

# Myelin Damage and Its Role in Alzheimer's Disease Pathology

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Myelin damage may be a driving force in Alzheimer's disease, making remyelination a promising therapeutic target.

### Quick Facts

- 44M+ people live with dementia worldwide — projected to triple by 2050
- 50–75% of all dementia cases are Alzheimer's disease
- 6.7M Americans aged 65+ live with AD today
- +145% rise in U.S. AD deaths, 2000–2019

### Background

- Demyelination is a major driver of cognitive decline and neurodegeneration in AD, not just a downstream symptom.
- Myelin insulates axons for rapid signaling; its loss impairs learning, memory, and decision-making.
- Damaged myelin diverts microglia from clearing amyloid- $\beta$ , accelerating plaque buildup.

### Objective

- Analyze the role of demyelination in cognitive decline associated with Alzheimer's disease.

### Methods

- Narrative review of preclinical animal models, human neuroimaging, and clinical trials of myelin integrity in AD.
- Examined three remyelination intervention classes: tissue engineering, neuromodulation, and pharmacologic.

### Healthy vs. Demyelinating Neuron

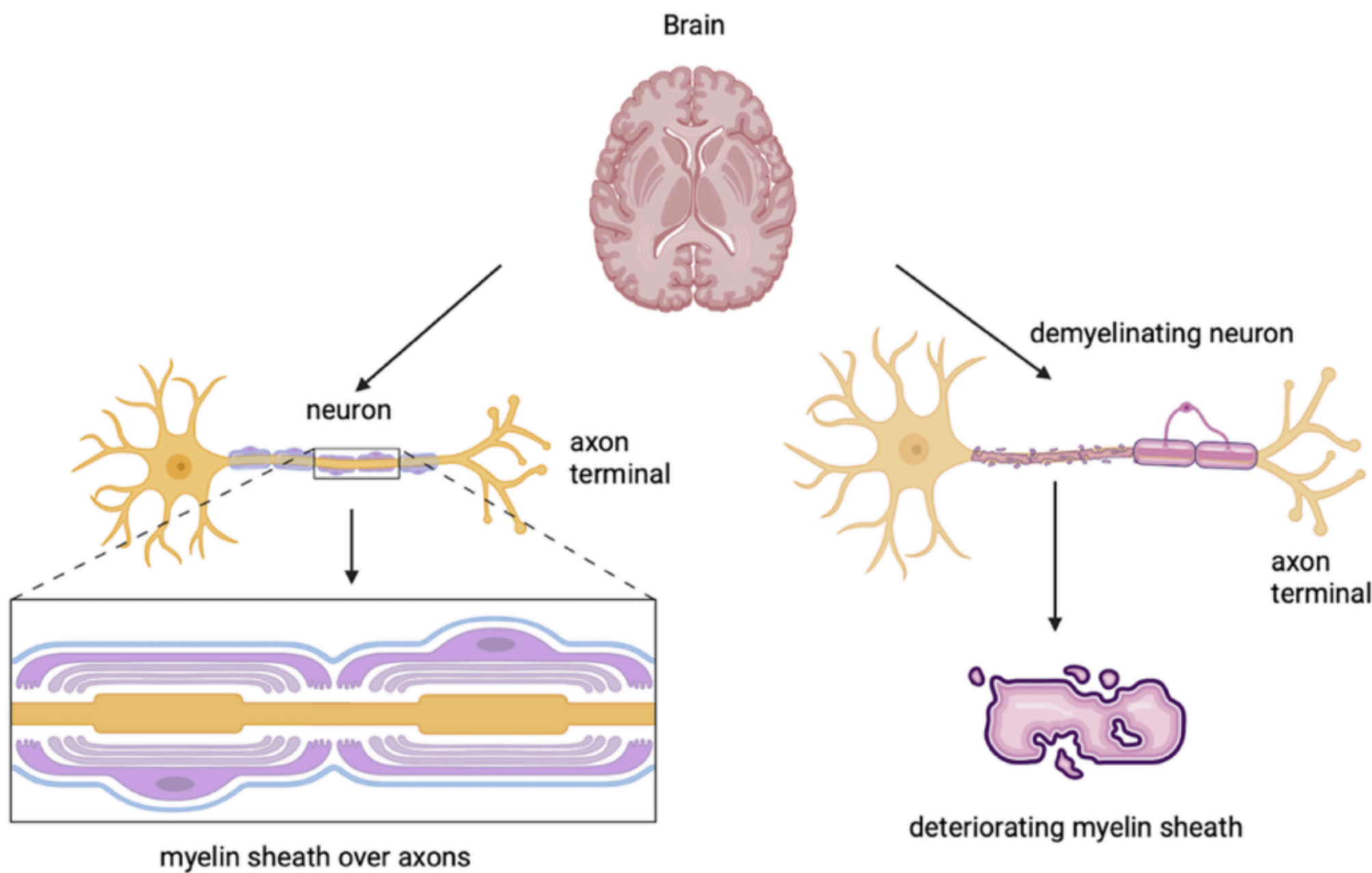


Figure 1. A healthy myelinated neuron vs. a demyelinating neuron with a deteriorating myelin sheath. Original figure created in BioRender by D. Develioglu.

### Findings

- Myelin loss drives amyloid- $\beta$  deposition and behavioral deficits in AD mouse models.
- T cell–mediated microglial activation triggers myelin pathology; depleting CD8<sup>+</sup> T cells improved memory in mice.
