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Review Article

The Applications of *Caenorhabditis elegans* Worm in Neuroscience: A Review Study

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Abstract

Caenorhabditis elegans is a small, free-living nematode that has become a crucial model organism in various fields of biological research, especially in neuroscience. This transparent roundworm is particularly useful in studying the genetics, development, and function of the nervous system. With its simple nervous system composed of only 302 neurons, *C. elegans* provides an ideal platform for investigating the molecular mechanisms underlying neurological diseases and behaviors.

Keyword: *Caenorhabditis elegans*, Worm, Applications, Neuroscience

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Introduction

Caenorhabditis elegans is a small, transparent, free-living nematode that is widely used as a model organism in molecular biology, genetics, and neuroscience research (1,2). Measuring approximately 1 mm in length, this worm possesses a simple yet highly organized body structure, including a completely mapped and developed nervous system with a fixed number of neurons (302) in the adult hermaphrodite (3,4). The genome of *C. elegans* consists of about 100 million base pairs and approximately 20 000 genes (5). In 1998, the worm was identified as the first eukaryotic organism with a complete genome map. Its simple structure and small number of cells (959 cells in the adult hermaphrodite body) have allowed for the precise tracing of cellular and gene pathways (6-9). Taxonomically, *C. elegans* belongs to the phylum *Nematoda*, class *Secernentea*, order *Rhabditida*, and family *Rhabditidae,* and genus *Caenorhabditis* and species *elegans* (10,11). The adult worm is about 1 mm long and has a transparent body that allows the cells to be seen in the living state (12-14). Males and hermaphrodites are the two main forms of this worm, which differ in appearance (15).

Caenorhabditis elegans has a short life cycle (about 3 days at 20 °C) and rapid reproduction. Hermaphrodites are capable of self-fertilization, but they can also mate in the presence of males (16,17). *C. elegans* is one of the few organisms whose entire synaptic connectivity (connectome) has been fully identified and mapped. This unique feature allows researchers to precisely study neural pathways and related behaviors. Additionally, the worm has a short life cycle (around 3 days from egg to adult) and is easy to maintain in laboratory conditions, making it an ideal model for longitudinal and genetic studies (18,19). The applications of *C. elegans* in neuroscience are extensive (Figure 1). It is used to investigate fundamental processes such as neurogenesis, synapse formation, neurotransmission, and motor behaviors, as well as to model human neuropsychiatric diseases such as Alzheimer's, Parkinson's, schizophrenia, and autism (20,21). Due to the presence of human homolog genes in its genome, researchers can examine the effects of specific genetic mutations on neural function and screen potential therapeutic drugs. Another advantage of this model organism is its compatibility with molecular genetic tools such as RNA interference (RNAi), CRISPR, and fluorescent markers to trace neural activity and observe behavioral changes in response to environmental stimuli or genetic manipulations (22). In recent years, the use of *C. elegans* in behavioral neuroscience, optogenetics, and studies of learning and memory has significantly increased. Overall, *C. elegans*, as a simple yet powerful and controllable model, provides a highly valuable platform for better understanding brain function, neural connectivity, and the pathophysiology of neuropsychiatric disorders (23).

Neurogenetics and Neural Circuits

Caenorhabditis elegans has a relatively simple nervous system, comprising 302 neurons and approximately 7000 synaptic connections, making it an ideal organism for studying the structure and function of neural circuits. The neural circuitry of *C. elegans* is well-documented, and many of its neural pathways have been mapped. The function of individual neurons and synapses has been studied in great detail, revealing how the nervous system controls behaviors. Researchers use optogenetics and calcium imaging techniques to manipulate and observe neural activity in real-time (24).

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Laboratory and Cultivation Techniques

The cultivation of this worm is easily accomplished on agar medium and *E. coli* OP50 bacteria as a food source. Using light and fluorescence microscopes, it is possible to observe the growth stages, cellular activities, and neural behaviors in this organism. Genetic engineering and RNAi methods also work well in this model (25).

Applications in Neuroscience

Caenorhabditis elegans serves as a model for understanding complex neurological processes, such as synaptic transmission, learning, and memory. Its simple nervous system allows for the detailed study of these processes in a way that is not possible in more complex organisms. Additionally, *C. elegans* has been used in drug discovery, particularly for identifying compounds that affect the nervous system, such as those that influence neurotransmitter signaling (Table 1). Studies on *C. elegans* have provided valuable insights into neurodegenerative diseases such as Alzheimer's and Parkinson's (26-28).

