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THE USE OF STEM CELLS IN THE TREATMENT OF NEURODEGENERATIVE DISEASES - CURRENT STATE OF RESEARCH AND CLINICAL PERSPECTIVES

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ABSTRACT

Introduction and aim: Neurodegenerative diseases, including Alzheimer's, Parkinson's, multiple sclerosis and amyotrophic lateral sclerosis, remain highly challenging due to their progressive course and lack of disease-modifying therapies. Stem cell-based strategies are increasingly investigated for their potential in neuroregeneration, immunomodulation and functional recovery. This study aims to summarize current evidence on stem cell applications in neurodegenerative diseases based on recent systematic reviews and meta-analyses.
Material and methods: A structured literature search was performed in PubMed, Medline and Google Scholar using the terms "stem cells," "neurodegenerative diseases," "clinical trials," "systematic review," and "meta-analysis." Eligible publications included English-language systematic reviews and human studies from 2015–2025. Over 30 relevant sources were analyzed by disease type and stem cell modality.
Results: Most studies report a favorable safety profile, particularly with mesenchymal (MSC), neural (NSC) and induced pluripotent stem cells (iPSC). Clinical trials in Parkinson's disease demonstrated measurable motor improvements, while applications in multiple sclerosis and spinal cord injuries showed immunomodulatory and functional benefits. Evidence in Alzheimer's disease and ALS remains limited and preliminary. Across conditions, heterogeneity of methods and small sample sizes reduce generalizability.
Conclusions: Stem cell therapy shows promise as an innovative approach in neurodegenerative disorders, though it remains experimental. Encouraging early outcomes highlight the need for large-scale, standardized and long-term trials to confirm efficacy, optimize protocols and ensure safety. Stem cells may become central to neuroregenerative medicine, but they are not yet ready for routine clinical use.

KEYWORDS

Stem Cells, Neurodegenerative Diseases, Clinical Trials, Neuroregeneration, Systematic Review, Mesenchymal Stem Cells

CITATION

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1. Introduction

Neurodegenerative diseases represent a group of chronic, progressive conditions characterized by the selective loss of structure or function of neurons. Among the most common are Alzheimer's disease (AD), Parkinson's disease (PD), multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS) and Huntington's disease (HD). These disorders are associated with substantial morbidity, impaired quality of life and significant socioeconomic burden. Despite advances in symptomatic treatment, there remains a critical lack of disease-modifying therapies that can halt or reverse the underlying neuronal degeneration.

Over the past two decades, stem cell-based therapies have gained considerable attention as a potential strategy to address the limitations of conventional treatments. Stem cells, defined by their self-renewal capacity and ability to differentiate into specialized cell types, offer hope for restoring damaged neural tissues, modulating immune responses and promoting endogenous repair mechanisms. Various types of stem cells—including mesenchymal stem cells (MSCs), neural stem cells (NSCs), embryonic stem cells (ESCs), and induced pluripotent stem cells (iPSCs)—have been investigated in preclinical and clinical settings for their regenerative potential in neurodegenerative conditions.

Emerging evidence from systematic reviews and meta-analyses suggests that some stem cell modalities may offer therapeutic benefits in select neurodegenerative diseases, particularly in PD and MS. However, the clinical application of these therapies remains at an early stage, with challenges related to standardization, long-term safety, ethical considerations and regulatory approval.

The aim of this review is to synthesize the current evidence on the use of stem cell therapies in the treatment of neurodegenerative diseases, focusing on the latest high-quality meta-analyses and systematic reviews. We present findings across major disease categories, evaluate the effectiveness and safety of various stem cell types, and discuss current clinical perspectives and future research directions.

2. Methodology

This review is based on a structured search of the scientific literature, focusing on systematic reviews and meta-analyses addressing the use of stem cell therapy in neurodegenerative diseases. The search was conducted between June and July 2025 in the PubMed, Medline, and Google Scholar databases using a combination of the following keywords:”stem cells”, ”neurodegenerative diseases”, ”Parkinson’s disease”, ”Alzheimer’s disease”, ”multiple sclerosis”, ”clinical trials”, ”systematic review”, ”meta-analysis”.

