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Myelin Damage and Its Role in Alzheimer's Disease Pathology

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Abstract

Recent research increasingly recognizes demyelination as a major contributor to the cognitive decline and neurodegeneration associated with Alzheimer's disease. Myelin, a sheath that insulates axons and enables rapid signal conduction, is essential for neuronal communication. The degeneration of myelin, which slows neuronal signaling, results in poor learning, impaired memory, and reduced decision-making capacity. Despite the many detrimental effects of demyelination, the specific mechanisms responsible for myelin damage remain unclear. Understanding these mechanisms leading to Alzheimer's disease is essential for developing effective treatment strategies to restore or preserve myelin integrity. Evidence from recent studies highlights promising approaches, including tissue-engineering methods like the use of hydrogel scaffolds and glial progenitor cell transplantation; neuromodulation approaches like neural stimulation and glutamate receptor modulation are also capable of fostering myelination. Additionally, there are also pharmacologic treatments like Lecanemab that may similarly support myelin preservation by reducing the processes culminating in myelin degradation. This review synthesizes findings from animal studies, human

neuroimaging, and clinical trials to evaluate current and emerging approaches to maintaining and repairing myelin. These results stress the importance of integrating cellular, molecular, and bioengineering approaches to advance therapeutic development. Strengthening myelin-targeting strategies may support earlier diagnosis, more personalized treatment, and improved long-term outcomes for patients. By identifying these therapeutic directions, this review emphasizes the significance of targeting myelin repair to slow Alzheimer's disease progression and mitigate the cognitive and behavioral effects associated with the disorder.

Keywords: Alzheimer's Disease, Myelin, Demyelination, Neural Tissue Engineering, Hydrogel Scaffolds

Introduction

Dementia affects over 44 million people worldwide and is expected to triple by 2050. Alzheimer's Disease (AD) is the biggest cause of dementia, and out of all cases of dementia, 50%–75% are classified as AD. AD mainly occurs later in life, significantly affecting those over 65; in fact, its prevalence doubles approximately every five years in those over 65 (Lane et al., 2017). Specifically, looking at those 65 and older, 6.7 million Americans experience AD-related dementia today. Its prevalence is continuously increasing; looking at the periods 2000 and 2019, the reported deaths due to AD increased by over 145% while deaths from diseases such as heart disease, HIV, and even stroke decreased (Alzheimer's Association, 2023). Moreover, this is a neurodegenerative disease with two different subtypes: amnesic and non-amnesic. Amnesia is the most common and is caused by problems with the medial temporal lobe memory system.

