Aging Pathobiology and Therapeutics 2026; 8(3): 345-348 ***345***
DOI: 10.31491/APT.2026.09.240

Creative Commons 4.0

The cricket brain: a tractable system for decoding neural aging

Gerald Yu Liao[a], Ariana Rhim[a], Jackson Wezeman[a], Warren Ladiges[a, b, *]

[a] *Department of Comparative Medicine, University of Washington School of Medicine, Seattle, WA, USA.*
[b] *Division of Gerontology and Geriatric Medicine, Department of Medicine, School of Medicine, University of Washington, Seattle, WA, USA.*

Abstract

Aging of the nervous system begins before overt cognitive impairment, yet identifying early predictors of neural vulnerability remains challenging in conventional vertebrate models. Crickets offer a complementary system in which sensory function, cognition, adult neurogenesis, and molecular mechanisms can be examined across a short, experimentally accessible lifespan. Their mushroom bodies support associative learning and memory while retaining adult-born Kenyon cells, providing a rare opportunity to link neuronal renewal directly to cognitive aging. Age-dependent changes in olfaction, vision, learning, and decision-making may further provide early behavioral signatures of declining neural function. Emerging genetic approaches, including preliminary evidence for adeno-associated virus delivery to the adult cricket brain, could extend this model from observation to causal intervention. Rather than serving as a miniature human brain, the cricket offers a simplified system for identifying conserved mechanisms of neural resilience and testing whether early sensory and behavioral changes predict, and potentially modify, subsequent cognitive decline.
Keywords: Aging, cricket, adult neurogenesis, cognitive decline, olfaction, neural resilience

Aging does not begin with dementia. Sensory processing, memory, and behavioral flexibility decline along distinct trajectories, with sensory dysfunction, particularly olfactory loss, often preceding cognitive impairment and neurodegenerative disease [1-4]. Yet establishing whether these early changes predict later neural vulnerability remains difficult in mammalian models, where lifespan, cost, and experimental complexity constrain longitudinal studies.

Crickets offer a complementary system in which neural aging can be followed across a short, experimentally accessible lifespan (Figure 1). The house cricket, *Acheta domesticus*, and tropical banded cricket, *Gryllodes sigillatus* (manuscript in progress), support sophisticated sensory learning, memory, and decision-making, while retaining proliferative neuroblasts within the adult mushroom bodies [5, 6]. In *A. domesticus*, olfactory preference, associative learning, memory, and decision-making follow distinct age trajectories, with altered decision dynamics preceding broader sensory and cognitive decline [7]. This makes the cricket particularly suited to asking whether early behavioral changes predict later neural vulnerability.

A mushroom body for an aging brain

The insect mushroom body is a higher-order associative center in which Kenyon cells transform sensory input into sparse representations shaped by neuromodulation and synaptic plasticity [8]. Its relevance to human aging lies not in anatomical homology to the hippocampus, but in shared computational principles of sparse coding, learning, and experience-dependent plasticity.

Crickets add a distinctive feature: mushroom-body neuroblasts generate new Kenyon cells throughout adulthood, and their proliferation is regulated by sensory experience [6]. Suppressing neurogenesis impairs olfactory learning and memory [9], while the insect-specific gene *oskar* interacts with the conserved transcription factor cAMP response element-binding protein (CREB) in neural progenitors to support long-term memory [10]. The cricket therefore permits neuronal renewal, experience, and cognition to be interrogated within the same aging circuit.

This becomes particularly powerful with age. Although the extent of adult hippocampal neurogenesis in humans remains debated, declining cellular and synaptic plasticity

* Corresponding author: Warren Ladiges
Mailing address: Department of Comparative Medicine, Division of Gerontology and Geriatric Medicine, Department of Medicine, School of Medicine, University of Washington, Seattle, WA, USA.
Email: wladiges@uw.edu
Received: 04 September 2026 / Accepted: 05 September 2026
Published: 30 September 2026

