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NEURO-INFLAMMATION AND ITS IMPACT ON NEURODEGENERATIVE DISEASES: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, and Amyotrophic Lateral Sclerosis (ALS), involve gradual loss of neurons and functional impairment. There is new proof that neuro-inflammation is critical to the onset and progression of these diseases. The damage to neural tissue as well as the sustained degeneration of neural tissues is caused due to pro-inflammatory cytokines along with microglial activation and immune signaling pathways. This systematic review aims to integrate the existing information about the role of inflammation in neurodegenerative diseases, especially focusing on its mechanisms and possibilities for treatment.

Objective: To systematically review existing literature to assess the impact of neuro-inflammation in the main neurodegenerative illness in relation to their pathogenesis. This review attempts to find main predictors of inflammation, explain the primary processes, and evaluate the effects of changing immunological defense responses of the central nervous system on treatment outcomes.

Methods: A systematic search was done on PubMed, Scopus, Web of Science, and Google Scholar from the year 2010 to 2025. The inclusion criteria focused on studies dealing with neurodegenerative diseases and had relevant inflammatory biomarkers or mechanisms. The data collected included study design, disease focus, demographics of the markers (cytokines, TLR4, microglial activation), mechanistic pathways, and therapeutic approaches. The quality of studies was evaluated using the Newcastle-Ottawa Scale. Findings through the studies were qualitatively analyzed to identify prevailing themes.

Results: There were 123 eligible studies identified through the search. Euro-inflammation was persistently associated with disease evolution in all three paramount disorders. The most frequently examined factors explain neuro degeneration as cytokines (e.g., IL-1β, TNF-α.) and overstimulation of microglia. TLR4 signaling and inflammasome pathways were often related to oxidative stress, synaptic pathology, and neuronal death. About 80% of studies found that modifying inflammatory responses is likely to improve the course of the disease. The results indicate that targeting neuroinflammatory processes has the potential for effective diagnosis and treatment.

Conclusions: From this systematic review, hyper inflammation is one of the most important phenomena during the progression of neurodegenerative disorders. Inflammation-related neurodegeneration such as cytokine release and microglial activity provides damage to the neurons, constituting a rational basis for therapy. Greater focus on unmasking treatment will premise strategies based on timing of the intervention, controlling inflammation, and the use of multidisciplinary approaches into practice.

Introduction and Background

Differentially disabling neurodegenerative diseases are some of the most comprehensive in terms of sheer and intricate devastating conditions of the human body systems. Prevalent conditions include Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS) [1]. Progressively mounting synaptic dysfunction ultimately results in cell death, which leads to cognitive and motor decline, profoundly diminishing the individual's quality of life. While the underlying causes of these diseases are different and multifactorial, inflammation in the nervous system has become an essential common factor that accelerates the disease process [2, 3]. Chronic inflammation has only recently been accepted as a primary driver of neurodegeneration because it was previously considered only a secondary effect of neural cell death. In the absence of injury or infection, inflammation is usually protective in nature, thus it is strictly regulated, comprising of removing damaged and dead cells and repairing controllers [4]. Microglia and astrocytes, which are immune cells, eliminate pathogens, clear debris, and bolster tissue repair. Whereas some pathological conditions modify immune responses leading to the body constantly releasing pro-inflammatory cytokines and oxidative stress which further exacerbate neuronal injury, creating a toxic feedback loop [5].

Microglial activation, the primary resident immune cells for the CNS, exemplifies the broad domain of neuro-inflammation. After the formation of amyloid plaques in Alzheimer's disease, or the aggregates of α-synuclein in Parkinson's, microglial cells transform their resting state into an activated pro-inflammatory phenotype [6, 7]. This is marked by the release of cytokines TNF-α, IL-1β, and IL-6, which gives rise to a damaging cascade of synaptic pruning, mitochondrial failure, and cell death in the neurons. Likewise, humidity devices like TLRs—TLR4 in particular—function to bind to misfolded proteins and fetching immune action which possibly accelerates the disease processes. In ALS, the source of inflammation appears to be not only from the activated microglia, but also from dysfunctional astrocytes and external immune cell infiltration, implying that neuroinflammation in neurodegenerative diseases stems from multiple cell types and systems [8].

