Early Trauma, Exaggerated Neuroinflammation, and Women's Neurodegenerative Risk

Research Question:

How early life trauma may lead to exaggerated neuroinflammatory responses in neurodegenerative diseases, especially in women.

Word Count: - 4046 words

Abstract

Early life stress (ELS) and trauma represent critical developmental risk factors that can fundamentally alter brain structure and function, with lasting consequences extending into adulthood. The relationship between early adversity and later neurodegenerative disease risk has emerged as a significant area of research.

Of utmost importance is understanding women's health, particularly, their differences between men that could make them more susceptible to such neuropsychiatric disorders. There exists also a consistent finding that women demonstrate greater vulnerability to stress-related neuropsychiatric disorders and certain neurodegenerative conditions, suggesting that there are sex-specific biological mechanisms underlying these associations.

This paper aims to conduct a review of the current standing literature between the decade of 2015-2025 that examines the epidemiological patterns, biological mechanisms, and sex differences that characterize the relationship between early life trauma and exaggerated neuroinflammatory responses in any and all neurodegenerative diseases, with emphasis on women.

Introduction

The term Early life stress (ELS) refers to traumatic or adverse experiences during childhood, such as childhood abuse and neglect (before the age of 18). It is a broad term that encompasses the several different kinds of adverse experiences a child may encounter which can have long-lasting negative impacts on a person's mental and physical health. ELS has been associated with increased risk for many psychiatric disorders for example but not limited to, depression, post-traumatic stress disorder (PTSD), and bipolar disorder (Famularo and Kinscherff, 1992).

A longitudinal work describes that ELS permanently alters the immune system and brain pathways, particularly the Hypothalamus-Pituitary-Adrenal (HPA) Axis. It triggers lasting biological changes- through HPA axis dysregulation and epigenetic alterations- that could set a primed state for future neuroinflammatory overreactions. Exposure to stress early in life has already been strongly linked to increased risks of neuro-developmental disorders (ex: ADHD and autism) although evidence isn't entirely consistent.

A central mechanism linking early-life experiences with later-life brain health is neuroinflammation: an inflammatory response linked with the brain and spinal cord. Additionally, early life experiences are said to set your lifelong inflammatory baseline. In healthy conditions, neuroinflammation serves a protective role to the body by clearing pathogens and cell debris. However, prolonged or inappropriate neuroinflammation can

damage the brain and even contribute to neurological disorders and conditions like dementia, Parkinson's, and Alzheimer's disease.

Of the more than six million people over 65 in the US who have Alzheimer's disease, almost two-thirds are women (Budson, 2022). It is found by numerous statistics that Alzheimer's disease disproportionately affects women, yet little is understood about how early adversity may predispose them to accelerated neurodegeneration. Although animal models have shown that maternal separation primes microglial hyper-reactivity, human evidence connecting early-life trauma to markers of brain aging remains limited. Understanding how early adversity influences neuroinflammatory trajectories is critical for identifying women at risk for premature cognitive decline.

To clarify the link between early trauma, sex differences, and neurodegenerative disease, this review examines four key areas: 1. The connection between early life trauma and neuroinflammatory pathways, 2. Microglia and sex differences in neuroinflammation, 3. Understanding estrogen and neuroprotection in women, and 4. Examining the link between neuroinflammation and neurodegenerative diseases.

Methodology

This paper presents a literature review of previously conducted research. This paper focuses on and analyzes how early life trauma may lead to exaggerated neuroinflammatory responses in neurodegenerative diseases, with a special emphasis in women. Sources were selected from Scispace and Google Scholar. A total of 43 papers were selected on the basis of keywords: "early life trauma" and neuroinflammation and "neurodegenerative disease" and (women OR female OR "sex differences") and (microglial OR cytokines).

Body

1. The connection between Early Life Trauma and neuroinflammatory pathways.

Early Life Stress (ELS) has emerged in recent times as one of the strongest predictors of immune dysregulation, with lasting effects that permanently alter the immune system and brain pathways, setting your lifelong inflammatory baseline. It chronically activates the Hypothalamus-Pituitary-Adrenal (HPA) axis, leading to prolonged glucocorticoid exposure that desensitizes glucocorticoid-receptor signaling and primes microglia for exaggerated neuroinflammatory responses. (Göver & Ślęzak, 2024).

