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REVIEW OPEN ACCESS

Temporal and Spatial Dynamics of Enteric Glial Cell Involvement in Parkinson's Disease: A Literature Review

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Abstract

Introduction: Enteric glial cells (EGCs) are critical regulators of gastrointestinal (GI) homeostasis and are implicated in early Parkinson's disease (PD) pathogenesis. Disruption of EGCs can trigger gut inflammation and propagation of pathological α-synuclein (α-syn) to the central nervous system (CNS). Investigating both the temporal dynamics of EGC activity across stages and spatial differences among gut regions is essential to identify when and where their shift from protective to pathological roles occurs. This review addresses these dynamics to understand PD progression better and propose EGC-targeted strategies.

Methods: A systematic search in May 2025 of PubMed and Google Scholar (Jan 2012–Apr 2025) yielded 842 articles. Prioritizing primary research on enteric glial cells in Parkinson's disease and excluding reviews or unrelated studies, 26 articles ultimately met the inclusion criteria for this review.

Results: Regarding temporal dynamics, animal models demonstrate that EGC activation and inflammation emerge in the prodromal phase, preceding motor deficits. Subacute toxin models exhibit variable glial stress responses, whereas chronic and protopathic models illustrate neurochemical remodeling and the potential spread of pathology from the ENS to the CNS. Spatially, animal studies indicate region-specific vulnerability: the gastric myenteric plexus exhibits early α-syn accumulation; the distal ileum and proximal colon display oxidative stress and neurotransmitter imbalances; and the sigmoid colon shows TRL4-mediated inflammation. In parallel, human clinical findings corroborate distinct regional alterations, particularly in the duodenum, characterized by reactive gliosis and α-syn aggregates, and the ascending colon, where elevated pro-inflammatory cytokines correlated with increased expression of reactive glial marker GFAP and the developmental marker Sox-10.

Discussion: The results support the hypothesis of PD pathology originating in the gut, with EGCs playing a critical role. Understanding these dynamics could help develop region-specific, EGC-based biomarkers for early diagnosis in the prodromal phase and guide targeted interventions. Future research should incorporate longitudinal tracking of EGC activity, single-cell multi-omics, and targeted interventions in PD models to establish causality.

Conclusion: EGCs respond to early gut dysfunction and influence subsequent PD progression. Their time and region-specific activation may explain not only GI symptoms but also PD pathology, suggesting possible biomarkers or treatment targets.

Keywords: Parkinson's disease; enteric glial cells; gut-brain axis; α-synuclein; enteric nervous system; gastrointestinal dysfunction; neuroinflammation

Introduction

Parkinson's disease (PD) is experienced by 1% of the population over the age of 60 worldwide [1]. PD is a progressive neurodegenerative disorder characterized by motor impairments and non-motor symptoms. Its hallmark features are loss of dopamine (DA) neurons and the aggregation of α-synuclein (α-syn) protein in the substantia nigra (SN) of the central nervous system (CNS) [2]. Non-motor gastrointestinal (GI) symptoms, such as chronic constipation, often precede motor and cognitive symptoms by many years and affect 60~80% of PD patients, only to significantly diminish quality of life [3, 4]. This temporal pattern aligns with Braak's hypothesis in that PD pathology may originate in the gut and that the pathological form of α-syn transmits to the brain via the vagus nerve [5, 6]. Recent studies claim that pathological changes within the enteric nervous system (ENS) may also play a pivotal role in the early stages of PD pathogenesis via the gut-brain axis [7, 8].

Enteric glial cells (EGCs) are a type of neuroglial cell critical to maintaining GI physiology in the ENS. EGCs are widely spread across various GI organs, such as the duodenum, ileum, and various regions of the colon (Figure 1) [9]. They are also distributed throughout all layers of the GI tract, including the mucosal, submucosal/myenteric plexus,

and muscular layers (Figure 2). EGCs are critical mediators of the gut-brain axis, influencing gut inflammation, epithelial barrier integrity, and neuronal survival while supporting enteric neurons. Disrupted EGCs impair gut homeostasis, contributing to inflammatory bowel disease (IBD) and neuroinflammation [10].