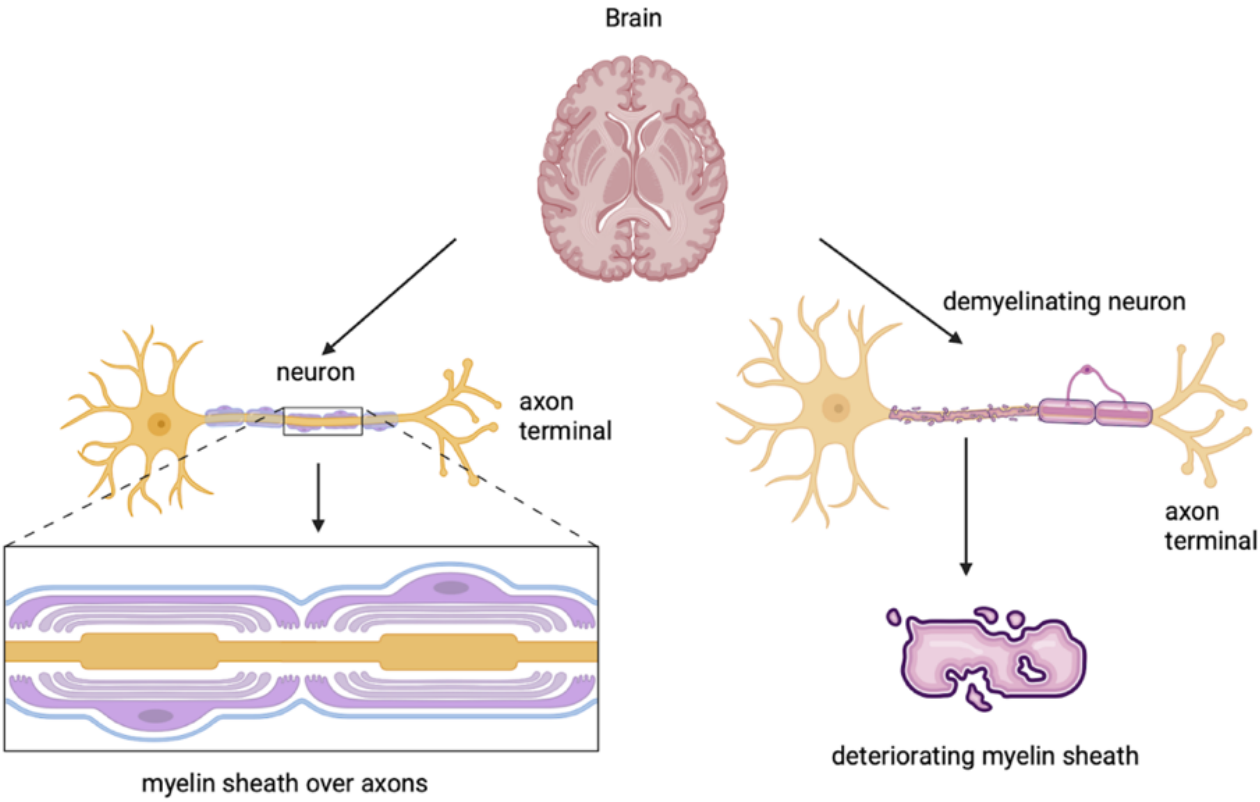
On the other hand, non-amnesic conditions affect one's executive functioning capabilities, such as organization, attentiveness, critical thinking, managing multiple responsibilities, challenges in learning and concentrating, and even control of one's behavior (Mantzavinos & Alexiou, 2017). The amnestic type is caused by neuritic plaques and neurofibrillary tangles, which result from the accumulation of amyloid-beta peptide—also called Aβ—in the most affected areas of the brain, including the medial temporal lobe and other structures in the neocortex.

In addition, ApoE can clear Aβ from the brain. It is a glycoprotein that acts as a ligand for receptors that mediate endocytosis of lipoproteins. ApoE2, ApoE3, and ApoE4 are three isoforms of this gene, but compared to ApoE2 and ApoE3, ApoE4 has a higher risk factor for both early and late onset AD. Furthermore, ApoE4 not only contributes to Aβ deposition and the plaques that accumulate outside neurons but also causes cerebral amyloid angiopathy, a marker for AD. It's associated with vascular damage in the brain, therefore leading to AD pathogenesis (Breijyeh & Karaman, 2020). Myelin is an important sheath in the brain and is composed of fats and proteins that surround nerve cells to accelerate the speed at which they send signals (Myelin, *Oxford Advanced Learner's Dictionary*, 2025). The myelin sheath does this by increasing the nerve signals of axons, which are threadlike parts of the nerve where impulses are sent from cell to cell (Axon, *Oxford Advanced Learner's Dictionary*, 2025). ApoE4 microglia, a non-nervous scavenging cell in the nervous system, also have a reduced efficiency in the clearance of myelin debris (Benveniste et al., 2004; Wang et al., 2022). Myelin debris is important because of its effect on the brain. Specifically, looking at how AD due to aging of the brain can affect oligodendrocytes and impact the structural integrity of the myelin sheaths, leading to neuroinflammation. Oligodendrocytes are a support cell for energy

metabolism in axons and neurons' health. Myelin is important, and when it is damaged, it can cause distraction to amyloid disease-associated microglia, which can clear amyloid plaques; hence, when they are distracted, they can promote Aβ plaque formation and increase the risk for AD (Figure 1).

Figure 1

Healthy vs. Deteriorating Myelin Covering Axons. This figure was created using Biorender by Duru Develioglu.