The structural brain effects of ELS include reduced hippocampal volume which is central to memory and stress regulation, and reduced prefrontal cortex volume which affects executive function, decision-making, and emotional regulation (McManus et. al 2021). This provides a direct link of ELS with poorer performance on memory tasks, processing speed, and attention. These effects remained decades later, showing long-term consequences (Cassiers

et. al 2019), while proving to be a strong predictor of adult depression and anxiety even in otherwise “healthy” adults.

ELS is also linked to dysregulation of the HPA axis as well as chronic low grade inflammation in adulthood, with findings often indicating elevated levels of proinflammatory cytokines in people with high ELS (Figg et. al 2019, Salleh et. al 2020). It was found that maternal stress during pregnancy and early postnatal life has measurable effects on children’s HPA-axis functioning (Simons et al. 2018). This is particularly important as the HPA axis and the locus coeruleus–norepinephrine system are vital in maintaining internal stability (homeostasis) during stressful events.

If stress reactions are too strong, prolonged, or poorly timed, they risk causing acute or chronic pathology and affect physical and mental health across the lifespan. Exposure to stress early in life is strongly linked to increased risks of neuro- developmental disorders like ADHD and autism- though evidence isn’t entirely consistent. ELS can reprogram gene expression via DNA methylation, providing a bridge between early stress and altered microglial or neuroimmune function later in life (Nicolaides et. al 2024).

This is supported by scientific evidence proving that adverse childhood experiences, such as neglect, abuse or maternal separation are consistently shown to reprogram the developing stress and immune systems, producing what this research describes as a “primed” inflammatory state, meaning that when someone encounters an infection, their body might overreact or fail to return to balance afterward (Cattane et. al 2022).

Reemst et. al 2022 found that microglia from ELS mice looked different than normal microglia, and their gene expression patterns showed an altered state- proving the “primed” state as discussed above. This meant that even without stress, their default mode was completely changed by early life experiences. When these mice were immune-challenged by lipopolysaccharide, ELS microglia reacted differently than the ones that were controlled. Some became over-reactive (stronger responses), others blunted (inflexible enough), either way their plasticity was disrupted. This proved that ELS may cause a kind of epigenetic reprogramming of microglia, and these changes last into adulthood.

It was also seen that while in this “primed” state, microglia were more likely to overreact to later stressors or pathological proteins, fueling chronic neuroinflammation and likely even contributing towards risk of neurodegenerative disease. By examining studies on both animals and humans, this section explores how ELS-induced changes in neuroimmune pathways establish the biological foundation for lifelong inflammatory risk.

In normal conditions, microglia extend arms (processes) and prune extra synapses. However, as found by Bolton et. al 2021, after ELS, microglia looked less active and reduced their synaptic pruning. This led to more excitatory synapses staying on neurons, meaning that stress neurons had become “overconnected,” leading to a hyperactive stress response. The study also examined MERtk (MER proto-oncogene tyrosine kinase). It is a protein that plays

crucial roles in the body's normal processes like tissue repair, immune regulation, and the clearance of apoptotic (dying) cells. It is a receptor microglia used to recognize and engulf synapses- and it was found that ELS reduced MerTK function. Because of these circumstances and the extra synapses, ELS animals showed lifelong stress hypersensitivity. This suggests a direct link between early life adversity, microglial dysfunction and long-term stress vulnerability.

In mice experiencing Neonatal Maternal Separation (NMS) i.e, mice that were separated from their mothers for several hours each day during the first two weeks of life- it was found that they exhibited depressive-like behaviors as an adult (Suman et. al 2025). This NMS, combined with amyloid-β oligomers to model Alzheimer's-like pathology, made mice perform with worse memory performance than normal. This showed that NMS and Aβ oligomers had additive/ synergistic effects, proving early trauma primes neural circuits and inflammatory pathways that amplify later neurodegenerative insult.

The same NMS was performed on both male and female mice, with findings indicating that maternal separation primed microglia differently in males and females (Garcia et. al 2023). It revealed that female mice showed more pronounced early Alzheimer's pathology, evidenced by higher amyloid deposition and stronger microglial activation in certain brain regions. This was further supported by findings of comparatively severe cognitive deficits (memory impairments) in females. Female brains were found to be more vulnerable to early trauma's priming effects, especially regarding neuroinflammation and amyloid pathology, adding a new sex-specific perspective to the topic. It is also found that female rats exposed to pre-pubertal stress (stress before sexual maturity) showed significantly higher corticosterone responses (the main stress hormone in rodents, analogous to cortisol in humans) compared to males when later exposed to stress (Brydges, 2020).

