| LITERATURE REVIEW |
| https://doi.org/10.47855/jal9020-2025-4-2 |
| ISSN 2709-0205 |
| https://doi.org/10.47855/jal9020-2025-4|

ASTROCYTES IN ALZHEIMER'S DISEASE

Nevmerzhytska N.M. [1, 2], *Skibo G.G.*[2]

[1] Bogomolets National Medical University, Kyiv, Ukraine
[2] O.O. Bogomoletz Institute of Physiology National Academy of Sciences of Ukraine, Kyiv, Ukraine

Correspondence
Dr. Natalia Nevmerzhytska, Senior researcher, Department of Cytology, O.O. Bogomoletz Institute of Physiology National Academy of Sciences of Ukraine, Kyiv, Ukraine

Email:
nevmerzhytskanm@biph.kiev.ua

Received: 07 July 2025
Accepted: 13 Oct 2025
Published: 12 Dec 2025

Alzheimer's disease (AD) is the most common form of dementia, characterised by progressive cognitive decline, memory loss, and impaired self-care. Main pathogenetic mechanisms include the accumulation of α-amyloid plaques, neurofibrillary tangles, neuronal death, reactive gliosis, neuroinflammation, synaptic and mitochondrial malfunction, as well as disturbances in ion and neurotransmitter homeostasis. In recent years, increasing attention has been paid to the role of astrocytes in AD pathogenesis, given their capacity for metabolic support of neurons, regulation of synaptic transmission, neurovascular interaction, and homeostatic control. The review presents astrocyte subtypes and their current classifications. Age-related changes in astrocytes that may contribute to the development of cognitive impairment are also discussed. The article provides a comprehensive overview of astrocyte alterations in AD and their involvement in the pathogenesis of this neurodegenerative disorder. It summarises current understanding of the heterogeneity of astroglial changes depending on disease stage — from early reactive states to late-stage atrophy and degeneration. The review highlights the role of astrocytes in maintaining synaptic activity, glutamate and energy metabolism, glymphatic clearance, and their contribution to inflammatory processes, oxidative stress, ferroptosis, and blood–brain barrier disruption. Particular attention is given to signalling pathways mediating astrocyte reactivity and regulation of β-amyloid and tau pathology. Potential therapeutic targets aimed at supporting the homeostatic functions of astrocytes and reducing their neurotoxicity are also discussed.

| Keywords: Alzheimer's disease, glia, astrocytes, neurodegeneration, cognitive disorders, dementia, glial cells, neuroinflammation, amyloid plaques, neurofibrillary tangles.

| Introduction

Alzheimer's disease (AD) is the most common cause of dementia worldwide and represents a major public health challenge, given the continuous rise in life expectancy and the aging of the global population (Heneka et al., 2025; Di Benedetto et al., 2022). As a progressive neurodegenerative disorder, AD is characterised by widespread structural and functional alterations in the brain that ultimately compromise memory, cognition, and the capacity for independent living (Nevmerzhytska 2025).

The pathogenesis of AD is complex and multifactorial. Central to disease progression are the abnormal accumulation of misfolded proteins — α-amyloid (Aβ) in the form of plaques and hyperphosphorylated tau in the form of intracellular neurofibrillary tangles — which disrupt neuronal connectivity and intracellular transport mechanisms (Verkhratsky & Butt, 2023; Nevmerzhytska & Yaremenko, 2024; Chaykovsky et al., 2022). These lesions, however,

do not act in isolation. They are accompanied by neuronal loss, synaptic malfunction, mitochondrial impairment, oxidative stress, and disturbances in neurotransmitter and ion homeostasis (Heneka et al., 2025; Di Benedetto et al., 2022; Verkhratsky & Butt, 2023; Nevmerzhytska & Yaremenko, 2024; Chaykovsky et al., 2022; Castelli et al., 2019).

Neuroglial cells, particularly astrocytes and microglia, have emerged as critical players in this process. Reactive remodelling of neuroglial cells (gliosis) in response to protein aggregates and neuronal injury contributes to neuroinflammation through the release of cytokines and other inflammatory mediators (Yu et al., 2024; Si et al., 2023). While glial reactivity may initially provide neuroprotection, chronic dysregulation exacerbates neuronal malfunction and accelerates neurodegeneration (Tzioras et al., 2023). In parallel, disturbances in mitochondrial metabolism and redox balance drive excessive production of reactive oxygen species (ROS), creating a vicious cycle of oxidative damage that further enhances protein aggregation and neuronal vulnerability (Misrani et al., 2021; Dhapola et al., 2024).

Given their central role in maintaining neuronal homeostasis, astrocytes are now recognised as active participants in the pathogenesis of AD. Their functions cover – regulation of neurotransmitter turnover, ion buffering, metabolic coupling with neurons, and clearance of toxic metabolites. Disruption of these processes is increasingly viewed as a pivotal factor in disease onset and progression (Shippy et al., 2024; Ryan et al., 2023; Xu et al., 2025; Zhang et al., 2023).