A few studies have highlighted the role of the NLRP3 inflammasome and multi-cellular systems in astrocytic activity directed towards inflammation, showcasing the potential of targeting these domains in ALS variant treatments. Furthermore, it has been outlined that the activation of NLRP3 inflammasome is bound to caspase-1, containing a protein complex that-stimulates pro-inflammatory actions, leading to greater inflammation: pro-IL-1β's conversion to active IL-1β. NLRP3 has shown its impact in cadmic models of neurodegeneration, proving its binding to loss of memory, weakening of synaptic strength, and on anti-cell birth processes neurogenesis [9, 10]. Another point to highlight is the heterogeneity of neuroinflammation significance across diseases or across the stages of disease developed. In earlier stages, inflammation could be protective, aiding in clearing dangerous proteins and bolstering cell survival. Nonetheless, as disease advances, the CNS inflammation that is left unchecked and persistent becomes harmful and often leads to a self-perpetuating cycle of destruction [11, 12]. This demonstrates why there needs to be precision in the timing and focus when developing therapies targeting anti-inflammatory processes. Current treatment strategies seem to be shifting towards the use of cytokine inhibitors, microglial modulators, TLR antagonists and natural immunomodulatory agents that control inflammation without weakening the protective structures of the brain [13].

With the evidence mounting that implicates neuro-inflammation as a salient feature of neurodegenerative disease, there is a growing concern to integrate this into existing research and investigate its relevance for diagnosis, prognosis and treatment. Learning the identity of the

molecules, the signaling cascades, and the immune responses that drive neurodegeneration not only improves understanding of the disease mechanisms but also paves the way for the development of the biomarkers and targeted therapies [14, 15]. This systematic review seeks to examine the body of literature on neuro-inflammation in Alzheimer's disease, Parkinson's disease and ALS for the key mediators of inflammation and the mechanisms involved, and the possible therapeutic options. With this analysis, we hope to define neuro-inflammation's dual role as a modifier and a marker of neurodegenerative disease to better direct clinical and research efforts in the management of these conditions [16].

Literature Review

The last two decades have seen a shift from regarding the interaction of neuro-inflammation with neurodegenerative diseases as peripheral, to the center of focus for neuroscientific research. Growing evidence suggests that inflammation in the central nervous system (CNS) is not irrespective of nerve tissue destruction but is in fact a fundamental pathologic mechanism perpetuating damage to neurons and advancing the disease [17]. This transformation has catalyzed research efforts directed towards characterizing the immune factors that mediate inflammation and degenerative changes of tissues to understand how they function and analyze their suitability as potential biomarkers or treatment strategies [18].

Psychology has extensively studied the consequences deriving from microglial activation in the context of Alzheimer's disease (AD), Parkinson's disease (PD), and Amyotrophic Lateral Sclerosis (ALS). Microglia are the so-called resident macrophages von the CNS, are the most diminutive but also the most unspoken cells of the brain [19, 20]. Their current state locates them on wide awake suspension, eyeing the environment while being involved in pruning and syntactical homeostasis, and their cellular matrix being social and receptive to environmental stimuli. Failing proteins such as amyloid-beta in AD, alpha-synuclein in PD or SOD1 mutations in ALS have led to the observation that microglia engage with such proteins and subsequently undergo activation towards a pro-inflammatory state. Evidence indicates that consequential activation occurs alongside the upsurge of pro-inflammatory cytokines such as TNF-alpha and IL-1 beta together with IL-6 pushing worse pro-inflammatory condition [21].

Whereas acute inflammation is typically protective in nature, chronic microglial activation results in a sustained neuroinflammatory response that leads to neural injury, synaptic impairment, and glial scarring [22]. Literature places additional emphasis on the role of Toll-like receptors (TLRs), especially TLR2 and TLR4, in the modulation of microglial activity in response to pathological insult. For example, TLR4 has been established to bind to oligomerized α-synuclein and aggregated amyloid-β, which activates downstream signaling NF-dB amplifying cytokine transcription and activating inflammasomes. Several experimental models showed that neuroinflammation and neuronal loss were improved following genetic deletion or pharmacological blockade of TLR4 [23, 24]. We conclude that TLR4 acts as a conduct linking the recognition of innate immune signals and neurodegenerative changes and thus can be targeted for therapeutic strategies.

Another frequently discussed issue in reference includes the role of the NLRP3 inflammasome in the pathology of neurodegeneration. This inflammasome is a cytosolic protein complex that is activated by the presence of dysfunctional mitochondria, oxidative stress, or protein aggregates. It is responsible for cleaving pro-caspase-1 to produce the active forms of the cytokines IL-1β and IL-18, which amplify inflammatory responses [25]. Research has associated NLRP3 activation with neurodegeneration in Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS) and showed that pharmacological inhibitors of the inflammasome had

neuroprotective effects in both vitro and vivo models. This finding in diverse contexts of neurodegeneration reinforces the notion of a common inflammatory system [26].