The inclusion criteria were:

- Articles published between **2015 and 2025**
- **Systematic reviews and/or meta-analyses** involving human subjects
- Studies published in **English**
- Reviews focused on one or more neurodegenerative diseases
- Availability of full-text articles

Exclusion criteria included:

- Studies involving only animal or in vitro models
- Narrative reviews, expert opinions, or editorials without systematic methodology
- Duplicate or outdated reviews superseded by more recent analyses

Articles were categorized according to the specific neurodegenerative condition addressed (e.g., Parkinson’s disease, Alzheimer’s disease, multiple sclerosis, ALS, spinal cord injury). Data extraction focused on:

- Types of stem cells used (MSC, NSC, iPSC, ESC, etc.)
- Routes and methods of administration
- Reported clinical outcomes (motor function, cognition, immune markers)
- Adverse events and safety profiles
- Study design and level of evidence

The selection and synthesis of literature followed the PRISMA guidelines for scoping reviews to ensure transparency and reproducibility.

3. Results

3.1 Alzheimer’s Disease (AD)

3.1.1 Preclinical Evidence

A 2025 meta-analysis of 14 studies assessing the therapeutic effects of intranasally administered stem cell derivatives in animal models of Alzheimer’s disease (AD) revealed a significant reduction in β-amyloid deposition, decreased neuroinflammation and reduced neuronal cell death. Additionally, inflammatory markers such as IL-1β and IBA-1 were significantly decreased [3].

Another systematic review focused on extracellular vesicles (EVs) derived from mesenchymal stem cells (MSCs), demonstrating improved cognitive performance in animal models, reduced β-amyloid accumulation and attenuated expression of inflammatory markers such as GFAP and pro-inflammatory cytokines. No significant changes in phosphorylated tau (p-Tau) levels were reported [1,2].

3.1.2 Systematic Reviews and Narrative Syntheses

Recent reviews highlight the potential of neural stem cells (NSCs) in replacing lost neurons, promoting synaptic plasticity and stimulating neurotrophic factors in preclinical models. However, their clinical application remains constrained by technical, ethical and immunological barriers [4].

MSCs derived from umbilical cord blood, adipose tissue or placenta have demonstrated a favorable safety and immunomodulatory profile. Systematic reviews report limited but promising early-phase clinical evidence, although significant variability exists in stem cell types, administration protocols and outcome measures [2,14].

3.1.3 Clinical Trials

A phase 2a randomized controlled trial investigating allogeneic MSCs in patients with mild AD showed that four monthly infusions were well tolerated and associated with trends toward reduced neurodegeneration, slower clinical decline and decreased levels of neuroinflammatory markers [5].

Other phase I trials using umbilical or adipose-derived MSCs confirmed safety and feasibility but reported limited cognitive improvement in short-term follow-ups. Larger trials with standardized methodologies are needed to validate these findings [15].

3.1.4 Summary of Evidence

- Preclinical models support the therapeutic potential of MSCs and NSCs in reducing hallmark AD pathology (amyloid burden, neuroinflammation) and enhancing cognitive outcomes [1-4].
- Clinical trials suggest that stem cell therapies are generally safe and well tolerated in early-stage AD, though efficacy remains inconclusive [5, 15].
- Key limitations include small sample sizes, short follow-up periods and methodological heterogeneity across studies [5, 14, 15].

3.2 Parkinson's Disease (PD)

3.2.1 Preclinical Evidence

Animal studies have demonstrated the neuroprotective and neurorestorative properties of various stem cell types in models of Parkinson's disease (PD). Systematic reviews of rodent models show that mesenchymal stem cells (MSCs) and neural stem cells (NSCs) improve dopaminergic neuron survival, increase striatal dopamine levels, and ameliorate motor deficits [6,7].

A 2023 meta-analysis of 22 preclinical studies found that transplanted stem cells led to significant improvements in behavioral performance, increased tyrosine hydroxylase-positive neurons and reduced neuroinflammation and oxidative stress markers [7].

Induced pluripotent stem cell (iPSC)-derived dopaminergic neurons have also shown promise in restoring function in MPTP-induced models of PD with some evidence of integration into host neural circuits [9,10].

3.2.2 Systematic Reviews and Evidence Synthesis

Recent systematic reviews emphasize the variability in cell sources, delivery routes (e.g., intracerebral, intrathecal, intravenous) and outcome measures used across studies, which complicates direct comparison [8].