Above in figure one, the difference between the neuron and the demyelinating neuron is shown, and improving oligodendrocyte health leads to strengthened myelin sheaths and can

delay the advancement of AD (Depp et al., 2023). Having strategies to combat this disease is essential, and currently, there are a few tissue engineering and treatment options. Tissue engineering has potential methods to increase myelination in the brain, and this can help combat the detrimental effects of AD. Tunable Conductive Hydrogel Scaffolds are one possible solution because they have the potential to increase myelination. Remyelination is possible due to its porous and conductive nature; the hydrogel scaffold also has tunable electrical and mechanical properties, which allow for the differentiation and modulation of cellular networks. This scaffold can mimic neural tissue properties, and when it is formed, the Neural progenitor cells (NPCs), which are incorporated into the scaffolds, make it so that neurite networks can form, therefore encouraging differentiation and myelinating oligodendrocytes (Tringides et al., 2022).

Another potential strategy for treatment is Glial Progenitor Cell Transplantation (GPC). Stem cells are differentiated into glial cells, specifically astrocytes; these astrocytes are important in the regulation of the central nervous system—also called CNS—and release hundreds of molecules involved in nerve tissue function. These secreted molecules play an important role in the pathophysiological processes that regulate neural stem cells and can modulate the integrity and function of the blood–brain barrier. Compared to other stem cells, GPCs do not replace neurons by integrating them into the neural network but instead differentiate into oligodendrocytes, which encourage a higher myelination of axons (Ekaterina Belousova et al., 2024). There are also treatment options such as stimulation and signaling. Repetitive transcranial magnetic stimulation (rTMS) is a promising therapeutic tool. More specifically, Intermittent Theta-burst Stimulation, which is a type of rTMS, has an increased electromagnetic stimulus that has been shown to enhance remyelination formation

and promote the differentiation of OPCs. It is also able to reduce neuronal injury in neurodegenerative diseases, and this can apply to AD. After this research, it was found that overall, this stimulation decreased myelin debris, thus countering the cause of AD (Feng et al., 2024). Signaling is also an up-and-coming option. Glutamate signaling can lead to myelin regeneration because of the activation of glutamate receptors at OPC-neuron synapses and oligodendrocyte precursor cell development. Specifically, D-Aspartate, which is a D-amino acid that is responsible for exerting modulatory actions at glutamatergic synapses, can be administered to improve cognitive deficits. Using an in *vivo* remyelination model, D-Aspartate during remyelination was able to improve motor coordination, greatly increase the number of small-diameter myelinated axons, and accelerate myelin recovery. It also reduced myelin loss and inflammation. It was also able to mature OPCs and accelerate developmental myelination in organotypic cerebellar slices (de Rosa et al., 2018). Overall, in this review, it was found that damage to myelin sheaths plays a critical role in AD progression and cognitive decline.

Ongoing research on Myelin Damage in AD Animal Studies

Table 1.

Animal Studies Investigating Myelin Damage and Its Contribution to Cognitive Decline

Last name et al.	Which cell type	Which scaffold	Outcome of the study

Depp et al. 2023.	Oligodendrocytes	5×FAD and APP NLGF mice with myelin gene knockouts ($CNP^{-/-}$, $PLP^{-/-}$)	Myelin loss promotes amyloid-β deposition, worsens behavioral deficits, impairs axonal energy metabolism, impaired increases disinhibition-like behavior.
Kedia et al. 2024.	$CD8^+$ T cells, Microglia	$CD8^+$ T cell depletion in mouse models	Depleting $CD8^+$ T cells improved memory/spatial learning, reduced anxiety-like behavior, and implicated $CD8^+$ T cells in promoting microglia-induced myelin damage.
Yu et al. 2022.	Oligodendrocytes	Icariin treatment in 3×Tg-AD mice	ICA improved cognition, reduced Aβ and tau pathology, increased myelin-related gene expression, and reduced myelin damage.
Shen et al. 2021.	Microglia	SIRPα inhibition in the AD model mice	SIRPα suppression promoted myelin debris clearance and potentially improved AD pathology.

Zheng et al. 2021.	Oligodendrocytes	Shenzhiling (SZL) treatment in APP/PS1 mice	SZL improved memory and cognition, protected myelin sheath, and stimulated myelin protein expression via signaling.