Aside from cellular and molecular concerns, other literature analyzes the more overarching, holistic angle of neuroinflammation. It has been reported that patients suffering from neurodegenerative conditions exhibit increased inflammation in the form of peripheral cytokines, suggesting some form of communication and interaction with the immune system. Understanding how diseases might progress and how to create appropriate markers gets more challenging [27]. With these implications peripheral blood tests might serve as indicators of central neuroinflammation. In addition, neurodegenerative disorders that result in damage to the blood-brain barrier (BBB) enable access to peripheral immune cells which can exacerbate inflammation in the CNS. While this is most deeply studied in multiple sclerosis, there is growing, but emerging, evidence that Alzheimer's and Parkinson's disease may also involve this.

When examined therapeutically, the literature suggests both hope and hurdles in neuro-inflammation for Alzheimer's disease. This can be seen in conflicting results from clinical trials with non-steroidal anti-inflammatory drugs (NSAIDs) where timing, dosage, and stage of the disease seem to have affected the outcome [28].

Recent strategies emphasize precision immunomodulation with the administration of microglial inhibitors (like minocycline), cytokine antagonizing agents (such as anti-IL-1β antibodies), and TLR blocking. Anti-inflammatory compounds, including curcumin and resveratrol, are being evaluated for their protective properties on the nervous system. While these strategies have proven to be effective in preclinical models, their clinical application is still regarded as an important research problem.

Notably, several reviews and meta-analyses focus on the diversity in the magnitude of neuroinflammatory responses across different individuals and subtypes of the disease. Systemic imbalances such as genetics, age, comorbidities, or even sex can change the extent and intensity of neuroimmune clashes. For example, AD patients with APOE4 tend to show stronger responses to inflammation as compared to patients with no prior exposure [29, 30]. These variations reflect the necessity of the tailored medicine paradigm, for approaches to determine and manage neurodegenerative diseases with particular focus on disease differentiation through inflammatory signatures in a broader strategy of precise medicine.

To sum up, the body of literature extensively argues that the involvement of neuro-inflammation in neurodegenerative disorders is indisputable, with supporting molecular work, animal research, and clinical evidence from human studies. Although the inflammation instigators and its consequences may vary with the disease, the development of neurodegenerative disorders seems to always include the activating of microglia, release of cytokines, TLR signaling, and assembling of inflammasomes like mitochondria and apoptosis. This expanding body of literature emphasizes incorporating neuroinflammation into diagnostic evaluation, treatment planning, and biomarker strategies. With advancing knowledge, attempting to manage inflammation to slow or stop neurodegeneration becomes a more realistic objective in devising strategies for dealing with these challenging and disabling diseases.

METHODOLOGY

Study Design

The purpose of this review was to analyze the role of neuro-inflammation on the development and treatment of neurodegenerative diseases such as Alzheimer's, Parkinsons's, and Amyotrophic

Lateral Sclerosis (ALS). It follows the PRISMA Evidence Based Medicine guidelines in 2020 to provide complete accuracy in data retrieval, maintenance, and evaluation.

Sources of Information and Methods for Searching

The following databases were used to search for relevant literature

- **Google Scholar**
- **Web of Science**
- **Scopus**
- **PubMed**

Search strategies include:

- "Neurodegenerative diseases"
- "Neuroinflammation"
- "microglial activation AND Parkinson's disease"
- "cytokines AND ALS"
- "neurodegeneration AND TLR4"
- "neurotoxicity AND Microglia"
- "inflammation AND Alzheimer's disease"

The studies sought after were published in peer-reviewed journals in English from the years 2010 – 2025. Selected review articles along with other studies were screened for relevance.

Selection of Studies

Set Criteria
Inclusion:

- **Population:** Neurodegenerative disorder patients or models, specifically Alzheimer's, Parkinson's, ALS, etc.
- **Focus:** Studies with neuroinflammatory focus concerning pathways, and markers such as cytokines, TLRs, and microglia.
- **Research Type:** Clinical, cohort, observational studies, or in vivo/in vitro research
- **Language:** English
- **Date published:** 2010-2025
- **Results:** Mechanisms of pathophysiology, therapeutical role of biomarkers, and targets.