PD is generally conceptualized in three stages: a preclinical phase (only pathological changes occur); a prodromal phase (early stage; only non-motor symptoms); and a clinical phase (onset of motor impairments accompanied by PD pathology) [11]. Since enteric glial activity, GI dysfunction, and inflammation have been observed during the prodromal phase, understanding the role of EGCs in PD is vital [12]. However, this review synthesizes evidence for prodromal (early) and clinical phases (subacute and chronic) of PD.

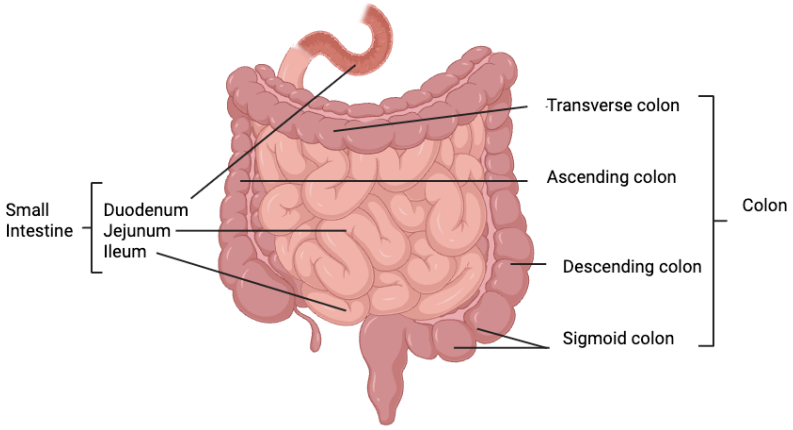

Figure 1. Anatomical regions of the GI tract in the ENS examined in this study. *Created with BioRender.com.*

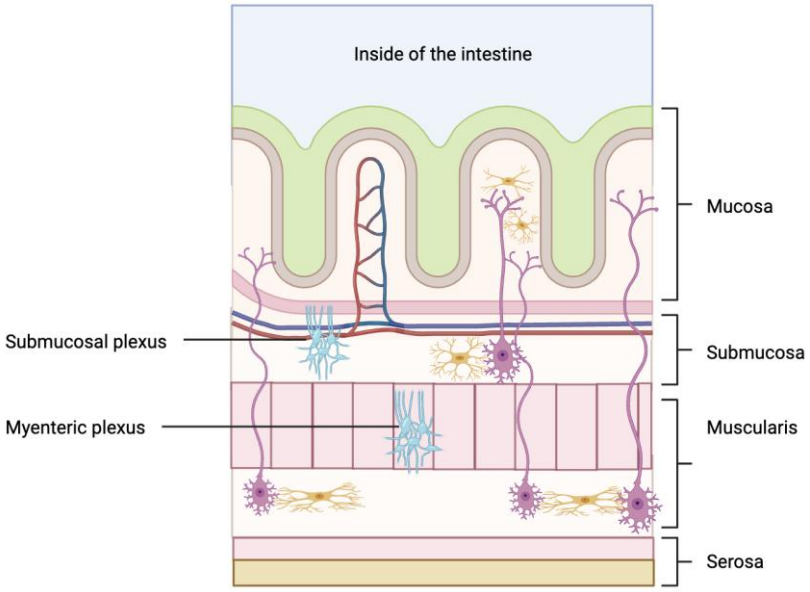

Figure 2. Tissue layers of the GI tract in the enteric nervous system. EGCs are shown in yellow, neurons in purple, and the neural plexuses—both submucosal and myenteric—in blue. These layers and cellular structures work together to regulate GI functions such as motility, secretion, and local reflexes. *Created with BioRender.com.*

Although research on the role of EGCs in PD has evolved, few reviews have comprehensively addressed the temporal dynamics (i.e., how EGC activity changes over time) and spatial dynamics (i.e., how EGC activity varies in different gut regions). This study synthesizes current findings on the temporal and spatial dynamics of EGCs in PD, with two primary objectives: 1) To provide an integrated view of EGC involvement in PD across different stages and gut regions/layers and 2) To identify gaps in current knowledge and propose potential EGC-targeted therapeutic interventions. Special attention is given to EGC reactivity across disease stages and gut regions to address the following key questions: How do EGCs transition from protective to pathological roles as

PD progresses, and what regional gut differences exist in their involvement? By integrating published data from humans, animals, and in vitro results, we propose novel EGC-based strategies to intervene in PD progression and provide future research directions.