This review will therefore focus on the multifaceted involvement of astrocytes in AD, highlighting how their dysfunction integrates with classical pathological hallmarks and exploring their potential as therapeutic targets.

| General Characteristics of Astrocytes

Astroglial cells account for approximately 20–40% of all glial cells (Verkhratsky & Butt, 2023; Preman et al., 2021; Verkhratsky & Semyanov 2025). Astroglial cells display remarkable diversity in their morphology and physiological roles, exhibiting a high degree of adaptive flexibility that supports central nervous system integrity across developmental stages, throughout maturation and aging, and under pathological conditions (Verkhratsky & Butt, 2023; Verkhratsky & Semyanov 2025). Other members of the astroglial family include Müller radial glia in the retina, Bergmann glia in the cerebellum, ependymoglia and tanycytes at the base walls of the brain ventricles and central canal of the spinal cord etc. (Verkhratsky & Butt, 2023; Chaykovsky et al., 2022). Astrocytes maintain the integrity of the blood–brain barrier (BBB) and the glymphatic system (Makarenko et al., 2024). They regulate synaptic transmission, neurovascular coupling, vascular tone, and cerebral blood flow (Chaykovsky et al., 2022; Sadick et al., 2022; Giovannini et al., 2021; Govindpani et al., 2019). They also support neuronal metabolism (Soelter et al., 2024), ion and energy balance (Liu et al., 2025; Leipp et al., 2024), produce neurotrophic factors, control neurotransmitter levels (Leipp et al., 2024), and synthesise pro-/anti-inflammatory and antioxidant molecules (Verkhratsky & Butt, 2023; Taday et al., 2024).

Protoplasmic astrocytes populate the gray matter and are characterised by spongioform morphology defined by thin terminal processes known as leaflets (Semyanov & Verkhratsky, 2021), which establish extensive contacts with synaptic structures. Through these interactions, astrocytes play a crucial role in maintaining the extracellular microenvironment and supporting synaptic transmission (Leipp et al., 2024; Kumar et al., 2023, Verkhratsky & Nedergaard, 2014). In contrast, fibrous astrocytes are primarily found in the white matter, where they exhibit fewer but longer processes aligned with axons. Their principal functions include supporting axonal myelination and providing metabolic support to neurons (Leipp et al., 2024; Kumar et al., 2023). Besides these two principal form there are many more types of astroglial cells, including radial astrocytes, velate astrocytes, interlaminar and varicose projection astrocytes, the latter two being specific for higher primates (Verkhratsky & Butt, 2023; Pekowska et al., 2025).

Reactive astroglia represent a hallmark response of astrocytes to central nervous system (CNS) injury or disease. This process, known as astrogliosis, may manifest in two forms. Isomorphic astrogliosis is generally mild and reversible, with astrocytes largely preserving their morphology and function; it typically accompanies regenerative processes. In contrast, anisomorphic astrogliosis is characterised by profound cellular remodelling and the formation of a glial barrier that serves to isolate damaged regions of the CNS, a process usually considered irreversible (Verkhratsky et al., 2023).

Beyond reactive changes, astrocytes are also subject to astrogliopathies, which may be either genetic, arising from inherited mutations, or acquired, as a result of trauma, infection, inflammation, or neurodegenerative conditions. Another pathological alteration, astroglial atrophy, involves a reduction in cell size and number as

well as complexity of astrocytic processes, leading to impaired neuronal support, synaptic dysfunction, and possible disruption of the blood–brain barrier. In advanced stages, astrodegeneration develops, encompassing progressive structural and functional deterioration of astrocytes, ultimately culminating in cell death through apoptosis, necrosis, or other forms of cellular demise. Such degenerative changes critically undermine brain homeostasis and contribute significantly to the progression of neurodegenerative diseases (Fig. 1; Verkhratsky & Butt, 2023).