This sex-specific perspective is further supported by the findings of Fleck et. al 2025, which proved that women who experienced more severe early-life stress tend to show reductions in total and subcortical gray matter volumes and an increase in third ventricular volume, a sign of brain tissue loss and a shrinkage in brain structures crucial for memory, emotion, and stress regulation. Findings indicate that severe stress in childhood seemed to accelerate brain aging. As these women grew older, parts of their brain shrank, and fluid spaces expanded, which can be linked to cognitive decline or risk for neurodegenerative diseases (Schuurmans et. al 2023) The study also identified significant nonlinear interactions between ELS severity and age indicative of neuroinflammation and neurodegeneration, respectively.

2. Microglia and sex differences in neuroinflammation

While early life trauma sets the stage for chronic neuroinflammation, its impact is not uniform across sexes. A growing body of evidence shows that microglia, the brain's resident immune cells, are sexually dimorphic in both development and function. Research indicates that male and female brains show different microglial densities, shapes, and activation states

during early development. These differences are hormone-driven and region-specific. Bordt et. al 2020 explains this concept in detail. It says that testosterone in males during perinatal development can be converted to estradiol in the brain, activating microglia and leading to sex-specific changes in brain wiring. For example: In the preoptic area (POA), estradiol-activated microglia promote the formation of male-typical synapses, which later underlie male sexual behavior.

While the 'mechanistic relationship between the sexually dimorphic neuroimmune system and the sex-specific outcomes of a pubertal immune challenge is unclear' as per Kolmogorova et. al 2021, evidence shows that social stress is associated with increased proinflammatory cytokine production in the locus coeruleus–norepinephrine system (LC) in female rats (Smiley et. al 2023). Microglial activity in the LC is crucial for manifestation of stress-induced behaviors, and its suppression during stress prevented heightened neuronal activity in LC typically observed in response to stress cues. This indicates that microglia plays a role in modulating neuronal responses to stress, underscoring the importance of considering sex-specific differences in neuroimmune responses and the potential for targeting microglia in therapeutic interventions for stress-related disorders.

The idea of sex-specific differences is reiterated by the evidence that male and female rat brains had different numbers and shapes of microglia during development, with males often having higher microglial density in certain regions and females showing different morphologies, indicating functional differences (Schwarz et. al 2012). Since rodent findings can be easily translated into humans, this showed that sex-specific differences are highly possible. However, it is also seen that these differences are region-dependent, meaning some brain areas are more vulnerable to sex-specific influences than others.

This provides a possible cellular-level explanation for why females may respond differently and even stronger to ELS (Logue et. al 2024). The stronger links between emotional abuse and depressive symptoms in females may reflect gendered patterns in emotional processing and coping mechanisms. Apart from structural differences, women may be more likely to internalize distress, leading to higher rates of depression following emotional maltreatment (O’Shields et. al 2023).

Since female microglia differ early in development, this combination could make them more reactive to ELS as well as move towards the tendency to develop exaggerated neuroinflammatory responses later in life.

FEMALE microglia	**MALE microglia**
Shifted towards glycolysis	Minimal or no shift
Aged compromised motility + did not adapt metabolism. Motility (observed via wound-healing assays) significantly reduced in microglia from aged female mice.	Aged had oxidative phosphorylation (efficient metabolism) + normal motility. Not that much in male.
Phagocytosis (the ability to clear debris) decreased with age in both sexes	**Phagocytosis** (the ability to clear debris) decreased with age in both sexes

Figure 1: Findings of Mela et. al (2023), original image

This hypothesis is further proved by molecular evidence that microglia in female mice were more vulnerable to acute immune challenge and aging- by metabolic shifts, reduced movement, and impaired clearance as compared to males (Mela et. al 2023, Ghannam et. al 2024) This reiterates the importance of including sex as a key variable in neuroimmune research.

In Figure 2, the findings note that female microglia experienced a shift toward glycolysis- which is associated with pro-inflammatory states and reduced function. Combined with inadequate metabolism, microglia may fail to clear pathological proteins and contribute to neurodegenerative cascades. Female microglia's heightened sensitivity may help explain why women are often more vulnerable to inflammation-driven brain diseases (e.g., Alzheimer's disease). The stressors studied- IFNγ, Aβ and aging- are directly relevant to neurodegenerative disease contexts, where microglial dysfunction accelerates disease progression, possibly proving why women were often more vulnerable.