Methods

A systematic literature search was conducted in May 2025 using the PubMed and Google Scholar databases. The search was restricted to peer-reviewed articles published in English between January 1, 2012, and April 30, 2025. The search strategy combined key concepts using Boolean operators (AND/OR). The primary search string used was: (("Parkinson's Disease" OR "PD") AND ("enteric glial cells" OR "EGCs" OR "enteric glia")) AND ("gut-brain axis" OR "alpha-synuclein" OR "enteric nervous system" OR "gastrointestinal"). The initial search yielded 842 entries and, after various eligibility screenings, 24 were ultimately used for this literature review. The remaining 2 citations are for the image reference and website. The detailed selection process, from identification to inclusion, is illustrated in the PRISMA flow diagram (Figure 3).

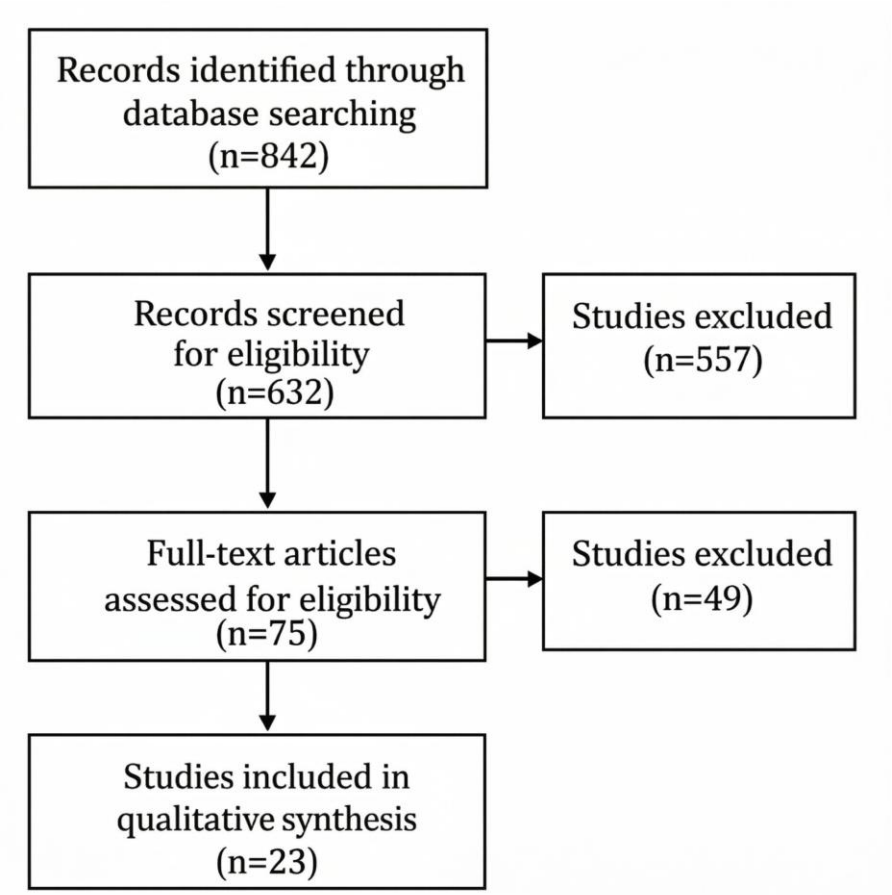

Figure 3. PRISMA flow diagram illustrating the literature search and selection process. *Created with Microsoft PowerPoint.*

Results

Temporal Dynamics of EGC Activation in PD

Animal models consistently suggest that EGCs exhibit dynamic and time-specific responses over the course of PD pathogenesis [12]. In fact, early EGC activation and gut inflammation often appear before the onset of motor symptoms or central nervous system (CNS) pathological markers. Together, these findings highlight that EGC responses evolve across PD stages to influence gut dysfunction and gut-to-brain symptom propagation.