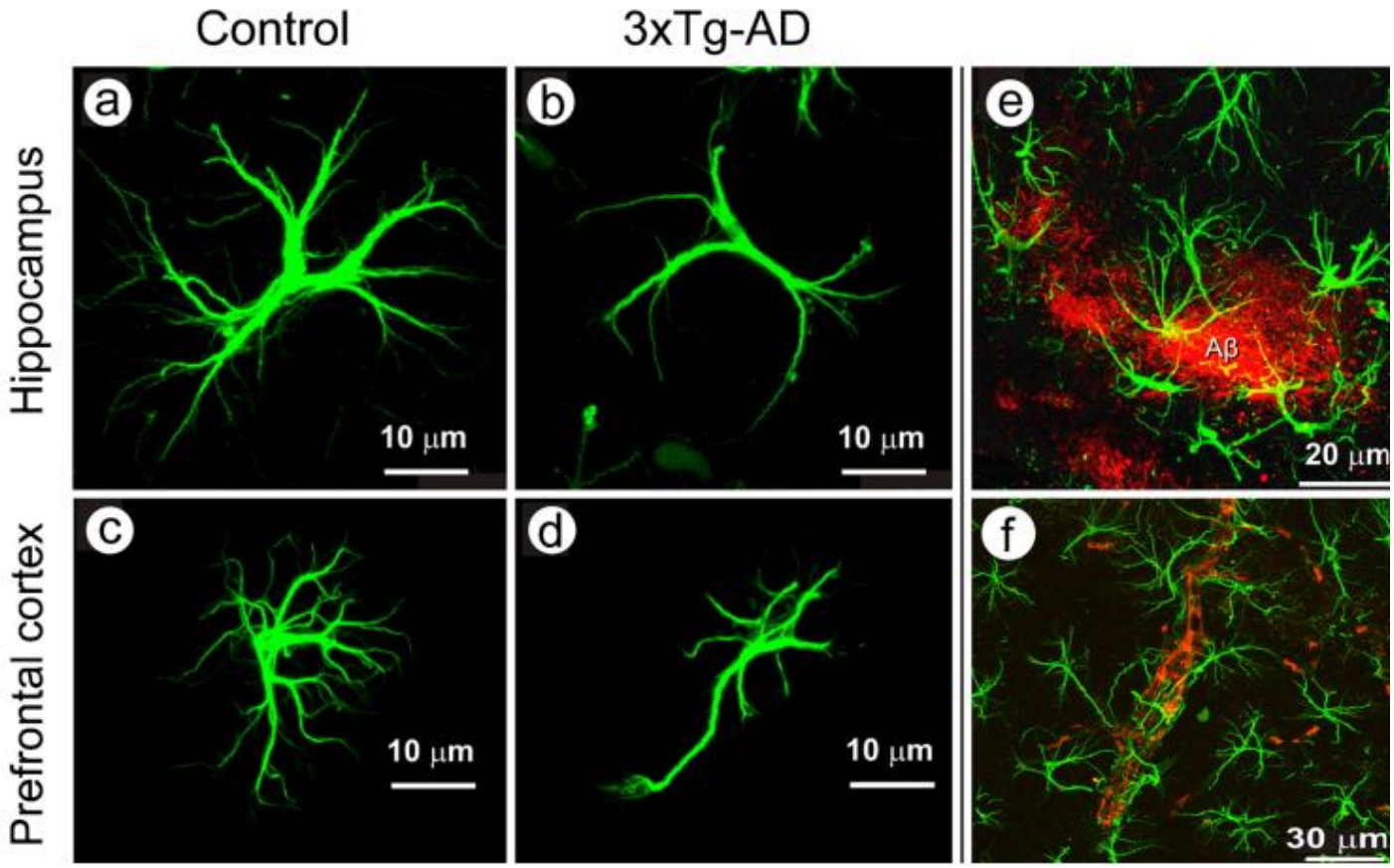

Figure 1. Astrodegeneration and astrogliosis at different stages of AD as seen in the 3xTG-AD mouse transgenic model. a–d: Images of GFAP-labelled protoplasmic astrocytes from hippocampus of 18-month-old control and 3xTg-AD mice (a, b) and from the prefrontal cortex of 3-month-old control and 3xTg-AD mice (c, d). e Confocal image showing hypertrophic astrocytes (green) concentrated around β-amyloid plaques (red). f Confocal image of hypertrophic astrocytes accumulated around vascular β-amyloid deposits (Verkhratsky et al., 2014).

| Ageing of Astrocytes

Astrocyte ageing is multifaceted and depends on CNS region, species, and other factors (Makarenko et al., 2024). In humans, the total number of astrocytes does not significantly change with physiological aging, although changes can occur in animal models (Makarenko et al., 2024). With age, astrocytes shrink and their morphology becomes less complex. Peripheral process atrophy leads to reduced synaptic coverage and may contribute to cognitive malfunction (Fig. 2; Verkhratsky & Butt, 2023; Popov et al., 2021; Popov et al., 2023; Makarenko et al., 2024).

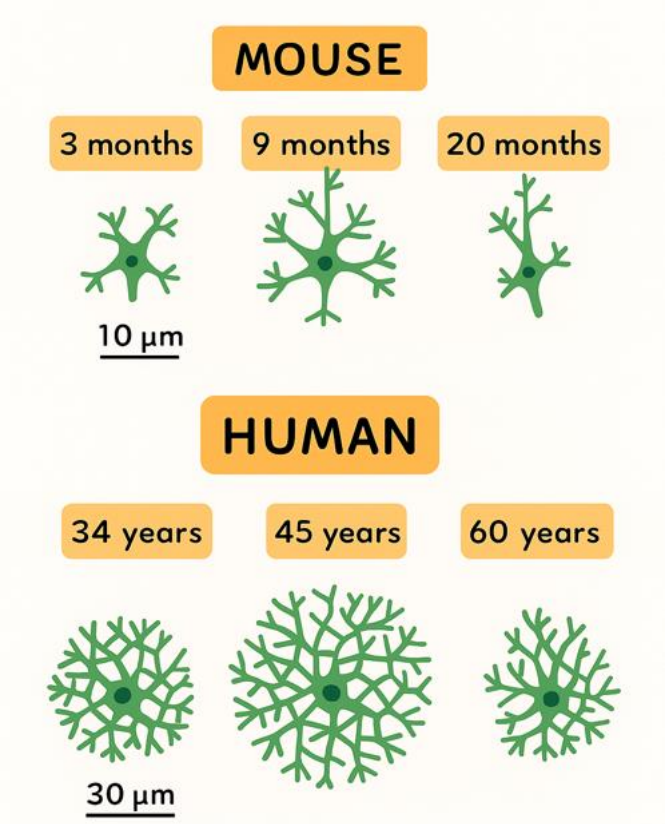

Figure 2. Morphological alterations of astrocytes associated with aging in mice and humans (AI-generated).