A comprehensive 2024 umbrella review concluded that MSC-based therapies offer moderate preclinical evidence for efficacy and strong evidence for safety with the best outcomes observed when cells are delivered intracerebrally [8].

iPSC technology allows for autologous cell-based therapies and modeling of patient-specific pathology. However, concerns remain regarding tumorigenic potential, ethical challenges, and scalability for clinical use [9,11].

3.2.3 Clinical Trials

Several early-phase clinical trials have explored the safety and feasibility of stem cell therapy in PD. A phase I trial using autologous iPSC-derived dopaminergic progenitor cells transplanted into the putamen of patients with advanced PD reported favorable safety outcomes and sustained improvements in motor function over 12 months, as measured by the Unified Parkinson's Disease Rating Scale [11].

An open-label study of MSCs administered intravenously demonstrated significant improvement in UPDRS Part III scores over a six-month follow-up, though placebo-controlled data are lacking [7].

A 2024 meta-analysis of clinical trials concluded that stem cell therapy is associated with moderate improvements in motor symptoms and quality of life but the overall level of evidence remains low due to small sample sizes and short follow-up durations [8].

3.2.4 Summary of Evidence

- Preclinical data strongly support the efficacy of MSCs, NSCs and iPSC-derived dopaminergic neurons in restoring dopaminergic function and improving motor symptoms in PD [6-10].
- Early-phase clinical trials demonstrate safety and feasibility with modest efficacy in symptom relief [7, 11].
- Methodological variability, limited long-term data and absence of large randomized trials remain key barriers to widespread clinical implementation [8, 11].

3.3 Multiple Sclerosis (MS)

3.3.1 Preclinical Evidence

Experimental autoimmune encephalomyelitis (EAE), the most widely used animal model of MS, has provided substantial insight into stem cell mechanisms. Mesenchymal stem cells (MSCs) have demonstrated immunomodulatory effects by shifting T helper cell polarization, inhibiting pro-inflammatory cytokine production, and promoting neuroregeneration [12]. A 2020 meta-analysis of MSC therapy in EAE models reported significant improvements in neurological scores, decreased inflammation, and enhanced remyelination [12].

Studies also show that neural stem cells (NSCs) and induced pluripotent stem cells (iPSCs) can differentiate into oligodendrocyte precursors, contributing to remyelination and neuroprotection. Human neural precursor cells have promoted axonal preservation and reduced demyelination in viral and toxin-induced MS models [13].

3.3.2 Systematic Reviews and Evidence Synthesis

Systematic reviews highlight the favorable safety profile of MSCs and their role in reducing inflammatory lesions in preclinical and early-phase clinical settings [14,17]. The regenerative and immunomodulatory potential of stem cells, particularly when administered intrathecally or intravenously, suggests a disease-modifying effect. Challenges include the heterogeneity of MSC sources, variability in administration protocols and differences in MS subtypes targeted across studies [14].

NSC-based therapies are under investigation for their ability to promote remyelination and restore functional synapses, although concerns regarding differentiation consistency and tumorigenic risk remain [13,15].

3.3.3 Clinical Trials

A Phase I trial using intrathecal administration of MSC-derived neural progenitors in progressive MS demonstrated feasibility with no serious adverse events and mild-to-moderate clinical improvement in some patients [16]. Another study involving intravenous MSCs showed reductions in gadolinium-enhancing lesions on MRI and improved EDSS scores, though placebo-controlled data remain limited [17].

A narrative review of ongoing trials indicates that MSCs are among the most studied cell types in MS with early evidence supporting their anti-inflammatory and neuroprotective effects [14,38]. However, rigorous phase II/III trials are still needed to confirm efficacy and define optimal protocols.

3.3.4 Summary of Evidence

- **Preclinical studies** strongly support MSCs' role in immunomodulation, neuroprotection and remyelination in EAE and viral models [12, 13].
- **Clinical trials** demonstrate safety and potential efficacy, particularly in progressive MS but lack large-scale, long-term data [16, 17].
- **Key limitations** include variability in stem cell sources, delivery methods and outcome assessment [14, 38].

3.4 Amyotrophic Lateral Sclerosis (ALS)

3.4.1 Preclinical Evidence

Preclinical studies using rodent models of ALS have shown that stem cell-based therapies may promote neuroprotection, delay disease progression and improve motor function. Mesenchymal stem cells (MSCs) have been shown to reduce neuroinflammation, support motor neuron survival and extend lifespan in SOD1-mutant mouse models [18,19]. Muse cells, a subtype of pluripotent-like stem cells, have demonstrated superior neuroprotective potential by suppressing glial activation and preserving motor neurons in ALS mouse models [18].