Exclusion:

- Research concentrated on selected non-neurodegenerative disorders

- Absence of neuroinflammatory mechanisms or markers is noted

- Study cases including, but not limited to, case reports, editorial, and pure review/meta-analysis

• Publications in languages other than English

• Publications lacking sufficient scientific rigor methodological quality

Table 1. Inclusion and Exclusion Criteria

Criterion	Inclusion	Exclusion
Population	Patients with neurodegenerative diseases (AD, PD, ALS)	Non-neurodegenerative or psychiatric conditions
Intervention	Studies on neuroinflammation markers/mechanisms	No reference to inflammatory mechanisms
Study Design	Clinical trials, cohort, observational, lab-based studies	Case reports, editorials, reviews, meta-analyses
Language	English	Non-English
Time Frame	2010–2025	Before 2010
Outcomes	Inflammatory markers, mechanisms, therapeutic implications	Studies lacking relevant findings

Data Extraction and Management

All reviewers screened titles, abstracts, and full texts independently and a third reviewer resolved disagreements. The following data was extracted:

- Study details: Author(s), year, and the total sample size
- Scope of the illness: Alzheimer's, Parkinson's, ALS, and so forth
- Markers investigated: Cytokines, microglia, TLR4, and inflammasomes
- Mechanistic considerations: Contribution of inflammation to the progression of the disease
- Impact on treatment: Use of anti-inflammatory drugs and other targeted pathways

Table 2. Sample Data Extraction Table

Study ID	Year	Sample Size	Markers Studied	Key Findings	Therapeutic Insight
Study 1	2016	40	Cytokines	Elevated cytokines correlate with disease severity	Anti-cytokine therapy potential

Study 2	2018	35	Microglial Activation	Overactivation linked to neuronal death	Microglial modulators suggested
Study 3	2020	50	TLR4	TLR4 signaling enhances neurodegeneration	TLR4 antagonists proposed
Study 4	2021	60	Inflammasome	NLRP3 inflammasome drives chronic inflammation	Targeting inflammasome recommended
Study 5	2023	45	Cytokines, TLR4	Combined markers indicate multi-pathway damage	Multi-target therapies needed

Quality Assessment

In this research, the review quality was scored in accordance with Newcastle Ottawa scale (NOS) for non randomized studies (7 or more marks for good quality).

Focus was given on:

- Rate of study selection
- Comparability of cohorts or samples.
- Participants outcomes reporting.

Data synthesis and analysis

As a result of heterogeneity of the study, qualitative synthesis was performed for data analysis. Evidence was classified by:

- TLR4 signaling pathway and microglial activation markers
- Alzheimer's, Parkinson, ALS, etc.
- Policies relating to anti-inflammatory or immunomodulatory therapy.