To clearly illustrate the temporal patterns of EGC activation, findings are organized into the prodromal/early phase, clinical/symptomatic phase, which includes subacute toxin models, and chronic progression models.

Due to the difficulties of examining the temporal changes of EGCs in humans, this section primarily reviews findings only from murine models. A summary of key pathological features and temporal dynamics of EGC activation across PD phases is provided in Table 1 for better understanding.

Table 1. Summary of primary research results for temporal dynamics of EGC activation across PD phases.

PD Phases	Key Pathological Features	Model / Subjects
Prodromal (Early) Phase	- Non-motor symptoms (e.g., constipation) - Early EGC activation (↓ S100β$^+$ and Sox-10$^+$ EGCs; ↑ GFAP expression) - Colonic inflammation (↑ IL-1β, TNF)	A53T α-syn transgenic mice – ENS pathology by ~12 weeks before motor onset
Clinical Phase – Early *(Subacute Response)*	- Rapid EGC stress response (↑ ROS, ↑ 4-HNE) within hours (MPTP) - α-syn aggregates in GFAP$^+$ EGCs - Delayed EGC reactivity with slower toxin (rotenone) at ~6 weeks	MPTP/probenecid model – acute toxin Rotenone model – slower-acting toxin
Clinical Phase – Established *(Chronic Progression)*	- Established CNS DA neuron loss - Enteric neurochemical shifts (↑ VIP, ↓ nNOS, ↓ D2R) - Slowed colonic transit - Structural and functional changes in EGCs	6-OHDA lesion model – ~4 weeks post-lesion

Prodromal (Early) Phase: EGC Activation Precedes CNS Pathology

In mouse models of early PD, enteric gliosis (defined as the activation and proliferation of EGCs) and subsequent colonic inflammation precede detectable CNS involvement [13]. Transgenic mice overexpressing human mutant α-syn (A53T, an alanine-to-threonine substitution at residue 53 of α-syn) showed a significantly reduced population of specialized EGCs in both the ileum and colon as early as 12 weeks of age. This is well before the onset of motor deficits, which only emerged at 36 weeks.

In these A53T mice, there was an early reduction in the number of S100-β positive glial cells at 12 weeks compared to wild type (WT) mice. S100-β serves as a calcium-binding protein that regulates intracellular calcium levels and provides essential neurotrophic support to enteric neurons. Similarly, significantly fewer developmental marker SRY-box transcription factor 10 (Sox-10)-positive glial cells were observed at 12 weeks in the colon. Sox-10 is a transcription factor that maintains the multipotent state of EGCs, enabling them to support tissue repair. This specific reduction of Sox-10-positive cells reflects the early vulnerability of the ENS to α-syn pathology.

Clinical Phase (Subacute Toxin Models)

In subacute toxin models, the temporal pattern of EGC activation varies significantly depending on the specific toxin and exposure period. In a chronic MPTP/probenecid mouse model, aggregated and nitrated α-syn, an oxidative stress-modified form, accumulates in glial fibrillary acidic protein (GFAP) EGCs of the gastric myenteric plexus [14]. Notably, even a single MPTP dose induces a change in glial stress response; within 3 hours, it causes a rapid burst of reactive oxygen species (ROS) and increased 4-hydroxynonenal (4-HNE; a lipid peroxidation marker) in gastric glia.

In contrast, the slower-acting toxin rotenone produces a more delayed glial response [14, 15]. Mice treated with rotenone did not show increased GFAP expression in the colon until around 6 weeks of exposure. No significant changes were observed at earlier time points (1-3 weeks) [16]. These differences suggest distinct temporal phases of EGC activation depending on the nature and duration of the insult.