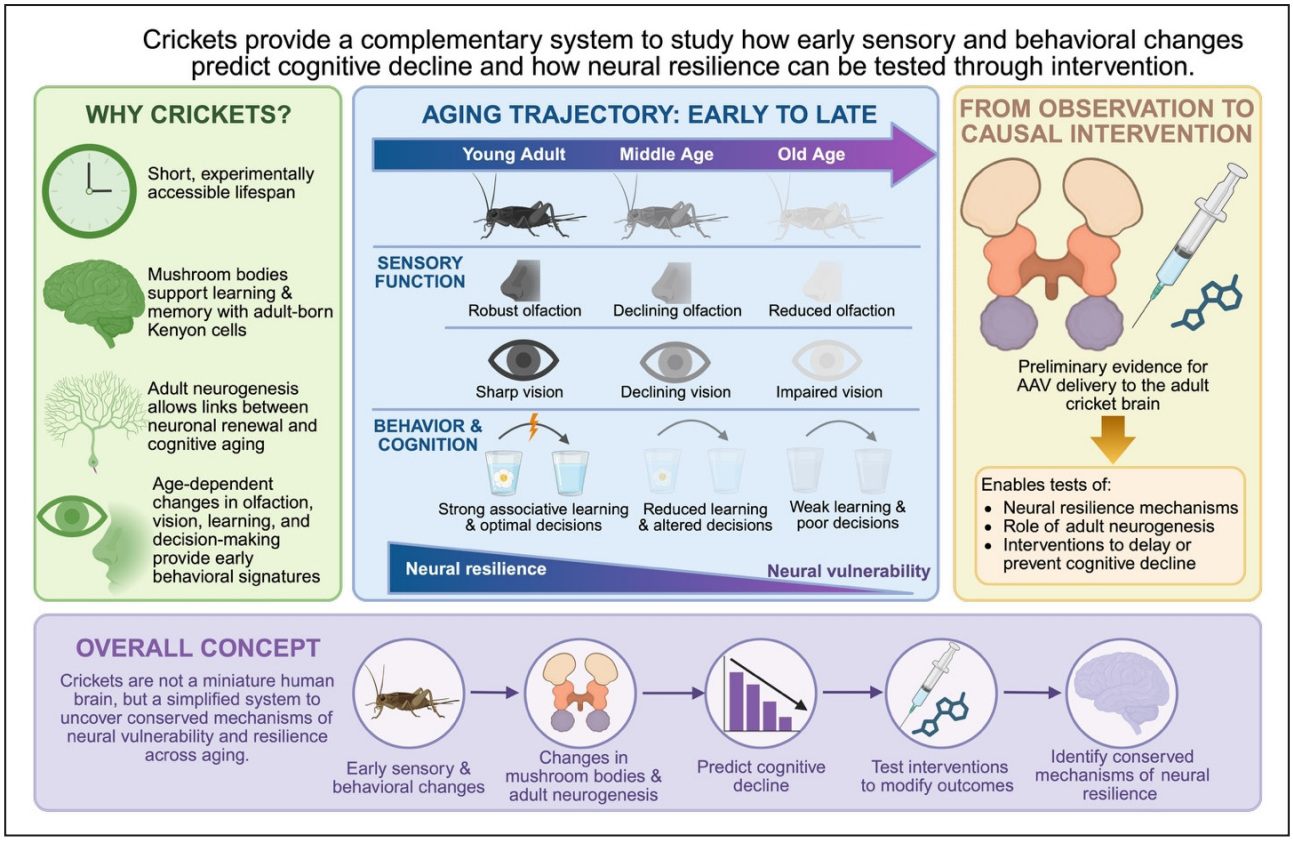


Figure 1. The cricket brain: a tractable system for decoding neural aging. Created in BioRender. https://BioRender.com/7zbcl2k.

are hallmarks of brain aging [11, 12]. In *Gryllus bimaculatus*, age-related long-term memory impairment can be rescued by activating nitric oxide–cyclic guanosine monophosphate (NO-cGMP) signaling [13], demonstrating that cognitive aging in crickets is experimentally modifiable rather than merely observable.

Smell, sight and early signatures of neural aging

Olfaction may provide an especially sensitive window into brain aging. In humans, olfactory dysfunction can precede cognitive decline and neurodegenerative disease [14]. In insects, olfactory information is transformed into sparse mushroom-body representations supporting discrimination and associative memory [15, 16]. Age-related changes in cricket olfaction may therefore provide an early readout of declining circuit function.

Vision offers a complementary measure. Visual and olfactory information converge on higher-order insect circuits, allowing multisensory experience to shape memory [17]. Tracking vision, olfaction, learning, and memory across individual lifespans could reveal whether sensory deterioration precedes, and predicts, later cognitive decline, providing experimentally testable biomarkers of biological brain age.

From observation to intervention

Genomic resources for crickets are also rapidly maturing: *A. domesticus* now has a chromosome-level, annotated reference genome containing approximately 29,000 predicted genes, providing a foundation for identifying candidate pathways, regulatory sequences, and molecular correlates of aging [18]. This growing genomic framework can complement longitudinal phenotyping while enabling increasingly informed design and interpretation of genetic interventions.