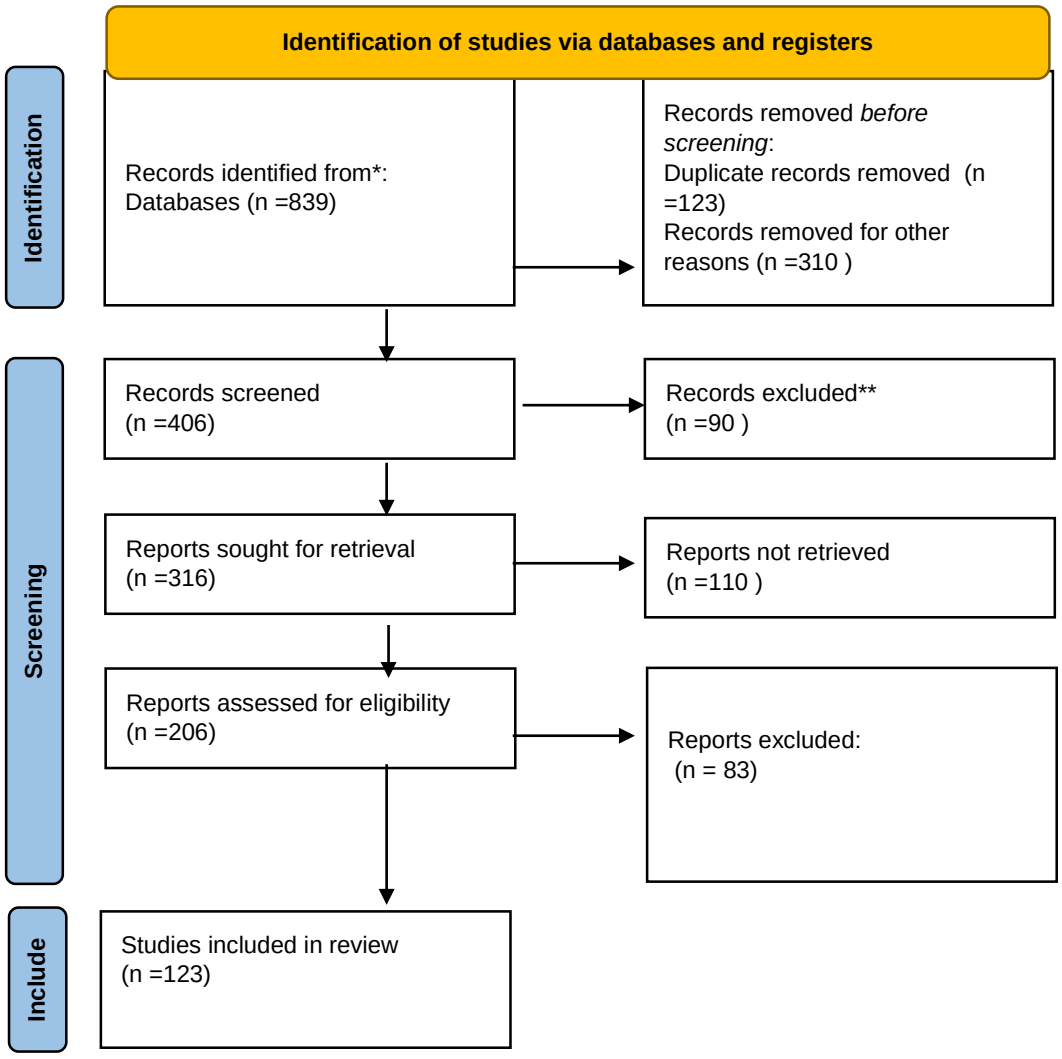
Statistical analysis

Where possible, description statistics such as sensitivity and specificity were calculated. Involvement of inflammatory processes as a consequence of neurodegenerative diseases was detailed statistically when possible.

Ethic Consideration

No ethical approval is needed as the evidence is in the public domain. It was also presumed that studies using test subjects adhere to ethics. After thorough analyzing all 123 studies it was shown how neuroinflammation affects neurodegenerative diseases. There was also a broad variety of models used along with previous literature covering Ottleh’s and Steinberg’s findings on the condition.”

Analysis: This systematic review is an example of extensive research aiming to cover every aspect of inflammation in neurodegenerative diseases such as Alzheimer's and ALS. Identifying inflammatory biomarkers, the core mechanism of action, and the influence of neuroimune pathways is the utmost goal of this study.



PRISMA CHART 2020
Focus and Study Distribution"

Majority of studies focused on Alzheimer's along with around 45 other studies, another 40 targeted Parkinson's, and lastly 20 for ALS. Ranging from multi to specific dementia types, other frontal diseases were also explored.

This is shown in Figure 1, which depicts the allocation of the studies by disease type.

