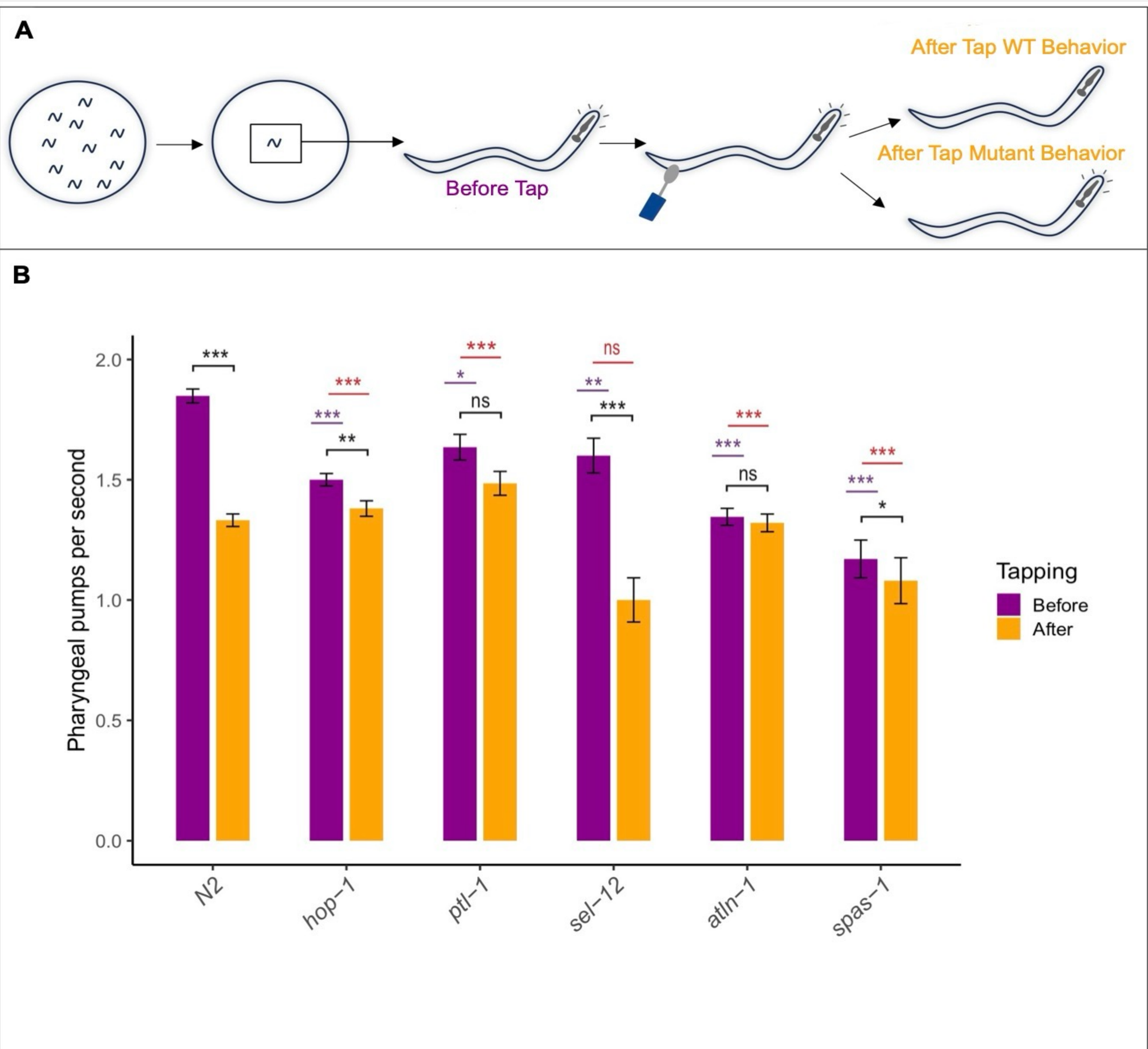
Objective & Approach

- Objective: To utilize *C. elegans* pharyngeal pumping behavior in the study of neurodegenerative disease. In addition to find possible links with psychiatric disease.



- 10 worms were placed at the L4 stage onto unseeded plates and the number of pharyngeal pumps (movements of the grinder in the terminal bulb) were recorded for 20 seconds
- Inhibition assays involved tapping each nematode near their tail with a worm pick.
- Pharyngeal pumping was then recorded for another 20 seconds. For every trial conducted both the control (N2, n=10) and a mutant (n=10) were assayed

Results



(A) Schematic of experimental paradigm. (B) Quantification of pharyngeal pumps per second. Purple bar, before tap; orange bar, after tap. Black lines, paired t-test (Before and after compared within genes) with Bonferroni correction; purple lines, Dunnett's test comparing pharyngeal pumping at base against N2 from two-factor ANOVA; red lines, Dunnett's test comparing the difference in pharyngeal pumping response (Before - After) from two-factor ANOVA. Asterisks convention: *** for p<0.001, ** p<0.01, * p< 0.05.

Future Directions

- Visual examination of movies acquired under both conditions to aid detection of subtle behaviors
- Additional genes would be considered, together with their possible interactions with the genes tested here, which would also be tested for neuron-specific function.

References and Funding

- Selvarathinam, H; Elkalil, A; Schargel, WE; Ghose, P (2024). Neurodegeneration-related genes influence *C. elegans* pharyngeal activity. *microPublication Biology*. [10.17912/micropub.biology.000897](https://doi.org/10.17912/micropub.biology.000897).

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QR Code to Publication