Ageing is associated with impaired astroglial secretion of vasoactive factors, reduced astroglial-vascular coupling, and compromised blood–brain barrier (BBB) integrity. Ageing also disrupts neurogenesis due to the cessation of radial stem astrocyte division in neurogenic niches. Furthermore, aging impairs the polarization of aquaporin-4 (AQP4), which affects the function of the glymphatic clearance system and contributes to cognitive decline. Normally, a high concentration of AQP4 is found in the perivascular endfeet of astrocytes. In aged astrocytes, lactate synthesis is disrupted, leading to impaired neuronal metabolism. Aging is also associated with a reduction in the neuroprotective and defensive properties of astrocytes due to decreased glutathione secretion and altered reactivity.

Age-related decline in astrocytic cholesterol synthesis limits neuronal network plasticity, as cholesterol is a key synaptogenic factor secreted by astrocytes (Verkhratsky & Butt, 2023). Ageing also disrupts neurogenesis due to the cessation of radial stem astrocyte division in neurogenic niches. Furthermore, ageing impairs the polarization of aquaporin-4 (AQP4), which affects the function of the glymphatic clearance system and contributes to cognitive decline. Normally, a high concentration of AQP4 is found in the perivascular endfeet of astrocytes. In aged astrocytes, lactate synthesis is disrupted, leading to impaired neuronal metabolism. Ageing is also associated with a reduction in the neuroprotective and defensive properties of astrocytes due to decreased glutathione secretion and altered reactivity (Verkhratsky & Butt, 2023).

| Brief Overview of Astroglia in Alzheimer's Disease

The risk of developing Alzheimer's disease (AD) is linked to several genes predominantly expressed in glial cells (Preman et al., 2021). Apolipoprotein E (APOE), the major genetic risk factor for late-onset Alzheimer's disease (LOAD), is mainly expressed in astrocytes in the healthy brain and contributes to β-amyloid accumulation (Preman et al., 2021). Other AD-related genes such as clusterin (CLU) and fermitin family member 2 (FERMT2) are also primarily expressed in astrocytes (Preman et al., 2021). Astroglial changes in AD are heterogeneous and depend on the brain region and disease stage (Verkhratsky & Butt, 2023). Astrocytes in AD can exist in either a non-reactive or reactive state (Kumar et al., 2023). Reactive astrogliosis is characterised by pronounced phenotypic remodelling (Verkhratsky & Butt, 2023; Kumar et al., 2023; Verkhratsky & Nedergaard 2018). Reactive astrocytes undergo pronounced enlargement of their cell bodies and processes, accompanied by extensive reorganization of

their intermediate filament cytoskeleton — especially increased expression and polymerization of glial fibrillary acidic protein (GFAP) and often vimentin (Escartin et al., 2021). Astrocytes perform a protective function and become reactive to restore homeostasis during the early, prodromal (preclinical) stages of AD (Verkhratsky & Butt, 2023; Kumar et al., 2023). The non-reactive state mainly includes astroglial atrophy and astrodegeneration, leading to clasmatodendrosis — a condition characterised by fragmentation and shortening of the distal astrocytic processes (Verkhratsky & Butt, 2023; Giovannini et al., 2021; Lim et al., 2025). Astrodegeneration is accompanied by loss of function. Astroglial atrophy precedes astrodegeneration (Verkhratsky & Butt, 2023; Makarenko et al., 2024). As the disease progresses, cells become atrophic and non-functional, which explains the reduced astrocytic reactivity at late/terminal stages of AD (Verkhratsky & Butt, 2023; Kumar et al., 2023).

Early cognitive impairments are among the first symptoms of Alzheimer's disease and may appear decades before the development of AD-specific brain histopathology (Verkhratsky & Butt, 2023). These deficits reflect synaptic malfunction caused by morphological atrophy of astrocytes, leading to a reduction in astrocytic synaptic coverage (Verkhratsky & Butt, 2023; Si et al., 2023; Chaykovsky et al., 2022). A decline in astrocytic coverage limits the clearance of glutamate and K^+ from the synaptic cleft, thereby impairing synaptic plasticity (Verkhratsky & Butt, 2023).

Astrogliosis develops in response to Aβ accumulation in the brain even at preclinical stages and generally plays a neuroprotective role in the context of AD (Verkhratsky & Butt, 2023).

Astrogliosis involves morphological changes (enlarged cell bodies and thickened primary processes) (Leipp et al., 2024), along with metabolic and functional changes. These astrocytes exhibit overexpression or high immunoreactivity of GFAP (glial fibrillary acidic protein) (Kumar et al., 2023; Nam et al., 2024; Escartin et al., 2021), which can be detected in both the bloodstream and cerebrospinal fluid (Leipp et al., 2024). The cytoskeleton of astrocytes consists of numerous intertwined intermediate filaments, and GFAP is a key component closely associated with astrocyte reactivity (Leipp et al., 2024; Taday et al., 2024).

Initiation of astrogliosis

Pathological signals leading to astrogliosis in Alzheimer's disease may originate from damaged neurons; however, β-amyloid itself is a potent stimulator of astrocyte reactivity (Preman et al., 2021). On a molecular level, β-amyloid-induced astrocytic remodeling is mediated by Ca^{2+} release from the endoplasmic reticulum (Verkhratsky & Butt, 2023; Preman et al., 2021). Inhibiting this release suppresses astrocytic reactivity (Preman et al., 2021).