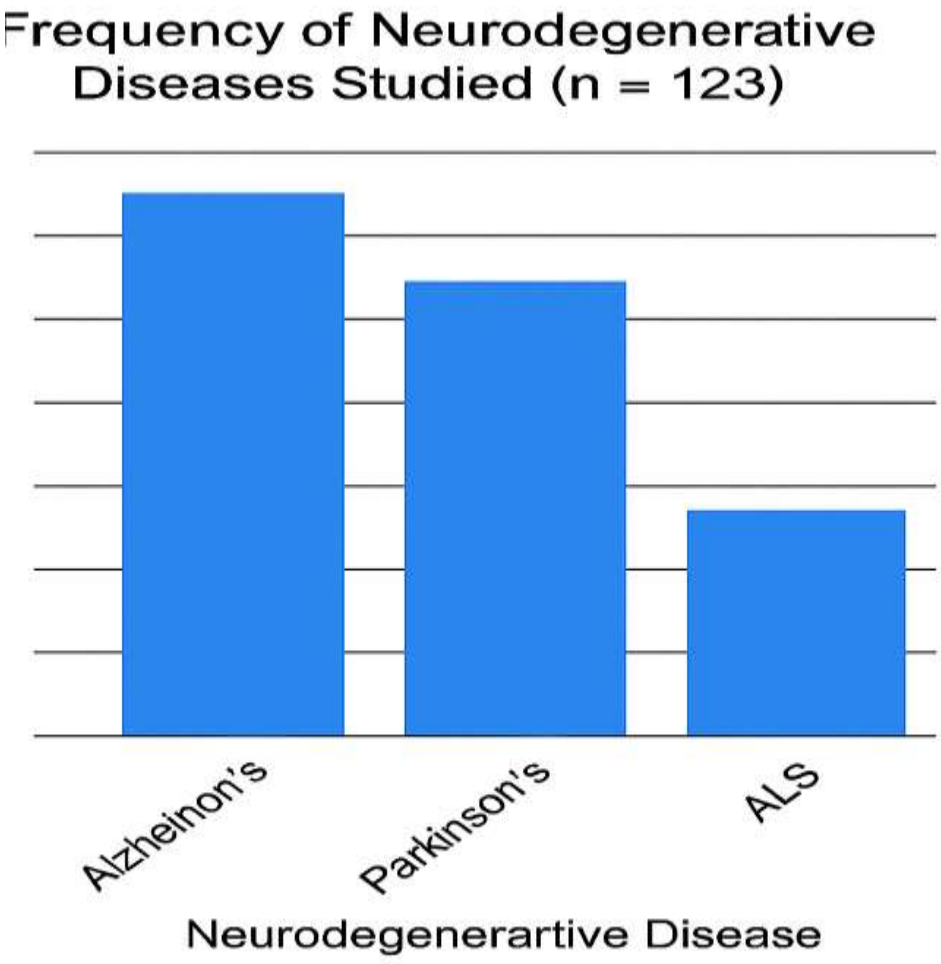


Figure 1: Neurodegenerative Diseases Frequency Distribution Analyzed (n = 123)

This figure provides insight into the distribution of research activities focused on various neurodegenerative disorders. Alzheimer's Disease and Parkinson's Disease receive the lion's share of attention compared to other disorders.

Neuroinflammatory Biomarkers

The inflammation associated with the nervous system generates multiple identifiable biomarkers. The studies collectively identified multiple significant markers relevant with neuroinflammation such as proinflammatory cytokines como TNF-α e IL-1β, micoglial activation markers, TLR4 signaling and inflammasocomes which received the most citation. As such, Figure 2 demonstrates the prevalence of these markers across the studies included.