Although Walker et. al 2019 did not contrast between male and female systems, its findings support that of the above while providing a clear relationship between ELS and neuroinflammation contributing towards neurodegenerative diseases. When quail chicks were exposed to ELS (stressful handling, unpredictable stressors), their immune systems didn't "reset" in adulthood. Instead, even long after the stress ended, they showed elevated expression of pro-inflammatory cytokines such as IL-1β and TNF-α- indicating a "primed" immune system that reacts faster, stronger, and longer to later stressors. This immune priming is linked to higher vulnerability for neurodegenerative diseases (like Alzheimer's, Parkinson's) because chronic low-grade inflammation accelerates brain damage.

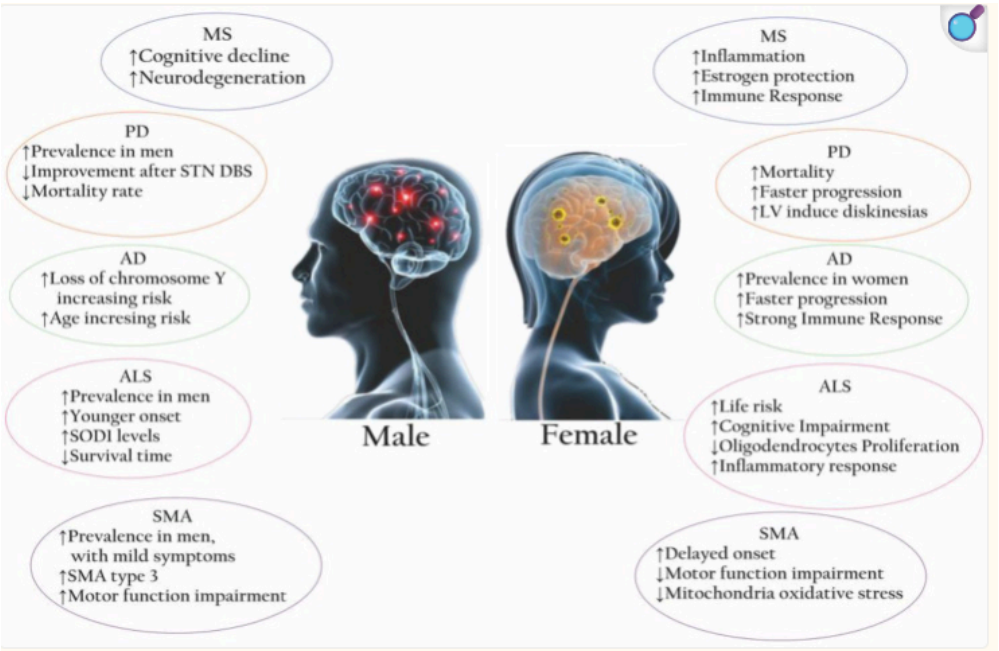

Figure 2: Differences between males and females as per Bianco et. al 2023.

The above proved sex-dependent profiles of microglia further amplify the existence of the hypothesis, only further supported by findings that neurodegenerative diseases also show sex related differences. This proves that neurodegeneration is sex-biased where men often show structural degeneration (neuronal loss, motor impairment) and women often show immune-driven and inflammatory mechanisms leading to faster progression.

Connecting this with ELA, behavioral changes of mice after repeated mild traumatic brain injury (rmTBI) showed that both male and female mice developed cold nociceptive hypersensitivity and exhibited negative affective states. This form of ELA also led to increased locomotor activity and risk-taking behavior in the mice. However, these negative effects were successfully reversed specifically in male mice after the use of an anti-inflammatory drug, minocycline. A significant sex difference was that minocycline was not able to reverse negative affect and pain hypersensitivities in female mice, further making the idea of a sexually dimorphic system concrete (Liu et. al 2023).

However, the same theory is not strongly researched yet. Based on self-reported data from 453 adults (267 women, 186 men) recruited via Amazon Mechanical Turk (MTurk), neither trauma (childhood or lifetime) nor gender alone predicted chronic inflammatory disease burden (Lacienski et. al 2019). It gave potential evidence that the trauma-to-inflammation pathway may be context-dependent, subtle, or mediated by intermediate mechanisms. Yet, the research was conducted upon self-reported data, which may not be entirely reliant, leaving the question of sex-specific differences still open.