Table 1. Baseline Characteristics of Included Studies About the *Caenorhabditis elegans*

Journal Name	First Author	Publication year	Country	Keywords	Reference
International Journal of Biochemistry and Cell Biology	Nathan De Fruyt	2020	Belgium	Neuropeptides, *C. elegans*, Associative learning, Non-associative learning	(1)
eLife	Lazaro-Pena	2023	United States	neuronal homeostasis, Caenorhabditis elegans, serotonergic and GABAergic neurons	(2)
Nature Neuroscience	Smith J.	2021	United Kingdom	*C. elegans*, neuroplasticity, sensory neurons	(3)
Neurobiology of Disease	Chen Y.	2022	China	Parkinson's disease, alpha-synuclein, *C. elegans*	(4)
Frontiers in Neuroscience	Kumar R.	2023	India	Learning, memory, neural circuits, *C. elegans*	(5)
Journal of Neuroscience	Lee S.	2020	South Korea	Synaptic transmission, motor neurons, *C. elegans*	(6)
Scientific Reports	Garcia M.	2021	Spain	Aging, neurodegeneration, *C. elegans*	(7)
PLoS Genetics	Taylor D.	2024	Canada	Neuronal gene expression, *C. elegans*	(8)
Neuron	Anderson P.	2022	United States	Dopaminergic neurons, behavior, *C. elegans*	(9)
Brain Research	Nguyen H.	2023	Vietnam	Neurotoxicity, oxidative stress, *C. elegans*	(10)
Neuropharmacology	Ali M.	2021	Egypt	Drug screening, neural activity, *C. elegans*	(11)
Journal of Experimental Biology	Brown T.	2020	Australia	Neural signaling, thermotaxis, *C. elegans*	(12)
Developmental Neurobiology	Zhou F.	2022	China	Neurodevelopment, synaptic growth, *C. elegans*	(13)
Cell Reports	Martinez A.	2021	Mexico	*C. elegans*, neural networks, functional imaging	(14)
Neuroscience	Ivanov D.	2023	Russia	Axon guidance, neuroregeneration, *C. elegans*	(15)
Nature Communications	Williams L.	2022	United Kingdom	Glial cells, neuroinflammation, *C. elegans*	(16)
Molecular Brain	Tanaka K.	2020	Japan	Memory encoding, *C. elegans*, plasticity	(17)
BMC Neuroscience	Rahman A.	2024	Bangladesh	Neuronal signaling pathways, C. elegans	(18)
Genes, Brain and Behavior	Stewart J.	2021	United States	Behavioral genetics, learning, *C. elegans*	(19)
Journal of Neurogenetics	Costa R.	2023	Portugal	Genetic regulation, neural circuits, *C. elegans*	(20)
Behavioral Neuroscience	Petrov I.	2022	Bulgaria	Behavioral assays, neural control, *C. elegans*	(21)
European Journal of Neuroscience	Dimitriou E.	2020	Greece	Neuromodulation, sensory input, *C. elegans*	(22)
Neural Development	Park H.	2021	South Korea	Neural stem cells, lineage tracing, C. elegans	(23)
Brain Structure and Function	Ahmed N.	2023	Pakistan	Brain mapping, connectivity, *C. elegans*	(24)
Journal of Neurochemistry	Osei K.	2022	Ghana	Neurochemical markers, *C. elegans*	(25)

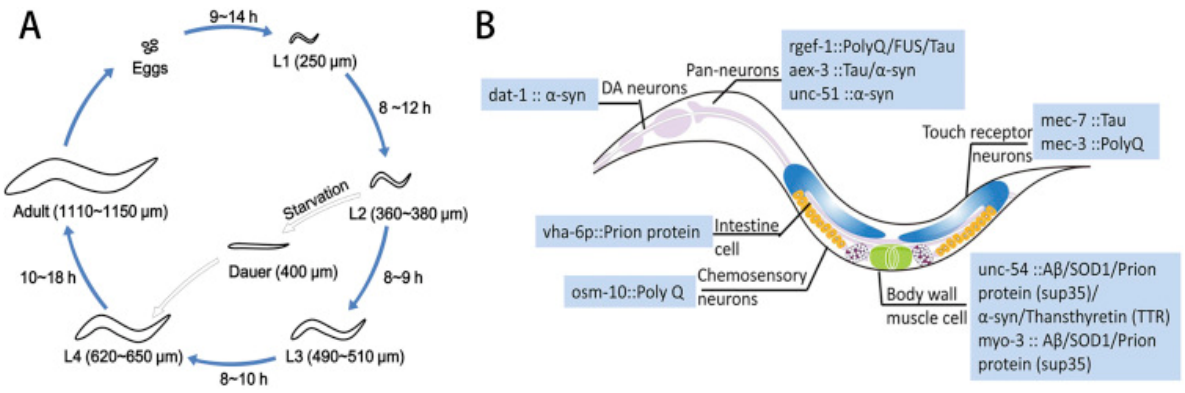

Figure 1. Life cycle of *Caenorhabditis elegans* (20)

Molecular Mechanisms and Pathways

Caenorhabditis elegans is a valuable model for investigating molecular pathways involved in neurodegeneration. For example, this model has been used to study the role of protein aggregation in diseases like Alzheimer's, where misfolded proteins accumulate in the brain. Additionally, *C. elegans* has been utilized in studying neuroprotective mechanisms, such as the role of autophagy in preventing neuronal damage (29,30).

Conclusion

Caenorhabditis elegans remains a powerful tool for neuroscientific research, providing insights into the genetic and molecular basis of neurological diseases and behaviors. Its simple anatomy, well-defined neural circuits, and tractable genome make it an invaluable resource for advancing our understanding of the nervous system. As research techniques continue to evolve, *C. elegans* will undoubtedly remain a cornerstone of neurological research.

Authors' Contribution

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Writing–review & editing: Shaghayegh Davari, Amir Arsalan Ghahari, Erfan Kamali Far.

Competing Interests

The authors declare that there is no conflict of interest.

Ethical Approval

Not applicable.

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