The principal limitation, therefore, is not simply genomic characterization but experimental access to the adult nervous system. Genetic tools are expanding in crickets, yet rapid manipulation of the adult brain remains limited. Adeno-associated virus (AAV), widely used for sustained transgene expression in mammalian neuroscience, could provide one route forward, although capsid tropism, promoter compatibility, and host-cell biology make successful application in insects uncertain [19-21].

Our preliminary experiments provide proof-of-concept for viral delivery in *A. domesticus*. Using an AAV construct adapted from a mammalian Alzheimer's disease model [22], crickets received intraperitoneal or intracranial injections. Fourteen days later, treated brains showed amyloid-β- and tau-immunoreactivity. Although capsid, promoter, dose, and delivery require optimization, these findings suggest that viral approaches may permit direct manipulation of the adult cricket nervous system.

If validated, AAV could shift the cricket from an observational model of neural aging to an interventional one.

Viral manipulation could be coupled to sensory behavior, memory, and mushroom-body neurogenesis to identify pathways that causally modify age-related decline. The aim is not to reproduce human Alzheimer's disease in an insect, but to exploit a short-lived nervous system to identify mechanisms of neural vulnerability and resilience for subsequent testing in vertebrate models.

A predictive model, not a miniature human

The value of the cricket brain lies not in anatomical resemblance to humans, but in experimental access to conserved features of neural aging. Proteostasis, metabolic homeostasis, and synaptic plasticity deteriorate with age across species [23, 24]. In crickets, these processes can be examined alongside adult neurogenesis, sensory function, and cognition within a single lifespan.

This creates an opportunity to move from describing aging to predicting it: do early sensory changes forecast memory loss? Can intervention redirect these trajectories? These questions mirror a central goal of human geroscience: identifying vulnerability before decline becomes irreversible [25].

No insect recapitulates the complexity of the human brain. But that simplicity is precisely the opportunity. The cricket brain may be most valuable not as a miniature human brain, but as a system in which the trajectory of neural aging can be observed, predicted, and ultimately altered.

Declarations

Author contributions: All authors contributed to the conception and writing of this commentary: Liao GY, Rhim A, Wezeman J, Ladiges W. All authors read and approved the final version of the manuscript.

Availability of data and materials: Not applicable.

Financial support and sponsorship: This work was supported by the National Institute on Aging of the National Institutes of Health under award number R01 AG067193 (PI, Warren Ladiges).

Conflicts of interest: Warren Ladiges is a member of the editorial board of *Aging Pathobiology and Therapeutics*. The authors declare that they have no conflicts and were not involved in the journal's review or decision regarding this manuscript.

Ethical approval and informed consent: Not applicable.

Consent for publication: Not applicable.

AI and AI-assisted tools statement: No AI tools were used in the preparation of this article.