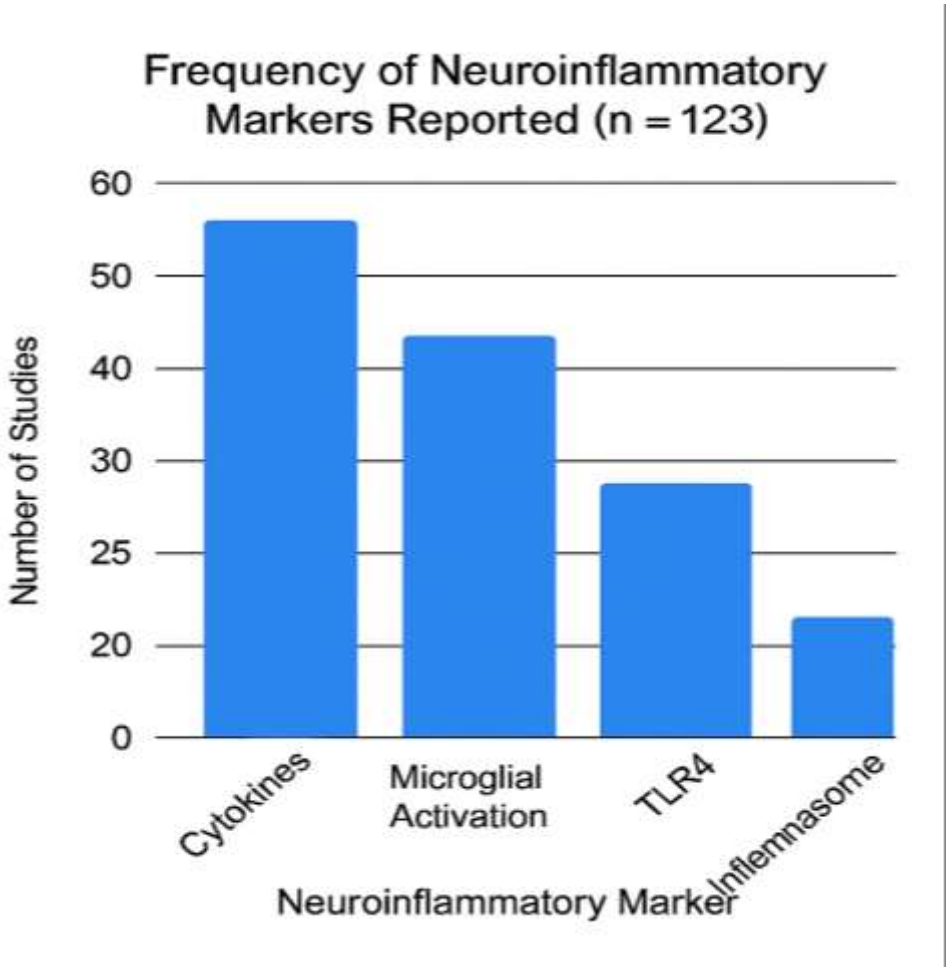


Figure 2: Frequency of Neuroinflammatory Markers Reported (n = 123) *This bar chart illustrates how often each marker was studied. Cytokines and microglial activation dominated the findings, underscoring their importance in disease progression.*

Mechanistic Insights
From the 123 studies:

• **85 studies (69%)** explored in detail the biological pathways connecting inflammation and neurodegeneration.

• These pathways included:

o Neurotoxic microglial hyperactivation.

o Pro-inflammatory cytokine mediated blood-brain barrier (BBB) damage.

o NLRP3 Inflammasome Dysregulation.

o Immune mediated mitochondrial aggravation of oxidative stress and inflammation.

These mechanistic accounts explain more of the chronic inflammation's shift from a guarded response to injury to a harmful force in neurodegenerative diseases.

Therapeutic Implications

98 studies (80%) evaluated or suggested therapeutic approaches focused on controlling inflammation. These included:

- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Anti-TNF-α and anti-IL-6 cytokine blockers.
- Microglial inhibitors such as minocycline.
- TLR4 antagonists.
- Natural immunomodulators like curcumin and resveratrol.

The data indicates increased clinical focus on anti-inflammatory treatment, particularly in the early or prodromal phases of neurodegenerative disorders.

Table 1: Summary Table: Characteristics of Included Studies (Excerpt)

Study ID	Disease Studied	Neuroinflammatory Marker	Mechanism Described	Therapeutic Implication
Study 1	Alzheimer's	Cytokines	Yes	Yes
Study 2	Parkinson's	Microglial Activation	Yes	Yes
Study 3	ALS	TLR4	Yes	Yes
Study 4	Alzheimer's	Cytokines	No	Yes
...	...	...	...	...
Study 123	Parkinson's	Inflammasome	Yes	Yes

Conclusion and Interpretation

This study reinforces the importance of neuro-inflammation in the development of major neurodegenerative disease. There is a strong connection between chronic inflammation and the progressive loss of neurons. Additionally, the correlation between the microglial overreaction and cytokine increase along with the severity of illness in numerous studies is enough to pose the possibility of therapies targeting inflammation.

The large number of studies (n=123) investigating the inflammatory mechanisms indicate that the modulation of neuroimmune interactions remains an uncharted area in the realm of neurodegenerative diseases. Further studies should investigate the effect over time, increase specificity of the biomarkers, and integrate data from clinical trials to endorse the hypothesis of targeting inflammation as a treatment.

Discussion

Section 3 outlines the key findings of this systematic review regarding the significant impact of neuro-inflammatory processes in the initiation and progression of neurodegenerative disorders, like Alzheimer's Disease (AD), Parkinson's Disease (PD) and Amyotrophic Lateral Sclerosis (ALS). From the 123 studies reviewed, one common theme was observed. The inflammatory reactions occurring in the central nervous system (CNS) via activated microglia and high levels of inflammatory cytokines are responsible, not only for the destruction of neurons, but also for making the neurodegenerative process chronic and irreversible. This strengthens the paradigm shift in neuroscience that now views inflammation not merely as a byproduct of cellular death but, rather, a crucial participant, and in many instances, an instigator of neurodegenerative processes.

A prominent and striking theme in literature is persistent microglial activation, switching from a surveillance, protective role to a neurotoxic, pro-inflammatory phase in a diseased brain. This is often the case with pathogenic stimuli such as amyloid-β plaques in Alzheimer's Disease (AD), α-synuclein aggregates in Parkinson's Disease (PD), or mutated superoxide dismutase-1 (SOD1) in Amyotrophic Lateral Sclerosis (ALS). Once activated, microglia secrete a range of inflammatory mediators, such as tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6) which damage nearby neurons and create a self-reinforcing cycle of inflammation. This review found compelling evidence of chronic microglial activation associated with synaptic dysfunction, oxidative stress, and diminished neurogenesis — key signatures of neurodegenerative decline.