Clinical Phase (Chronic Toxin Models)

Chronic PD models highlight how damage to the CNS directly triggers major neurochemical changes and glial reactivity in the ENS. In rat models of chronic PD using 6-hydroxydopamine (6-OHDA)-induced nigrostriatal lesions, significant enteric alterations were observed [17]. Around 4 weeks post-lesion, rats exhibit marked neurochemical shifts in the distal ileum and proximal colon. These include increased vasoactive intestinal peptide (VIP) and decreased inhibitory neuronal nitric oxide synthase (nNOS) expression in the myenteric plexus. These changes correlate with reduced dopamine D2 receptor expression and slower colonic transit, contributing to the severe constipation observed [17]. Alterations in EGC activity have also been reported in these affected regions, suggesting a link between central dopaminergic injury and downstream enteric glial remodeling.

Spatial Dynamics of EGC Involvement in PD

EGC changes in PD also vary across GI regions (Figure 1) and tissue layers (Figure 2), revealing spatially distinct vulnerabilities. For clarity, the pathological changes of EGCs across the stomach, small intestine, and colon are highlighted below. An overview of the key pathological features based on different gut regions and layers, and their implications for PD pathogenesis, is provided in Table 2.

Table 2. Summary of regional and layer-specific EGC pathology in the GI tract and its implications for PD.

Gut Region & Layer	Key Pathological Features	Model / Subjects	Implications for PD Pathogenesis
Gastric Myenteric Plexus (stomach)	Early accumulation of aggregated, phosphorylated (p-syn), and nitrated (n-syn) α-syn in EGCs	MPTP/probenecid-treated mice	Stomach may act as an initial site for early α-syn pathology; region-specific targeting could prevent gut-to-brain spread
Small Intestine			
– **Duodenum (mucosa/submucosa)**	Aggregated α-syn co-localized with neurons; ↑ GFAP+ EGC density & size (reactive gliosis).	Human PD patients (early & advanced).	Persistent gliosis may sustain inflammation independent of PD stage
Colon			
– Ascending Colon (mucosa/muscular)	↑ GFAP & TNF-α before CNS injury • Mild inflammation and reduced fecal water content by week 1; Early protective upregulation of occludin & GDNF that declines by week 2 (loss of protection)	6-OHDA PD mouse model	Shows early EGC activation shifting from protective to pro-inflammatory state; supports early colon involvement in PD
– Ascending Colon (mucosa)	Elevated TNF-α, IFN-γ, IL-6, IL-1β mRNA • ↑ GFAP & Sox-10; unchanged S100β • Strong correlation between cytokine elevation and glial dysregulation	Human colonic biopsies from PD patients	Indicates IBD-like inflammation and EGC dysregulation in PD colon
– **Sigmoid Colon (myenteric plexus)**	↑GFAP+ EGC activation; barrier disruption; ↑inflammatory markers; TLR4-dependent inflammatory signaling	Rotenone-induced PD mice.	Key site for inflammation/barrier breakdown; potential target for localized anti-inflammatory therapy; highlights TLR4-dependent glial activation

Stomach: Gastric Myenteric Plexus

Animal Evidence:

In toxin-induced animal models, the gastric myenteric plexus is identified as a highly vulnerable region where EGCs exhibit pathological α-syn accumulation at the early stage of disease. MPTP/probenecid-treated mice, which showed induced α-syn levels in the SN, also exhibited early accumulation of aggregated phosphorylated (p-syn) and nitrated (n-syn) α-syn in EGCs of the gastric myenteric plexus [14, 18].

Small Intestine

Duodenum

Human Evidence:

Human biopsy studies reveal that the duodenum is a prominent site of pathology, characterized by significant EGC activation and α-syn aggregation in both mucosal and submucosal layers [19]. These duodenal wall biopsies were analyzed from patients with advanced PD. IHC analysis (Immunohistochemistry) showed that aggregated α-syn was present in the duodenal mucosa and submucosa of all PD patients, including those in early disease stages. (IHC is a technique that uses antibodies to visualize specific proteins in tissue.) These α-syn aggregates were specifically localized to neuronal structures.