- In humans, myelination genes are downregulated, and white-matter integrity declines with AD.
- Remyelination strategies (scaffolds, cell transplants, rTMS, Lecanemab, 40 Hz gamma) show repair potential.

### Remyelination Strategies in Alzheimer's Disease

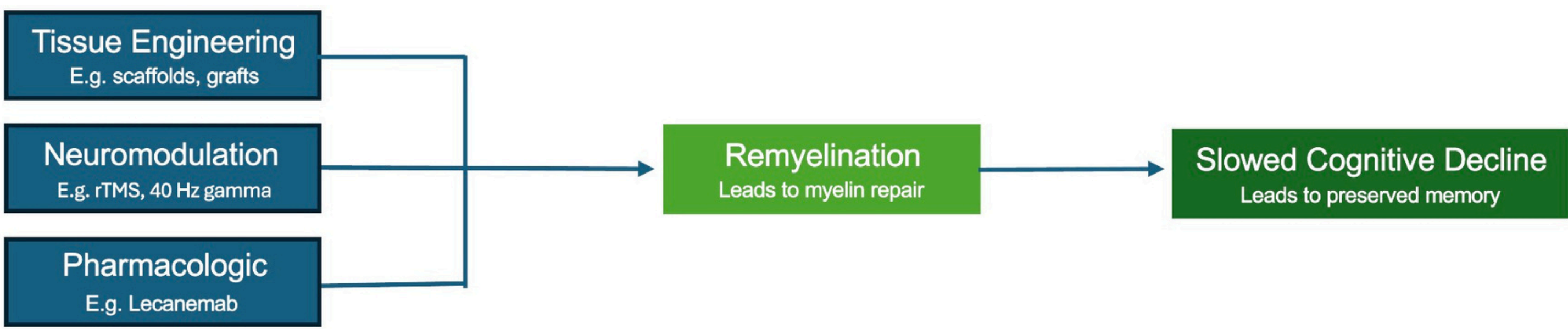


Figure 2. A Three intervention classes converge to promote remyelination, supporting preserved memory and slowed cognitive decline. Original figure created in BioRender by D. Develioglu.

### Key Takeaways

- Demyelination is a major driver of cognitive decline in Alzheimer's disease, not just a downstream symptom.
- Protecting and restoring myelin is possible through tissue engineering, neuromodulation, and amyloid-targeting drugs such as Lecanemab. This is a promising therapeutic frontier.
- Early, combined intervention to preserve myelin integrity could slow disease progression and improve cognitive outcomes.

### Conclusions

- Demyelination is a driver of Alzheimer's, not just a downstream symptom.
- Protecting and restoring myelin, through tissue engineering, neuromodulation, and amyloid-targeting drugs, is a promising therapeutic frontier.

### Future Directions

- Refine and human-test myelin-repair methods such as scaffolds and cell transplants.
- Combine stem cells, brain stimulation, and drugs rather than relying on any one alone.
- Use genetic risk screening (APOE4) and MRI to detect AD earlier and personalize treatment.

### References

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