Myelin damage is evident in AD, and by using animal models as shown in Table 1, there is a definitive correlation. Preclinical studies using mouse models of Alzheimer's disease have demonstrated that myelin damage is closely associated with inflammation, which tends to increase with age. This inflammation and injury, therefore, can promote amyloid-β deposition and increase the risk of AD. Myelin is a compacted glial membrane that enhances axonal conduction speed. Part of myelin, however, is not compact, and these regions enable oligodendrocytes to supply metabolic support to neurons. These components in the structure of myelin, however, result in a slow and difficult turnover of protein and lipid. Because of this difficulty and the long lifetime of oligodendrocytes, their structure might be responsible for myelin deterioration with age. Aβ deposition is speculated to be driven by myelin deterioration, and in mouse models of amyloidosis, this study used mice by introducing varying levels of myelin damage. Human neuropathology cannot determine if myelin is the cause or outcome of neuronal AD. This study investigated whether myelin loss acts as a driver of amyloidosis by using two experimental animal models of AD (5×FAD and APP NLGF). They combined AD mouse models with genetically modified mice that have mild myelin damage and found that mice lacking CNP showed axonal swelling due to collapsed cytosolic channels in the myelin sheath. The mice also lacked PLP, so their myelin

lacked stability, hindered axonal energy metabolism, and, at an older age, led to axonopathy. Looking also at the neuropsychiatric symptoms seen in patients with AD, this study resulted in the conclusion that myelin dysfunction and amyloid pathology are responsible for making behavior deficits worse, and this was presented in mice through their disinhibition, a lack of impulse control, which is also common in humans with AD (Depp et al., 2023).

In another study, behavioral deficits were also analyzed using the Barnes maze test; $CD8^+$ T cells are linked to myelin damage, and when these cells were depleted, the mice had improved memory and spatial learning performance. $CD8^+$ T cells are linked to myelin damage because, just like anxiety is a symptom present in those with AD, these cells induced anxious behavior in mice. $CD8^+$ T cells also encourage the accumulation of microglia, which are activated by interferons and, after activation, damage myelin, proving to have myelin-damaging activity; checkpoint inhibitor treatment, which boosts the activity of cells such as $CD8^+$ T cells, resulted in an increase in myelin dysfunction, and they noted an increase in anxiety-related behaviors in those mice. In response to damaged myelin in mice, they observed $OLIG2^+$ cells, $PDGFR\alpha^+$ oligodendrocyte progenitor cells, premyelinating $BCAS1^+$ cells, and mature $CC1^+$ oligodendrocytes, which are all indicative of a regenerative response in 5xFAD mice, yet their behavioral deficits stayed constant (Kedia et al., 2024). One study wanted to see how they could slow/stop myelin degeneration to stop AD by using icariin (ICA), a prenylated flavonol glycoside capable of improving cognitive function in AD model mice. Using 3 × Tg-AD mice the Morris water maze and Y maze tests were performed to assess the learning and memory of the mice and by performing an immunofluorescence analysis of Aβ1-42 deposition and myelin basic protein, it was found that ICA treatment improved the learning and memory of these model mice by reduced Aβ deposition as well as

tau protein phosphorylation in the hippocampus which are responsible for the progressment of AD. Using mice, ICA increased myelin-related gene expression and reduced myelin damage (Yu et al., 2022). Researchers suppressed SIRPa and found that the inhibition of this protein led to a clearing of myelin debris. SIRPa is a phosphatase non-receptor type substrate 1 tyrosine-protein which aids in transporting important signaling proteins to the cell membrane, where they contribute to synapse function and development. Under normal conditions, SIRPA suppresses microglial phagocytic activity to maintain myelin integrity. However, in early stages of AD, this same inhibition suppresses microglia from clearing phagocytosing Aβ fibrils, which contributes to AD progression. This study newly introduced the higher concentration of SIRPa in mice with AD and is a promising area for further research (Shen et al., 2022). In an animal study examining how Shenzhiling oral liquid protects the myelin sheath against AD, for three months, APP/PS1 mice were treated with SZL or donepezil. The SZL treatment proved to improve cognitive function and memory and reduce oligodendrocyte and myelin sheath. SZL was found to have a neuroprotective effect on the myelin sheath because of its stimulation of myelin proteins' expression during AD. The phosphatidylinositol-3-kinase (PI3K)/Akt-mTOR signaling pathway is also essential in controlling myelin protein translation, myelination, and the differentiation of oligodendrocytes in the central nervous system (Zheng et al., 2021).

Human Studies

Table 2.