In the duodenal mucosa and submucosa, there was also a significant increase in both the density and size of GFAP+ EGCs, indicating prominent reactive gliosis [19]. This persistent glial activation suggests a sustained inflammatory microenvironment in the duodenum that may contribute to PD-related gut dysfunction even before pronounced motor decline.

Colon

Ascending Colon: Cytokine Elevation and Glial Dysregulation

Animal Evidence:

EGCs in the colon mucosa demonstrate a clear change over time, initially protecting and transitioning into a state of promoting inflammation and gut movement problems. In the 6-OHDA mouse model of PD, GFAP and the pro-inflammatory cytokine TNF-α increase in both the mucosal and muscular layers of the colon before CNS injury [12]. One week later, mice show mild colonic inflammation, reduced fecal water content (indicating intestinal dysmotility), and increased glial activation. Protective responses included upregulation of tight junction protein occludin and glial cell line-derived neurotropic factor (GDNF) but declined by week two [12]. The decline of the initial protective factors (occludin, GDNF) by week two,

despite the early glial activation, shows the transition from protective to a pro-inflammatory state.

Human Evidence:

Collectively, human data suggest a clear association between colonic inflammatory activation and enteric glial dysregulation in PD. In human studies focused on the colon, PD patients showed significantly increased mRNA levels of pro-inflammatory cytokines in the ascending colon compared to healthy controls. These cytokines included TNF-α, IFN-γ, IL-6, and IL-1β. This finding reflects an inflammation similar to that seen in IBD [16, 20]. Alongside this heightened inflammation, expression of the glial markers GFAP and developmental glial marker Sox-10 was also significantly elevated in colonic biopsies from PD patients. In contrast, S100-β expression remained unchanged [20]. The changes in GFAP and Sox-10 expression correlated strongly with the increased cytokine levels, suggesting that EGCs become activated or dysregulated as a response to local inflammation.

Sigmoid Colon: Barrier Disruption and Inflammatory Signaling

Animal Evidence:

In rotenone-induced PD mouse models, increased GFAP+ EGCs are observed in the myenteric plexus. This response is dependent on TLR4-mediated pro-inflammatory signaling. (TLR4 signaling is a key pathway that recognizes pathogens and triggers inflammation.) In terms of regions, the sigmoid colon shows the most changes, including compromised intestinal barrier integrity and elevated inflammatory markers [11]. This evidence suggests that EGC activation and gut inflammation are concentrated in the colon during early PD. This highlights the colon as a key site of vulnerability and potential intervention.

Discussion

PD is a progressive neurodegenerative disorder marked by chronic motor impairment from DA neuron loss [2]. However, many PD patients experience GI symptoms that often precede motor impairments by years and are related to early dysfunction in the ENS [3, 4]. EGCs have emerged as key mediators in maintaining gut homeostasis and regulating the gut-brain axis [5, 6]. Growing evidence from both human and animal studies suggests that early glial and neuronal changes in the gut may contribute to PD pathogenesis [7, 8]. To summarize the findings: In murine models, reactive gliosis often precedes motor symptoms, indicating a clear temporal progression. Similarly, human studies found that pathological alterations of enteric glia span the entire GI tract. These cells are distributed throughout all tissue layers—from the mucosa to the muscularis—and exhibit diverse, region-specific functions that are increasingly implicated in the pathology [9].