3. Understanding estrogen and neuroprotection in women.

If sex-biased microglial activity explains women's heightened inflammatory reactivity, estrogen provides the counterbalance that protects the female brain. Estrogen decreases microglial overactivation, reduces production of pro-inflammatory cytokines and protects against neuroinflammation triggered by stress, injury, or neurodegenerative pathology (Rao et. al 2019, Rahman et. al 2019). It enhances mitochondrial function and reduces oxidative damage in neurons, preventing cell death while promoting synaptic plasticity in the hippocampus and cortex (Petrovska et. al 2022).

Women have higher estrogen levels during reproductive years, which may explain lower incidence or delayed onset of some neurodegenerative diseases. The loss of estrogen during menopause increases susceptibility to neuroinflammation and cognitive decline. Estrogen normally suppresses excessive microglial activation and trauma-primed microglia may respond more strongly if estrogen protection is lost later in life (Rahman et. al 2019).

Chronic stress is said to alter aromatase activity and can even reduce the ability to make estrogen. This causes changes in estrogen receptors, and if altered, even the estrogen that is produced may not work properly. (Rao et. al 2019) The same effects were found after a genetic knockout model (KO) was created with an ERβ deletion, leading to significant mitochondrial dysfunction especially in females, characterized by reduced mitochondrial membrane potential which is also observed in Alzheimer's disease pathology, maybe link between ERβ deficiency and AD progression (Long et. al 2011).

This connects stress with hormonal disruption and exaggerated inflammation possibly leading to future brain vulnerability. In women, loss of estrogen's protective effect (especially during stress or later in menopause) could even accelerate neurodegeneration. This provides a biological rationale for considering female-specific vulnerability in neuroinflammatory diseases and Alzheimer's.

The clinical significance of estrogen loss becomes most evident during midlife and surgical interventions. Rahman et al. (2019) emphasized that the menopausal transition removes a crucial layer of neuroimmune protection, explaining the sharp rise in Alzheimer's disease prevalence among older women. This is due to the fact that surgery/anesthesia reduces synaptic plasticity in the hippocampus, and may trigger stress responses, inflammation, and neural stress. This even impairs the ability of hippocampal neurons to form and maintain synapses. It indirectly even reduces synaptic plasticity, manifested as memory deficits/ cognitive dysfunction- especially in vulnerable populations (elderly). It is found that estrogen supplementation rescues this decline. Researchers (Tan et. al 2023) injected estrogen directly into the hippocampus of animal models, and observed restored synaptic plasticity where neurons reconnected properly, and memory performance was improved in behavioral tests.

This is further evidenced in Rose et. al 2019 when Selective Estrogen Receptor Modulators (SERMs)- i.e. drugs that act like estrogen in selective tissues- activated ERα and ERβ (estrogen receptors) in neurons and glia, reducing Aβ-induced cell death which is toxic in

Alzheimer's Disease (AD). They suppress microglial overactivation and decrease pro-inflammatory cytokines (IL-1β, IL-6, TNF-α). This reduces oxidative stress in neurons and supports synaptic plasticity, improving learning and memory in experimental models. SERMs can even provide neuroprotection in post-menopausal females, when ovarian estrogen is low, without the systemic risks of hormone replacement therapy. This explains the molecular pathways of protection against Aβ toxicity: microglial modulation, anti-inflammatory signaling, antioxidant defense, and synaptic support.

The below table thirds the neuroprotective role of estrogen and presents adjusted odds ratios (HR = hazard ratio) for developing dementia or Parkinson's disease (PD) after ovarian removal surgery (oophorectomy) at different ages in premenopausal women. Unilateral oophorectomy is the removal of one ovary while bilateral oophorectomy = removal of both ovaries.

Overall interpretation of the values revealed that younger women are at much higher risk as compared to older and the earlier the ovaries are removed, the higher the risk of dementia or PD. This shows that estrogen loss matters, as removing ovaries reduces estrogen, which plays a neuroprotective role. These hormonal fluctuations may even trigger neuroinflammation, oxidative stress, and synaptic dysfunction in the brain, increasing susceptibility to disorders like Alzheimer's disease.