Demyelination and Its Role in AD Pathology in Humans

Last name et al.	Which cell type	Which scaffold (model/intervention)	Outcome of the study
Lu et al. 2014	White matter (myelinated axons)	DTI imaging of the frontal lobe and corpus callosum in 12 AD patients vs. 12 controls	Reduced white matter integrity was observed, especially in the splenium; breakdown in late-myelinating regions correlated with emotional numbness in AD patients.
Tomimoto et al. 2004.	Axons (white matter)	Post-mortem brain tissue from 22 AD, 6 Binswanger's, 3 LVOD, 6 controls	Anterior corpus callosum atrophy is more pronounced in AD and LVOD; axonal damage is confirmed via immunohistochemical analysis, and it is strongly correlated with AD pathology.
Allen et al. 2017.	Myelinating glial cells	Transcriptome analysis of 940 post-mortem AD brain samples	Myelination-related gene networks were downregulated in AD, suggesting impaired myelin maintenance and a role in disease progression.

Tian et al. 2004.	Oligodendrocytes, vascular cells	Post-mortem tissue from 137 AD brains	Myelin loss is common alongside cerebral amyloid angiopathy and arteriosclerosis; some myelin loss occurred independently, indicating other contributing factors to degeneration.
Miller et al. 2008.	Oligodendrocytes, neurons	Post-mortem transcriptional network analysis	High co-expression of PSEN1 with myelin genes suggests PSEN1 may be involved in glial-neuronal signaling and linked to neurodegeneration in AD.

Imaging studies are also essential in analyzing how AD affects the brain, as shown in Table 2. In one imaging study, 12 AD patients were examined compared to 12 control patients, and using four DTI metrics, researchers assessed their frontal lobes and anterior section of the corpus callosum. They examined these regions using fractional anisotropy, axial diffusivity, radial diffusivity, and mean diffusivity. The frontal lobe is a vulnerable late-myelinating region, and the genu white matter in the corpus callosum is an early-myelinating region. AD patients showed a numerical trend towards poorer integrity of the corpus callosum—specifically the splenium region— and the white matter breakdown in the late-myelinating regions exhibited emotional numbness as a symptom, which shows this study's

translation into the behavior associated with AD (H Lu et al., 2014). In fact, while analyzing post-mortem brain tissue, researchers studied 22 brains with AD: 9 presenile onset, 13 senile onset, 6 Binswanger's disease, 3 LVOD — both forms of vascular dementia — and 6 non-neurological control brains. The corpus callosum in this study shrank at the anterior part of the brain in AD and LVOD most compared to the control. Using immunohistochemistry, researchers observed axonal damage in the corpus callosum, and this atrophy was measured to be directly correlated with AD (Tomimoto et al., 2004).

One study aimed to analyze how conserved brain myelination networks are altered in AD by examining post-mortem brain tissue. Researchers analyzed 940 brain transcriptomes in AD patients and identified transcriptional co-expression networks involved in myelination that were downregulated in AD compared to control samples. This downregulation suggests a reduction in myelination activity, which is strongly correlated with AD and the progression of neural impairment (Allen et al., 2017).

In another study, researchers examined brain tissue of 137 post-mortem AD patients and measured myelin loss, cerebral amyloid angiopathy, and arteriosclerosis. Amyloid buildup, artery hardening, and myelin loss were all common, and although myelin loss was linked to artery hardening, in some cases, myelin loss occurred without the occurrence of artery hardening, which suggests that different vascular problems might be a contributing factor to consider when analyzing white matter damage in AD (Tian et al., 2004). Lastly, one more post-mortem tissue analysis study suggests a role of presenilin 1 in the neurodegenerative process of AD. Examining transcriptional networks in AD and identifying 12 modules relating to synaptic processes, immune response white matter, and metabolic

processes helped in the recognition of 9 that related to AD progression. 2 showed the link between AD and aging, several genes also supported this suspected correlation, and the high coexpression of presenilin 1—PSEN1—with myelin proteins, suggesting a role for PSEN1 in glial-neuronal activity and a possible relation to neurodegeneration in AD (A. Miller et al., 2008).

Myelin Damage on Cognitive Decline in Clinical Trials

Table 3.