The temporal dynamics of EGC involvement in PD are significant for understanding disease progression and identifying potential therapeutic interventions. Increasingly, EGCs are recognized as active modulators in both the initiation and propagation of PD pathology. In the prodromal phase, EGC activation before detecting CNS involvement is evident. This temporal relationship suggests that EGCs function as early indicators, initiating inflammatory and immune responses that accelerate the progression of PD. Notably, these glial changes are confined to the gut at this stage, preceding any CNS pathology. In the prodromal (early) phase, a study from A53T mice proposed that the loss of EGCs disrupts the coordination of gut motility and removes essential neuroprotective support, leading to neuronal oxidative stress and functional impairment. Experimental toxin-induced models reveal that EGC responses vary by stimulus. MPTP rapidly induces oxidative stress and glial activation, whereas chronic exposures, such as rotenone, elicit slower and less pronounced responses [14]. This suggests that EGC activity is context-dependent, potentially neuroprotective or pathogenic. In chronic models, neurochemical alterations in enteric neurons and glia accompany DA neuron degeneration in the CNS, showing a reverse influence along the gut–brain axis in which CNS pathology impacts peripheral tissues. Similarly, chronic CNS injury modulates gut glial activation, supporting a bidirectional interplay between CNS and ENS pathology [5, 12]. Gut-to-brain transmission models further implicate EGCs in the α-syn propagation from the intestinal wall to the CNS [19]. These studies support the hypothesis that PD pathology may originate in the gut, with EGCs helping transmit or amplify pathological signals along the gut–brain axis.

Across different gut regions, EGC activation occurs with α-syn aggregation, inflammatory signaling, and neurochemical disturbances; however, the patterns are not uniform. In the gastric myenteric plexus, early aggregated α-syn appears in proximity to vagal nerve terminals, suggesting an initial defensive mechanism against pathogenic signals, which may potentially initiate gut-to-brain propagation [14]. In the duodenum, persistent glial activation and GFAP upregulation create a pro-inflammatory environment. At the same time, oxidative stress in the distal ileum and proximal colon correlates with early constipation via disrupted VIP and nNOS signaling [17]. Further complexity is seen in the colon: the sigmoid region shows TLR4-mediated barrier dysfunction, while the ascending colon mirrors IBD-like inflammation [16, 20].

However, despite accumulating evidence supporting the involvement of EGCs in PD pathogenesis, several key limitations remain, which future studies should address.

First, the causal relationship between EGC activation and PD progression remains unclear; it is unknown whether EGC reactivity is a driver of pathology or merely a secondary response to α-syn aggregation. Establishing causality requires future EGC-targeted manipulation in PD mouse models using techniques such as conditional

knockouts or genetic modulation of engineered proteins to determine whether glial alterations exacerbate or attenuate pathology.

Second, our understanding is limited by studies relying on single-time-point observations or samples from advanced-stage PD patients, which obscures early glial changes. To overcome this, future studies must incorporate longitudinal experimental designs, such as using reporter mice (e.g., GFAP, Sox-10) for real-time tracking of EGC activation across PD stages.

Third, the molecular mechanisms behind the switch from protective to pathological EGC phenotypes are poorly defined. To clarify these mechanisms, single-cell transcriptomic and proteomic analyses of human GI biopsies across different gut regions and disease stages are crucial. This approach would help identify early-stage biomarkers and distinguish between functionally distinct EGC subtypes.

Finally, the upstream signaling events and environmental triggers (e.g., microbiota, diet, or toxins) that directly influence EGC behavior are not well understood. Therefore, the role of microbiota-EGC-immune crosstalk needs further investigation, as gut microbial metabolites may directly influence enteric glial phenotypes and inflammatory responses.

Understanding the timing, location, and molecular context of EGC involvement in PD is crucial for redefining the gut-brain axis as a targetable component of PD pathophysiology. Overcoming current limitations may uncover novel diagnostic biomarkers and therapeutic strategies that exploit the glial compartment of the ENS, enabling intervention before irreversible neurodegeneration occurs. Current therapeutic strategies for PD-related gut dysfunction, such as Guanylate cyclase C (GCC) agonists and 5-Hydroxytryptamine 4 (5-HT4) receptor agonists, which are known to increase intestinal fluid secretion, demonstrate limited efficacy [3]. Given that most patients are diagnosed with PD in the clinical (mid/late) phase, considering the temporal dynamics of PD is noteworthy [21]. Early biomarkers in the gut may serve as a predictive tool to detect PD-related changes before the onset of motor symptoms. In the prodromal phase, EGC activation markers, including increased GFAP expression, decreased S100β, and elevated pro-inflammatory cytokines (IL-1β, TNF) in colonic or duodenal biopsies, could be potential indicators [14, 20]. Additionally, 4-HNE accumulation may serve as a biomarker of early oxidative stress in gastric EGCs [14]. Targeting the receptor-mediated pathways could address the upstream regulation and target EGCs and DA neurons. In addition, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) such as liraglutide and exenatide have demonstrated efficacy in reducing both EGC and microglial inflammation, while simultaneously improving gut motility and DA neuron survival [22, 23].