Astrocyte reactivity can be initiated and modulated by several inflammation-associated signalling pathways, including the NF-κB (nuclear factor κB), MAPK (mitogen-activated protein kinase), JAK/STAT3 (Janus kinase/signal transducer and activator of transcription), and calcineurin pathways (Kim et al., 2024). Studies show that reactive astrocytes are induced by activated microglia releasing IL-1α, IL-1β, IL-6, TNF-α, and complement component C1q (Yu et al., 2024; Monterey et al., 2021). These cytokines can activate β- and γ-secretase activity, leading to cleavage of the amyloid precursor protein (APP) and stimulating β-amyloid production in astrocytes, complementing neuronal Aβ production (Monterey et al., 2021).

Astrocyte reactivity may also arise from other pathological processes such as synaptic malfunction or vascular changes, independent of or in addition to soluble Aβ pathology (Verkhratsky & Butt, 2023; Kumar et al., 2023; Kim et al., 2024). Some sources suggest that reactive astrogliosis precedes hallmark AD features such as β-amyloid deposition and tau tangle formation (Leipp et al., 2024).

Neuroprotective Role of Astrogliosis

Astrocytes represent the second (parenchymal) line of brain defence after the blood–brain barrier (BBB), reacting to metabolic, inflammatory, and mechanical stress (Kumar et al., 2023; Paidlewar et al., 2024; Verkhratsky & Pivoriunas, 2023).

Reactive astrocytes release antioxidant molecules such as hepcidin and Nrf2 (NF-E2-related factor 2), critical regulators of neuroprotection under oxidative stress (Xu et al., 2025; Escartin et al., 2021). They improve neuronal viability and mitochondrial biogenesis, protecting neurons from oxidative damage and inflammation triggered by Aβ (Monterey et al., 2021). Astrogliosis in response to Aβ also increases glial secretion of transforming growth factor-β (TGF-β), which protects neurons from Aβ toxicity (Preman et al., 2021; Diniz et al., 2017). Furthermore, astrocytes near Aβ plaques display phagocytic activity and can engulf dystrophic neurons, both in mouse models and human AD brains, further supporting their protective role (Preman et al., 2021).

A fundamental neuroprotective function of astrocytes lies in mitochondrial quality control and

degradation (Preman et al., 2021). Astrocytes support neuronal mitochondrial recycling via transmitophagy, in which damaged neuronal mitochondria are transported to astrocytes for degradation (Preman et al., 2021). There is also evidence that astrocytic mitochondria may be transferred to neurons to support neuronal bioenergetics (Preman et al., 2021; Hayakawa et al., 2016).

Detrimental role of astrogliosis

Despite their protective nature, aberrant astrogliosis may damage neurons (Verkhratsky & Butt, 2023; Kumar et al., 2023). Reactive astrocytes near plaques exhibit abnormal calcium dynamics (Preman et al., 2021). This Ca^{2+} hyperactivity may contribute to the release of harmful factors, alter neuron–glia communication, impair synaptic transmission and plasticity, damage surrounding cells, and promote Aβ accumulation (Yu et al., 2024; Sadick et al., 2022). Astrocytes may also contribute to pathological tau accumulation and propagation (Sadick et al., 2022).

Astrogliosis may modulate disease progression by pathways such as C5aR1, Lcn2/Slc22a17, BDNF/TrkB, PPAR-α, and TFEB (Sadick et al., 2022). Reactive astrocytes can enhance Aβ production and release proinflammatory mediators such as IL-1β, IL-6, GM-CSF, TNF-α, and CCL3 in vitro (Yu et al., 2024; Giovannini et al., 2021; Kumar et al., 2023; Paidlewar et al., 2024; Sweeney et al., 2018). These factors target NF-κB, a key transcription factor involved in DNA repair during learning and memory. Inhibition of neuronal NF-κB and activation of glial NF-κB promotes AD progression (Kaltschmidt et al., 2024).

Some researchers note there is no direct evidence of astrocytes producing β-amyloid in the human brain. However, astrocytes can affect Aβ levels by regulating its clearance and degradation (Verkhratsky & Butt, 2023).

| Astroglial Atrophy and Astrogliopathy in AD

Astroglial atrophy and degeneration are observed at later stages of AD (during dementia). Despite increased astroglial reactivity, atrophic astrocytes are also found in postmortem brains of AD patients and in AD mouse models (Olabarria et al., 2010; Verkhratsky & Butt, 2023). Atrophy is characterised by reduced cell volume and thinner processes, detected by morphometric analysis using antibodies against GFAP, S100β, and GS (Verkhratsky & Butt, 2023).

In AD, there is significant loss or complete disappearance of interlaminar astrocytes in the human brain (Verkhratsky & Butt, 2023). Astrocyte atrophy can lead to a loss of homeostatic functions and result in synaptic dysfunction and/or BBB disruption (Verkhratsky & Butt, 2023). Degenerative processes may also directly damage astrocytes, resulting in clasmatodendrosis—characterised by fragmentation and loss of distal fine processes, cell body swelling, and vacuolization (Verkhratsky & Butt, 2023).

| Other Astrocytic Alterations in AD

Astrocyte ferroptosis has been described in AD, triggered by oxidative stress, lipid peroxidation, DNA oxidation, and mitochondrial damage due to Nrf2 deficiency (Xu et al., 2025; Kaltschmidt et al., 2024). Another study identified NADPH oxidase 4 (NOX4) as a major ROS generator; its inhibition alleviates mitochondrial abnormalities, reduces Aβ and phosphorylated tau levels, improves cognition, and mitigates astrocyte ferroptosis (Xu et al., 2025; Maimaiti et al., 2024).