Clinical Trials Assessing Methods to Slow Cognitive Decline and Demyelination

Last name et al.	Which cell type	Which scaffold (model/intervention)	Outcome of the study
Da et al. 2024.	Patients ≥55 with mild cognitive impairment or mild-moderate AD	40 Hz simultaneous audio-visual stimulation + MRI	Reduced white matter atrophy and myelin loss compared to sham treatment
Van Dyck et al. 2022.	Patients 50–90 with early AD and confirmed amyloid	Lecanemab (IgG1 monoclonal antibody targeting Aβ)	Slowed cognitive decline and reduced amyloid burden; side effects led to discontinuation in 7%

Fieremans et al. 2013.	15 healthy, 12 MCI, 14 AD patients	Diffusion kurtosis imaging	Differentiated white matter integrity across groups; corpus callosum metrics linked to processing speed
Bartzoskis et al. 2003.	General population across the aging spectrum	MRI analysis of transverse relaxation rates (genu & splenium regions)	Genu showed an earlier and faster decline in myelin integrity, linked to amyloid β-peptide toxicity
Vogt et al. 2021.	73 healthy middle-aged adults, no prior statin use	40 mg simvastatin daily vs. placebo + neuroimaging	Preserved white matter volume and microstructure; ~30% effect mediated by serum cholesterol reduction

Clinical trials are vital in providing data to draw conclusions that are promising in advancing the treatment of AD and remyelination, as shown in Table 3. Reducing myelin loss is an essential part of these clinical trials, one of which is a non-invasive gamma sensory stimulation that also uses an MRI to perform white matter volume and myelin content assessments. There were 33 participants given the treatment that completed the study, and 20 participants given a placebo treatment that completed the study. All participants were 55 or

above (Cognito Therapeutics, Inc., 2021). The treated group's clinical trial was for 6 months and consisted of a 1-hour 40 Hz simultaneous audio-visual sensory stimulation. These patients had mild cognitive impairment or mild to moderate AD, and using a volumetric MRI, atrophy and regional differences were measured. Through combined stimulation treatment, patients experienced a reduction in white matter atrophy and myelin loss compared to those with the sham treatment (Da et al., 2024).

Currently, on the market, there is an FDA-approved drug called Leqembi or Lecanemab that targets early AD. This drug targets the accumulation of aggregated Aβ, which, as I mentioned, is thought to lead to AD. Lecanemab is a humanized IgG1 monoclonal antibody that binds to these Aβ protofibrils. In an 18-month phase 3 clinical trial with people from 50-90 years old with early AD and confirmed amyloid, participants were given Lenecanemab. Researchers measured the change from baseline to the end of the trial based on the Clinical Dementia Rating–Sum of Boxes (0-18), the Alzheimer's Disease Assessment (0-90), and the Alzheimer's Disease Composite Score (0-1.97); the higher the score, the worse the cognitive impairment. In all the tests listed, the Lecanemab had a lower score than the placebo, showing a decrease in neurodegeneration.

The Alzheimer's Disease Cooperative Study–Activities of Daily Living Scale for Mild Cognitive Impairment was also a test researchers used, which is from 0-53 and but the lower the score, the greater the cognitive impairment. In this test, the Lecanemab had a higher score, and from these trends, researchers saw a greater reduction of amyloid burden in those with the drug than with the placebo. Leqembi did come with adverse effects, such as edema, hemorrhaging, headaches, and falls; hence, 7% of patients taking Lencanemab had to

stop drug usage, and it is essential to keep studying ways to improve cognitive function in those with AD while making it safer (H. van Dyck et al., 2022). This study creates an association between white matter integrity and AD. Myelin is an important part of white matter, and maintaining its integrity is essential to limit AD progression. Diffusion kurtosis imaging was used to detect microstructural abnormalities in neural impairment of varying intensities, starting from healthy aging to those with severe AD. Researchers scanned the brains of 15 healthy people, 12 with mild cognitive impairment, and 14 with AD. This imaging was able to effectively differentiate white matter microstructure in these different groups and saw that the white matter metrics in the corpus callosum were strongly linked to processing speed in those with mild cognitive impairment (Fieremans et al., 2013). An MRI was used to analyze myelin breakdown, its impact on brain aging, and its link to AD. They looked at an early myelinating region of the brain, the splenium, which contains sensory axons responsible for vision. They also examined a later myelinating region of the brain, the genu, which connects prefrontal association cortices. They calculated the transverse relaxation rates of the genu and splenium, which is an indirect measure of the structural integrity of white matter. In the genu, they observed an accelerated decline beginning around age 31, whereas the splenium showed a more gradual decline at about one-third the rate. These findings suggest that in AD, this age-related degeneration is exacerbated across the brain, consistent with the effects of amyloid β-peptide toxicity or another extracellular mechanism (Bartzokis et al., 2004).