Adjusted odd ratio for dementia after unilateral oophorectomy			
Age at surgery (years)	Hazard ratio	CI 95%	P value
<43	1.74	0.97–3.14	0.06
43–48	1.68	1.06–2.66	0.03
>48	1.09	0.74–1.61	0.66
Adjusted odd ratio for dementia after bilateral oophorectomy			
<34	4.61	2.52–8.43	<0.0001
34–41	1.23	0.67–2.26	0.51
>41	1.50	1.05–2.13	0.03
Adjusted odd ratio for PD after bilateral oophorectomy			
<38	2.85	1.28–6.35	0.001
38–45	1.38	1.28–6.35	0.42
>45	1.38	0.92–3.03	0.09

Table 1.

Utero-ovarian surgery and neurological disturbances in premenopause.

Cases of cognitive impairment/dementia and Parkinson disease (PD) in women with unilateral (813) and bilateral (676) oophorectomy: For a nonmalignant disease, in Olmsted County, Minnesota (USA) during 1950–1987, followed up the death or the finish of study at 2001–2006 (Rocca et al. [32]).

Figure 3: Utero-ovarian surgery and neurological disturbances in premenopause. (Figure taken from Russu et. al 2018)

While estrogen normally protects the brain, chronic stress can undermine this shield. Recent studies have also revealed that estrogen activates several genes associated with Alzheimer's disease (AD) (Ratnakumar et. al 2019). One of these genes is APOE, known to increase AD risk if it's a certain variant (Wang et. al 2020). This shows that estrogen doesn't just affect reproductive systems- also modulates brain pathways that can influence neurodegeneration. A loss of estrogen during menopause may also interact with genetic vulnerability to Alzheimer's, making women more susceptible at certain life stages.

Along with the effect of ELS on the brain for accelerated aging, estrogen modulates gene expression in pathways relevant to neurodegeneration- and this combination may make women more vulnerable to conditions like Alzheimer's, especially if ELS or social/diagnostic biases delay recognition and treatment.

4. Examining the link between neuroinflammation and neurodegenerative diseases.

Neuroinflammation consistently emerges as a central pathway driving neurodegenerative disease. Genetic and molecular studies show that risk factors for Alzheimer's and Parkinson's converge on microglial dysfunction and immune dysregulation (Boyd & Avramopoulos 2022; Ripa 2023).

Many genes linked to Alzheimer's (AD) and Parkinson's (PD) control microglial function, immune signaling, or the brain's ability to regulate inflammation. Brain injury, stress, infections, or toxins can even "prime" microglia into an overactive state, pushing the brain toward degeneration. It is evidenced that neuroinflammation isn't secondary- but rather it's central to neurodegenerative diseases. Traditionally, scientists thought inflammation was just a reaction to plaques (in AD) or Lewy bodies (in PD). However, inflammation might be the driver that makes these diseases worse.

Although Alzheimer's and Parkinson's are two different (memory vs. motor symptoms) diseases, the underlying inflammatory signatures are very similar. So instead of seeing AD and PD as entirely separate, researchers are encouraged to see them as different "faces" of a common inflammatory vulnerability. This evidence suggests treatments that target neuroinflammation could even help both diseases.

An important factor of not only the body but also in neurodegenerative diseases, microglia are considered to be double-edged swords. Although they serve a protective role by clearing Aβ plaques associated with AD, and even support neuronal survival while maintaining homeostasis, they may also be harmful. Chronic activation of microglia produces pro-inflammatory cytokines, oxidative stress, and worsens tau pathology. Excess IL-1β, IL-6, TNF-α produced amplifies neuronal damage and synaptic dysfunction (Shah et. al 2024, Ripa et. al 2023). IL-6 contributes to neurodegeneration by impairing neurogenesis and promoting glial reactivity while TNF-α triggers oxidative stress and apoptosis in neurons. The coordinated release of these inflammatory molecules by microglia links immune dysregulation directly to cognitive decline in AD.

Apart from the above, prior stress or trauma such as ELS can "prime" microglia, making them more reactive to later insults like Aβ accumulation. Targeting microglial activation could help slow AD progression.