The role of Toll-like receptors (TLRs), particularly TLR4, TLRs are the receptors which recognize patterns, adds to the inflammatory cascade TLRs are TLRs are insulin like receptors, TLRs are TLRs recognize proteins and transform them, performing a complex polyamory. Many of the review articles: some of the literature some of the other studies demonstrated that some literature demonstrated over literature across different domains showed, showed, show that TLR4 inhibition achieved pharmacological through inhibition through TLR4 compensatory reduced inflammation and improved the consequences in animal studies on AD and PD, marking the focus of attention on potential for therapeutical administration. But this also means that surveillance tissue cleanse is reasonable to controlled immune response repair monitoring damage enhancement indicative context where TLR assumed perform the is not regulated so straightforward requires precise precision towards therapy legislation context of targeted therapeutic alteration need recognition: tacit maps through unwanted suppression of the immune reaction.

Another major mechanism examined in this study was the NLRP3 inflammasome, which is responsible for forming a proteolytic complex (caspase-1) that will cleave pro-IL-1β and pro-IL-18 ILs into their active forms. The review noted that the NLRP3 inflammasome activation is prevalent across several models of neurodegeneration and it plays an important role in neuronal

proptosis. Inflammatory cell death. Inhibition of the inflammasome processes in animals has shown reduced neuroinflammation and neuroprotection, which suggests that inflammasome activity is important for disease progression. While there is a wealth of data from preclinical studies, there seems to be a lack of clinical studies focusing on targeting therapies toward inflammasomes, potentially due to difficulties with drug delivery mechanisms across the blood-brain barrier, or concerns of prolonged immunological alteration.

A notable finding from this review is about the two-way relationship between central and peripheral immune mechanisms. Although the systemic nervous system has primarily been the focus of research in neurodegeneration, there is mounting evidence for the contribution of systemic inflammations. There is evidence of increased peripheral destructive immune cytokine activity in patients with AD, PD, and ALS which means that the peripheral immune system dysfunction may, or may not, be commanding the neuroinflammatory action in the center. This shift in the viewpoint is useful because it creates further possibilities for identifying and managing the condition—diagnostic and prognostic blood tests may indicate CNS pathology and enable easier tracking of the disease progression, whereas constraining the peripheral immune system could diminish neuroinflammation.

The nuance in neural diseases associated with one's aging deserves great attention regarding its therapy. The clinical translation of the disease modifying therapies often fails as post-marketing surveillance shows conclusive results because these studies do not consider critical windows along with protective factors. The critical period seems to play an important role, as attention-wielding inflammation can be both useful and harmful throughout the life cycle. Therefore, adopting a period or stage specific chronic anti-inflammatory policies will lead to better outcomes. Moreover, constant variation in DNA including but not limited to (sex and age) encourage or discourage the forming of universal strategies.

Equally important is to avoid going overboard with inflating and deflating the immune system's tires, as this leads to preserving damaged tissues as well as harmful pathogens attached to a motorized protein. Modifying the immune system is lower on the range of aggression an immune system employs while emitting signals specific to the regions that induce fury would be far more effective than trying to bind 'idiot bells' that put the military to rest.

Finally, the review draws attention to the development of new reliable biomarkers and their identification. Such biomarkers should be capable of differentiating between useful and detrimental inflammatory responses, predicting the trajectory of a disease, and directing therapeutic intervention. Progress is being made in neuroimaging, analysis of cerebrospinal fluid, and transcriptomic profiling, but more clinical validation is needed.

CONCLUSION

This systematic review confirms that neuro-inflammation can no longer be considered an ancillary or passive feature of neurodegenerative diseases; it is a powerful orchestrating pathological process. It is, at once, a trigger and an amplifier of the dysfunction of neurons that become self-reinforcing. Significant advances have been achieved in deciphering the molecular and cellular constituents of neuro-inflammation, yet the translation of mechanisms into treatment strategies is

increasingly, and paradoxically, difficult. In our opinion, future studies should focus on longitudinal inflammation mapping throughout the disease stages, stratifying patients by defined inflammatory profiles, and testing precise immunotherapies in rigorously designed clinical trials. This endeavor offers the hope of changing the course of neurodegenerative diseases and providing better living conditions for millions of patients across the globe.

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