References

1. Salthouse T. Consequences of age-related cognitive declines. *Annu Rev Psychol*, 2012, 63: 201-226. [Crossref]
2. Whitson H, Cronin-Golomb A, Cruickshanks K, Gilmore G, Owsley C, Peelle J, *et al*. American Geriatrics Society and National Institute on Aging Bench-to-Bedside Conference: sensory impairment and cognitive decline in older adults. *J Am Geriatr Soc*, 2018, 66(11): 2052-2058. [Crossref]
3. Olofsson J, Ekström I, Larsson M, & Nordin S. Olfaction and aging: a review of the current state of research and future directions. *i-Perception*, 2021, 12(3): 20416695211020331. [Crossref]
4. Papadatos Z, & Phillips N. Olfactory function reflects episodic memory performance and atrophy in the medial temporal lobe in individuals at risk for Alzheimer's disease. *Neurobiol Aging*, 2023, 128: 33-42. [Crossref]
5. Liao G, Dai S, Bae E, Singh S, Klug J, Pettan-Brewer C, *et al*. Morphological features of the domestic house cricket (*Acheta domesticus*) for translational aging studies. *Geroscience*, 2025, 47(5): 6487-6511. [Crossref]
6. Cayre M, Strambi C, Charpin P, Augier R, Meyer M, Edwards J, *et al*. Neurogenesis in adult insect mushroom bodies. *J Comp Neurol*, 1996, 371(2): 300-310. [Crossref]
7. Liao G, Klug J, & Ladiges W. Age-related cognitive decline in house crickets reveals conserved patterns of sensory and learning deficits across the lifespan. *Geroscience*, 2026, 48(3): 3789-3802. [Crossref]
8. Aso Y, Sitaraman D, Ichinose T, Kaun K, Vogt K, Belliart-Guérin G, *et al*. Mushroom body output neurons encode valence and guide memory-based action selection in *Drosophila*. *Elife*, 2014, 3: e04580. [Crossref]
9. Scotto-Lomassese S, Strambi C, Strambi A, Aouane A, Augier R, Rougon G, *et al*. Suppression of adult neurogenesis impairs olfactory learning and memory in an adult insect. *J Neurosci*, 2003, 23(28): 9289-9296. [Crossref]
10. Kulkarni A, Ewen-Campen B, Terao K, Matsumoto Y, Li Y, Watanabe T, *et al*. *oskar* acts with the transcription factor Creb to regulate long-term memory in crickets. *Proc Natl Acad Sci U S A*, 2023, 120(21): e2218506120. [Crossref]
11. Boldrini M, Fulmore C, Tartt A, Simeon L, Pavlova I, Poposka V, *et al*. Human hippocampal neurogenesis persists throughout aging. *Cell Stem Cell*, 2018, 22(4): 589-599.e585. [Crossref]
12. Tobin M, Musaraca K, Disouky A, Shetti A, Bheri A, Honer W, *et al*. Human hippocampal neurogenesis persists in aged adults and Alzheimer's disease patients. *Cell Stem Cell*, 2019, 24(6): 974-982.e973. [Crossref]
13. Matsumoto Y, Matsumoto C, Takahashi T, & Mizunami M. Activation of NO-cGMP signaling rescues age-related memory impairment in crickets. *Front Behav Neurosci*, 2016, 10: 166. [Crossref]
14. McLaren A, & Kawaja M. Olfactory dysfunction and Alzheimer's disease: a review. *J Alzheimers Dis*, 2024, 99(3): 811-827. [Crossref]
15. Turner G, Bazhenov M, & Laurent G. Olfactory representations by *Drosophila* mushroom body neurons. *J Neurophysiol*, 2008, 99(2): 734-746. [Crossref]
16. Lin A, Bygrave A, de Calignon A, Lee T, & Miesenböck G. Sparse, decorrelated odor coding in the mushroom body enhances learned odor discrimination. *Nat Neurosci*, 2014, 17(4): 559-568. [Crossref]
17. Vogt K, Schnaitmann C, Dylla K, Knapek S, Aso Y, Rubin G, *et al*. Shared mushroom body circuits underlie visual and

ANT PUBLISHING CORPORATION | All Rights Reserved

olfactory memories in *Drosophila*. *Elife*, 2014, 3: e02395. [Crossref]
18. Dossey A, Oppert B, Chu F, Lorenzen M, Scheffler B, Simpson S, *et al*. Genome and genetic engineering of the house cricket (*Acheta domesticus*): a resource for sustainable agriculture. *Biomolecules*, 2023, 13(4): 589. [Crossref]
19. Ling Q, Herstine J, Bradbury A, & Gray S. AAV-based *in vivo* gene therapy for neurological disorders. *Nat Rev Drug Discov*, 2023, 22(10): 789-806. [Crossref]
20. Gao J, Gunasekar S, Xia Z, Shalin K, Jiang C, Chen H, *et al.* Gene therapy for CNS disorders: modalities, delivery and translational challenges. *Nat Rev Neurosci*, 2024, 25(8): 553-572. [Crossref]
21. Wang J, Gessler D, Zhan W, Gallagher T, & Gao G. Adeno-associated virus as a delivery vector for gene therapy of human diseases. *Signal Transduct Target Ther*, 2024, 9(1): 78. [Crossref]
22. Darvas M, Keene D, & Ladiges W. A geroscience mouse model for Alzheimer's disease. *Pathobiol Aging Age Relat Dis*, 2019, 9(1): 1616994. [Crossref]
23. Mattson M, & Arumugam T. Hallmarks of brain aging: adaptive and pathological modification by metabolic states. *Cell Metab*, 2018, 27(6): 1176-1199. [Crossref]
24. López-Otín C, Blasco M, Partridge L, Serrano M, & Kroemer G. Hallmarks of aging: an expanding universe. *Cell*, 2023, 186(2): 243-278. [Crossref]
25. Kennedy B, Berger S, Brunet A, Campisi J, Cuervo A, Epel ES, *et al*. Geroscience: linking aging to chronic disease. *Cell*, 2014, 159(4): 709-713. [Crossref]

Cite this article as: Liao GY, Rhim A, Wezeman J, & Ladiges W. The cricket brain: a tractable system for decoding neural aging. *Aging Pathobiol Ther*, 2026, 8(3): 345-348. doi: 10.31491/APT.2026.09.240