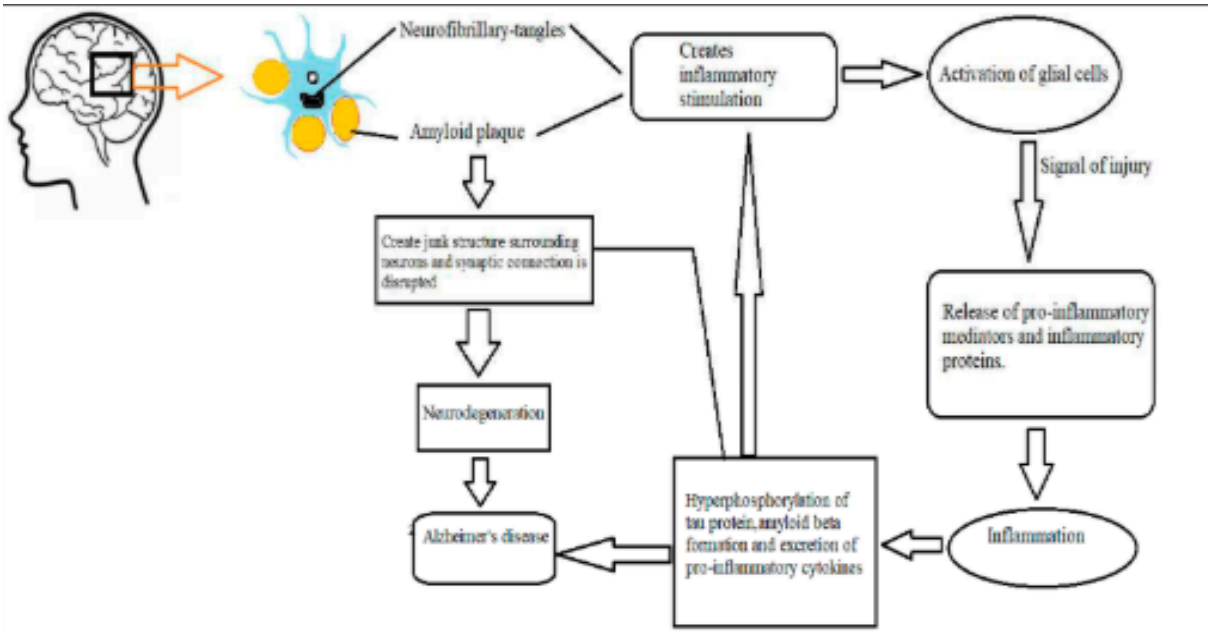

Figure 4 (Ripa. et al 2023): This diagram illustrates the neuroinflammatory cascade in Alzheimer's disease (AD) where amyloid plaques and tau tangles trigger glial activation, leading to chronic neuroinflammation, which drives neuronal death and Alzheimer's progression.

Apart from neurodegenerative diseases it has been found that depression, which is a psychiatric disorder, is widely linked to elevated inflammation. Evidence shows that patients with major depressive disorder (MDD) show increased levels of proinflammatory cytokines like IL-6, IL-1β, TNF-α, and even CRP (Beurel et. al 2020). Exposure to these cytokines (e.g., during infections or interferon-α treatment) often induces depressive-like behavior, creating an endless cycle of further inflammation. Multiple triggers merge as ELS, microbiome changes, genetic predispositions, and stress all can fuel inflammation contributing to depression. Just as depression and inflammation are entwined, neurodegeneration may be fueled by a similar loop- especially if early trauma shifts inflammatory set points.

If women manifest stronger inflammatory responses (due to microglial priming or hormonal interactions), this loop can amplify and accelerate neurodegenerative processes.

Together, these findings highlight neuroinflammation as the final common pathway through which early trauma, sex differences, and hormonal decline converge, explaining women's elevated risk for neurodegenerative disease.

Conclusion

Early life trauma leaves a biological "memory" in the brain and immune system that persists across the lifespan. By priming microglia, disrupting HPA axis regulation, and reprogramming stress-immune pathways, trauma establishes a heightened inflammatory baseline that increases vulnerability to later insults. In women, these effects are amplified by

sex-specific neuroimmune differences and the loss of estrogen's protective role during menopause or surgical interventions. Together, these processes accelerate neuroinflammation, synaptic dysfunction, and neurodegenerative cascades, helping to explain why women disproportionately suffer from Alzheimer's disease and other inflammation-driven disorders.

The evidence reviewed here highlights neuroinflammation as the final common pathway where biology (microglial priming, hormonal changes) and lived experience (early adversity) converge. Importantly, it underscores the need for sex-aware neuroscience and medicine-from basic research that incorporates female models, to clinical strategies that account for women's trauma histories and hormonal transitions.

Future work must aim to develop biomarkers that capture trauma-primed inflammation, design interventions that restore neuroimmune balance, and address cultural and diagnostic barriers that delay recognition in women. By integrating biological mechanisms with psychosocial realities, research can move toward precision prevention and treatment strategies that reduce the disproportionate neurodegenerative burden borne by women.

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