Altogether, these findings indicate that EGCs respond to PD-related insults at very early stages, even before CNS involvement. Initially, EGCs may serve a protective role by transiently upregulating occludin and GDNF [12]. However, with ongoing α-synucleinopathy and chronic stress, EGCs can shift into a reactive and pro-inflammatory state that may contribute to further neurodegeneration and gut-brain axis disruption. These dynamic, phase-specific changes in EGC behavior underscore their potential role as both early biomarkers and modulators of disease progression in PD. The sigmoid colon shows robust EGC activation linked to barrier dysfunction and TLR4-mediated inflammatory signaling, which may facilitate the peripheral spread of pathogenic α-syn [16]. The ascending colon displays two-phase glial responses—initially protective, later pathogenic—suggesting an early intervention window. Widespread upregulation of pro-inflammatory cytokines and glial markers in colonic mucosa mirrors patterns seen in IBD, implying shared mechanisms of chronic inflammation [20]. Collectively, these findings underscore the enteric contribution to PD, suggesting that regional EGC dysfunction may trigger or amplify PD pathology.

Conclusions

Emerging evidence suggests that EGCs play an active role in PD pathogenesis, particularly in the early prodromal stage [7, 8]. EGCs in different layers and regions of the gut are activated at various time points, which may help explain why most PD patients initially experience GI symptoms. This review suggests that EGCs may act not only as early responders to gut dysfunction and α-syn aggregation but also as active modulators of PD progression. Their transition from protective to pro-inflammatory suggests that EGCs may serve as both biomarkers and therapeutic targets. However, whether EGC activation causes PD or merely responds to it, the underlying molecular mechanism of EGC remains unclear. In the long term, time and region-specific studies may clarify the precise role of EGCs in PD pathogenesis.

List of Abbreviations

4-HNE: 4-hydroxynonenal
5-HT4: 5-hydroxytryptamine 4
6-OHDA: 6-hydroxydopamine
α-syn: alpha-synuclein
CNS: central nervous system
DA: dopamine
EGC: enteric glial cell
ENS: enteric nervous system
GCC: guanylate cyclase C
GDNF: glial cell line-derived neurotropic factor
GFAP: glial fibrillary acidic protein
GI: gastrointestinal tract
GLP-1 RAs: glucagon-like peptide-1 receptor agonists
IBD: inflammatory bowel disease

IFN-γ: interferon gamma
IHC: immunohistochemistry
IL-1β: interleukin 1 beta
IL-6: interleukin-6
MPTP: 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
nNOS: nitric oxide synthase
PD: Parkinson's disease
ROS: reactive oxygen species
SN: substantia nigra
Sox-10: SRY-box transcription factor 10
TLR4: Toll-like receptor 4
TNF-α: tumor necrosis factor alpha
VIP: vasoactive intestinal peptide

Conflicts of Interest
The authors declare that they have no conflicts of interest.

Ethics Approval and/or Participant Consent
This review did not require ethics approval and/or participant consent because this is a literature review where experiments of animal or human were not conducted.

Authors' Contributions
SK: made substantial contributions by performing literature search, contributed to the analysis and interpretation of the selected literature, drafted the initial manuscript, critically revised the manuscript, created the figures, and gave final approval of the version to be published.
JP: contributed to the analysis and interpretation of the selected literature, drafted the initial manuscript, critically revised the manuscript, and gave final approval of the version to be published.

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