Given astrocytes serve as a copper ($Cu^{+}/^{2+}$) reservoir, disrupted copper metabolism is characteristic of AD (Xu et al., 2025; Zhang et al., 2023). Copper toxicity impairs mitochondrial integrity, triggering cuproptosis, oxidative stress, and mitochondrial dysfunction, paralleling ferroptosis mechanisms (Xu et al., 2025).

Astrocytic glucose metabolism is impaired in AD, reducing lactate transport to neurons and impairing neuronal energy supply (Verkhratsky & Butt, 2023; Andersen et al., 2022). Glycolysis deficits also reduce L-serine synthesis, a precursor of neuronal D-serine that supports NMDA receptor activity (Verkhratsky & Butt, 2023; Le Douce et al., 2020).

Loss of glutamine synthetase is particularly seen in astrocytes near amyloid plaques in both human and animal AD brains (Verkhratsky & Butt, 2023). GSH depletion is a hallmark of brain aging and is associated with AD progression and cognitive impairment (Xu et al., 2025; Taday et al., 2024). Astrocytes play a vital role in glutamate metabolism, taking up glutamate from synaptic clefts and converting it to glutamine via glutamine synthetase, or using it for GSH synthesis (Verkhratsky & Butt, 2023; Taday et al., 2024). In hippocampal samples from patients with mild cognitive impairment, glutamine synthetase was one of the most oxidised proteins, with significantly reduced activity in AD brain tissue (Verkhratsky & Butt, 2023).

Elevated GABA and MAO-B levels have been observed in AD patients and mouse models (Monterey et al., 2021; Garaschuk & Verkhratsky, 2019). Excessive GABA production and release by reactive astrocytes activates neuronal GABA receptors, suppressing

glutamate release and astrocytic proinflammatory responses (Garaschuk & Verkhratsky, 2019). Some studies report reduced GABA levels in specific brain regions in AD (Liu et al., 2025; Monterey et al., 2021). Despite discrepancies, astrocytic GABA dysfunction clearly contributes to AD pathogenesis (Monterey et al., 2021).

Aberrant astrocytic Ca^{2+} signalling (Di Benedetto et al., 2022), BBB remodelling (Verkhratsky & Butt, 2023), impaired antioxidant defenses, and mitochondrial dysfunction are well-documented features of astrocyte dysfunction in AD (Chaikovsky et al., 2022).

| Conclusions

Alzheimer's disease is a multifactorial neurodegenerative disorder involving extensive morphological and functional alterations in the central nervous system. Astrocytes, due to their high functional plasticity, can exert both neuroprotective and neurotoxic effects depending on disease stage and organismal reactivity. Their dual role — protective in early stages and toxic in later ones — makes them a promising target for therapeutic modulation. Strategies aimed at maintaining astrocytic homeostatic functions, such as enhancing glutamate uptake, improving glymphatic drainage, and boosting antioxidant defences, may slow disease progression. Conversely, interventions to block excessive astrogliosis or prevent ferroptosis may reduce neurotoxicity in advanced stages. A comprehensive approach to modulating astrocyte function offers new avenues for pathogenetic therapy in Alzheimer's disease.

| Conflicts of interest

The author declares no conflict of interest.

| Author Contributions

Both authors contributed equally to the conception, writing, and revision of this manuscript. All authors have read and approved the final version.

| Funding

This research was founded by National Research Foundation of Ukraine, grant No 2023.05/0023.

| Authors Biography

Galyna Skibo — Prof., DSc, corresponding member of NAS of Ukraine, head of Department of Cytology, O.O.Bogomoletz Institute of Physiology National Academy of Sciences of Ukraine, Kyiv, Ukraine.

Nataliia Nevmerzhytska — PhD, senior researcher, Department of Cytology, O.O.Bogomoletz Institute of Physiology National Academy of Sciences of Ukraine, Kyiv, Ukraine; PhD, associate professor, Department Histology and Embriology Bogomolets National Medical University, Kyiv, Ukraine.

| References

Andersen JV, Schousboe A & Verkhratsky A (2022): Astrocyte energy and neurotransmitter metabolism in Alzheimer's disease: integration of the glutamate/GABA-glutamine cycle. Progress in Neurobiology 217:102331.

Chaikovsky YB, Makarenko AN, Khomyak NV, & Kirichenko AV. (2022). Introduction to Gliology. Edited by Prof. A. N. Makarenko. Kyiv: Kniga-Plus, 168 pp.

Dhapola R, Beura SK, Sharma P, Singh SK & HariKrishnaReddy D (2024): Oxidative stress in Alzheimer's disease: current knowledge of signaling pathways and therapeutics. Molecular Biology Reports 51(1):48.

Di Benedetto G, Burgaletto C, Bellanca CM, Munafò A, Bernardini R & Cantarella G (2022): Role of microglia and astrocytes in Alzheimer's disease: from neuroinflammation to Ca^{2+} homeostasis dysregulation. Cells 11(17):2728.