Another clinical study used longitudinal neuroimaging in order to acquire data from 73 cognitively unimpaired, healthy middle-aged adults who had not been treated with statins (cholesterol-lowering medications) for 18 months. These adults were given 40 mg of

simvastatin daily or a placebo. ANCOVA models were used to analyze the effect of simvastatin on white matter, gray matter, and white matter hyperintensities. They also analyzed covariates (age, sex, and APOE4 status) and changes in total cholesterol. Researchers found that the simvastatin group presented a notable preservation of radial diffusivity, global white matter fractional anisotropy, and white matter volume. It was found that ~30% of simvastatin's effect on white matter microstructure was mediated by serum cholesterol reduction. This enabled scientists to conclude that simvastatin effectively preserved white matter microstructures and their volume in healthy middle-aged adults, and future research can help determine this drug's long-term effects on cognition (M. Vogt et al., 2021). This research's preservation of white matter, and therefore myelin in the brain, is a promising pathway for myelin damage that can lead to AD.

Future Directions

In terms of future directions for treatments to reduce myelin deterioration and slow AD progression, remyelination and neuroprotection strategies are quite promising. Pre-clinical tissue engineering methods, such as hydrogel scaffolds and glial progenitor cell transplantation, have strong potential. Future research should focus on making these strategies more effective and optimized in their target of remyelination and oligodendrocyte integration, and differentiation. Scientific research would benefit from seeing these methods' effect on cognitive function for humans, and if the same results are collected, proving their viability. Glial progenitor cell transplantation, if combined with stimulation therapies like rTMS, as I mentioned, has the potential to improve and foster repair mechanisms. Stimulation therapies provide a non-tissue engineering treatment approach, and non-invasive

strategies such as anti-inflammatory approaches can also be an encouraging direction. Looking at icariin, checkpoint inhibitors, and $CD8^+$ mice revealed inflammation's contribution to myelin deterioration and the behavioral deficits associated with this damage. In humans, however, anti-inflammatory compounds could have the same effect, where microglia and T cell pathways are targeted in order to combat demyelination. Early diagnosis for AD is essential to start combating the effects of the disease, and imaging models like DTI, MRI, and diffusion kurtosis imaging are promising tools.

Considering the current clinical treatment strategies available, Lecanemab has shown some success in preserving white matter, and pharmaceutical companies such as Lilly do have promising AD treatments, but myelin deterioration-specific medicine is not a staple on the market, so future clinical trials would benefit from including a form of maintaining myelin integrity. To prioritize remyelination in treatments, I believe drugs, stimulation, stem cell therapy, and scaffolds should be looked at for combinatory therapies. In the future, detecting the covariate APOE4 in people before symptoms are shown could help tailor treatments.

Conclusion

The studies and promising treatments presented both show that myelin sheath deterioration is a driving factor in AD but also emphasize the urgency for clinical strategies

that can preserve and restore myelin integrity to slow cognitive decline. Myelin sheath damage is truly a key contributor to AD because of its role in mental decline and neurodegeneration. Studies in animal models, human imaging, and clinical trials all show links between demyelination and white matter deterioration in AD pathology. Current treatments offer some benefits but do not effectively target myelin repair. Tissue engineering methods such as hydrogel scaffolds and GPC transplantation are up-and-coming, but so are stimulation and signaling treatments like rTMS, glutamate signaling modulation, and pharmacological and molecular approaches like Icariin, checkpoint inhibitors, SIRPA inhibition, shenziling oral liquid, simvastatin, and Lecanemab. In conclusion, to optimally slow AD progression and improve patients' life quality, research on myelin's role in the AD mechanism is essential because of the potential for therapy, tissue engineering, and drug development.

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