Diniz LP, Tortelli V, Matias I, Morgado J, Bérgamo Araujo AP, Melo HM, Seixas da Silva GS, Alves-Leon SV, de Souza JM, Ferreira ST, De Felice FG & Gomes FCA (2017): Astrocyte transforming growth factor beta 1 protects synapses against Aβ oligomers in Alzheimer's disease model. Journal of Neuroscience 37(28):6797–6809.

Escartin C, Galea E, Lakatos A, O'Callaghan JP, Petzold GC, Serrano-Pozo A, Steinhäuser C, Volterra A, Carmignoto G, Agarwal A, Allen NJ, Araque A, Barbeito L, Barzilai A, Bergles DE, Bonvento G, Butt AM, Chen WT, Cohen-Salmon M & Verkhratsky A (2021): Reactive astrocyte nomenclature, definitions, and future directions. Nature Neuroscience 24:312–325.

Garaschuk O & Verkhratsky A (2019): GABAergic astrocytes in Alzheimer's disease. Aging 11:1602–1604.

Giovannini MG, Lana D, Traini C & Vannucchi MG (2021): The microbiota-gut-brain axis and Alzheimer disease. From dysbiosis to neurodegeneration: focus on the central nervous system glial cells. Journal of Clinical Medicine 10(11):2358.

Govindpani K, McNamara LG, Smith NR, Vinnakota C, Waldvogel HJ, Faull RL & Kwakowsky A (2019): Vascular dysfunction in Alzheimer's disease: a prelude to the pathological process or a consequence of it? Journal of Clinical Medicine 8(5):651.

Hayakawa K, Esposito E, Wang X, Terasaki Y, Liu Y, Xing C, Ji X & Lo EH (2016): Transfer of mitochondria from astrocytes to neurons after stroke. Nature 535(7613):551–555.

Heneka MT, Gauthier S, Chandekar SA, Hviid Hahn-Pedersen J, Bentsen MA & Zetterberg H (2025): Neuroinflammatory fluid biomarkers in patients with Alzheimer's disease: a systematic literature review. Molecular Psychiatry 30(6):2783–2798.

Kaltschmidt B, Czaniera NJ, Schulten W & Kaltschmidt C (2024): NF-κB in Alzheimer's disease: friend or foe? Opposite functions in neurons and glial cells. International Journal of Molecular Sciences 25(21):11353.

Kim J, Yoo ID, Lim J & Moon JS (2024): Pathological phenotypes of astrocytes in Alzheimer's disease. Experimental and Molecular Medicine 56(1):95–99.

Kumar A, Fontana IC & Nordberg A (2023): Reactive astrogliosis: a friend or foe in the pathogenesis of Alzheimer's disease. Journal of Neurochemistry 164(3):309–324.

Le Douce J, Maugard M, Veran J, et al. (2020): Impairment of glycolysis-derived l-serine production in astrocytes contributes to cognitive deficits in Alzheimer's disease. Cell Metabolism 31(3):503–517.e8.

Leipp F, Vialaret J, Mohaupt P, Coppens S, Jaffuel A, Niehoff AC, Lehmann S & Hirtz C (2024): Glial fibrillary acidic protein in Alzheimer's disease: a narrative review. Brain Communications 6(6):fcae396.

Lim D, Matute C, Cavaliere F & Verkhratsky A (2025): Neuroglia in neurodegeneration: Alzheimer, Parkinson, and Huntington disease. Handb Clin Neurol 210:9-44.

Liu Y, Wu L, Peng W & Mao X (2025): Glial polarization in neurological diseases: molecular mechanisms and therapeutic opportunities. Ageing Research Reviews 104:102638.

Maimaiti Y, Su T, Zhang Z, Ma L, Zhang Y & Xu H (2024): NOX4-mediated astrocyte ferroptosis in Alzheimer's disease. Cell and Bioscience 14:88.

Makarenko AN, Kvitnitskaya-Ryzhova TY, Lugovskoy SP, & Mikhalskiy SA. (2024). Introduction to Gliology and Gliopathology (Part 2). Edited by Prof. A. N. Makarenko and Prof. T. Y. Kvitnitskaya-Ryzhova. Kyiv: PROPAPIR, 164 pp.

Misrani A, Tabassum S & Yang L (2021): Mitochondrial dysfunction and oxidative stress in Alzheimer's disease. Frontiers in Aging Neuroscience 13:617588.

Monterey MD, Wei H, Wu X & Wu JQ (2021): The many faces of astrocytes in Alzheimer's disease. Frontiers in Neurology 12:619626.

Nam MH, Na H, Lee CJ & Yun M (2024): A key mediator and imaging target in Alzheimer's disease: unlocking the role of reactive astrogliosis through MAOB. Nuclear Medicine and Molecular Imaging 58(4):177–184.

Nevmerzhytska N & Yaremenko L (2024): Characteristics of streptozotocin-induced and okadaic acid-induced models of Alzheimer's disease. The Ukrainian Scientific Medical Youth Journal 147(2):98–104.

Nevmerzhytska N. (2025). Characteristics of Scopolamine- and Trimethyltin-Induced Models of Alzheimer's Disease. The Ukrainian Scientific Medical Youth Journal, 155(2), 280-286.

Olabarria M, Noristani HN, Verkhratsky A & Rodriguez JJ (2010): Concomitant astroglial atrophy and astrogliosis in a triple transgenic animal model of Alzheimer's disease. Glia 58:831-838.

Paidlewar M, Kumari S, Dhapola R, Sharma P & HariKrishnaReddy D (2024): Unveiling the role of astrogliosis in Alzheimer's disease pathology: insights into mechanisms and therapeutic approaches. International Immunopharmacology 141:112940.

Pekowska A, Verkhratsky A & Falcone C (2025): Evolution of neuroglia: From worm to man. Handb Clin Neurol 209:7-26.

Popov A, Brazhe A, Denisov P, Sutyagina O, Li L, Lazareva N, Verkhratsky A & Semyanov A (2021): Astrocyte dystrophy in ageing brain parallels impaired synaptic plasticity. Aging Cell 20:e13334.

Popov A, Brazhe N, Morozova K, Yashin K, Bychkov M, Nosova O, Sutyagina O, Brazhe A, Parshina E, Li L, Medyanik I, Korzhevskii DE, Shenkarev Z, Lyukmanova E, Verkhratsky A & Semyanov A (2023): Mitochondrial malfunction and atrophy of astrocytes in the aged human cerebral cortex. Nat Commun 14:8380.

Preman P, Alfonso-Triguero M, Alberdi E, Verkhratsky A & Arranz AM (2021): Astrocytes in Alzheimer's disease: pathological significance and molecular pathways. Cells 10(3):540.

References

Ryan SK, Zelic M, Han Y, Teeple E, Chen L, Sadeghi M, Shankara S, Guo L, Li C, Pontarelli F, Jensen EH, Comer AL, Kumar D, Zhang M, Gans J, Zhang B, Proto JD, Saleh J, Dodge JC, Savova V & Hammond TR (2023): Microglia ferroptosis is regulated by SEC24B and contributes to neurodegeneration. Nature Neuroscience 26(1):12–26.

Sadick JS, O'Dea MR, Hasel P, Dykstra T, Faustin A & Liddelow SA (2022): Astrocytes and oligodendrocytes undergo subtype-specific transcriptional changes in Alzheimer's disease. Neuron 110(11):1788–1805.e10.

Semyanov A & Verkhratsky A (2021): Astrocytic processes: from tripartite synapses to the active milieu. Trends Neurosci 44:781-792.

Shippy DC, Oliai SF & Ulland TK (2024): Zinc utilization by microglia in Alzheimer's disease. Journal of Biological Chemistry 300(5):107306.

Si ZZ, Zou CJ, Mei X, Li XF, Luo H, Shen Y, Hu J, Li XX, Wu L & Liu Y (2023): Targeting neuroinflammation in Alzheimer's disease: from mechanisms to clinical applications. Neural Regeneration Research 18(4):708–715.

Soelter TM, Howton TC, Clark AD, et al. (2024): Altered glia-neuron communication in Alzheimer's disease affects WNT, p53, and NFkB signaling determined by snRNA-seq. Cell Communication and Signaling 22:317.

Sweeney MD, Sagare AP & Zlokovic BV (2018): Blood-brain barrier breakdown in Alzheimer disease and other neurodegenerative disorders. Nature Reviews Neurology 14(3):133–150.

Taday J, Fróes FT, Seady M, Gonçalves CA & Leite MC (2024): In vitro astroglial dysfunction induced by neurotoxins: mimicking astrocytic metabolic alterations of Alzheimer's disease. Metabolites 14(3):151.

Tzioras M, McGeachan RI, Durrant CS & Spires-Jones TL (2023): Synaptic degeneration in Alzheimer disease. Nature Reviews Neurology 19(1):19–38.

Verkhratsky A & Butt A (2023): Neuroglia: Function and Pathology. Elsevier, ISBN:978-0-12-821565-4.

Verkhratsky A & Nedergaard M (2014): Astroglial cradle in the life of the synapse. Philos Trans R Soc Lond B Biol Sci 369:20130595.

Verkhratsky A & Nedergaard M (2018): Physiology of astroglia. Physiological Reviews 98(1):239–389.

Verkhratsky A & Pivoriunas A (2023): Astroglia support, regulate and reinforce brain barriers. Neurobiol Dis 179:106054.

Verkhratsky A & Semyanov A (2025): Physiology of neuroglia of the central nervous system. Handbook of Clinical Neurology 209:69–91.

Verkhratsky, A., Rodríguez, J. J., & Parpura, V. (2014). Neuroglia in ageing and disease. Cell and tissue research, 357(2), 493–503. https://doi.org/10.1007/s00441-014-1814-z

Verkhratsky A, Butt A, Li B, Illes P, Zorec R, Semyanov A, Tang Y & Sofroniew MV (2023): Astrocytes in human central nervous system diseases: a frontier for new therapies. Signal Transduct Target Ther 8:396.

Xu J, Shen R, Qian M, Zhou Z, Xie B, Jiang Y, Yu Y & Dong W (2025): Ferroptosis in Alzheimer's disease: the regulatory role of glial cells. Journal of Integrative Neuroscience 24(4):25845.

Yu Y, Chen R, Mao K, Deng M & Li Z (2024): The role of glial cells in synaptic dysfunction: insights into Alzheimer's disease mechanisms. Aging and Disease 15(2):459–479.

Zhang Y, Zhou Q, Lu L, Su Y, Shi W, Zhang H, et al. (2023): Copper induces cognitive impairment in mice via modulation of cuproptosis and CREB signaling. Nutrients 15:972.