Human neural stem cells (NSCs) and induced pluripotent stem cells (iPSCs) have also shown promise in replacing degenerated motor neurons and integrating into host neural circuits. However, the differentiation potential, immunogenicity and tumorigenicity of pluripotent-derived cells remain active areas of investigation [20].

3.4.2 Systematic Reviews and Evidence Synthesis

Recent systematic reviews and comparative studies of stem cell therapies in ALS models suggest that MSCs and NSCs offer the most consistent neuroprotective effects [21]. Meta-analyses highlight variability in efficacy depending on cell type, delivery route and disease stage at intervention. MSCs are favored for their immunomodulatory and trophic properties, while iPSCs are increasingly explored for their capacity to generate patient-specific motor neurons [21,22].

Safety concerns regarding uncontrolled proliferation and tumor formation persist, particularly with pluripotent-derived products. NSCs and MSCs have demonstrated favorable safety profiles in preclinical settings, though standardization in protocols is lacking [17].

3.4.3 Clinical Trials

Clinical trials involving intrathecal or intracerebroventricular administration of MSCs and NSCs have generally shown good tolerability and safety [17,23]. A Phase I trial using lumbar intraspinal injection of NSCs in 12 ALS patients demonstrated no serious adverse events and modest functional stabilization in a subset of participants [16].

Recent reviews highlight promising trends toward improved motor scores and prolonged survival but emphasize the need for larger, controlled trials with longer follow-up to establish clinical efficacy [21,23].

3.4.4 Summary of Evidence

- **Preclinical models** support the efficacy of MSCs, NSCs and Muse cells in promoting neuroprotection, preserving motor function and reducing neuroinflammation in ALS [18–20].
- **Early-phase clinical trials** confirm safety and feasibility but therapeutic benefit remains inconclusive [16, 17, 23].
- **Challenges** include limited trial sizes, short observation periods and lack of standardization in cell preparation and delivery [17, 21, 22].

3.5 Spinal Cord Injury (SCI)

3.5.1 Preclinical Evidence

Stem cell therapies have shown significant regenerative potential in preclinical models of spinal cord injury (SCI), mainly through mechanisms such as reduction of inflammation, promotion of axonal regeneration, remyelination and functional synapse formation [28-30].

A 2023 meta-analysis of 27 animal studies demonstrated that mesenchymal stem cell (MSC) transplantation leads to significant improvements in locomotor recovery , especially when administered during the subacute phase post-injury [31].

Neural stem cells (NSCs) and oligodendrocyte precursor cells (OPCs) have also been shown to integrate into the host spinal cord tissue, promote remyelination and support synaptic plasticity [32,33].

Induced pluripotent stem cells (iPSCs) have been used to generate transplantable neuronal populations that facilitate axonal regrowth and restore neural circuit function in SCI models [34,35].

3.5.2 Systematic Reviews and Evidence Synthesis

Systematic reviews emphasize that MSCs exert strong immunomodulatory and trophic effects in SCI, their administration can reduce glial scarring and secondary injury cascades [30,36].

A 2024 systematic review noted that cell origin (autologous vs. allogeneic), dosage and delivery method significantly influence outcomes with intrathecal and intralesional administration generally offering more pronounced benefits than intravenous injection [37].

Umbrella reviews of regenerative strategies also highlight the potential synergy between stem cells and biomaterials (e.g., hydrogels, scaffolds) to enhance cell survival, localization and neural regeneration [38].

3.5.3 Clinical Trials

Several early-phase clinical trials have evaluated the safety and preliminary efficacy of stem cell therapy in SCI patients. A 2023 open-label trial using autologous bone marrow-derived MSCs administered intrathecally in patients with chronic thoracic SCI showed improvement in motor and sensory scores in 40% of participants over a 12-month period [39].

A phase I/II study using iPSC-derived neural progenitor cells (NPCs) implanted into the lesion site demonstrated no major safety concerns and suggested possible motor function gains in some participants [35].

A systematic review published in 2024, encompassing 14 trials, concluded that stem cell therapies are generally safe and show moderate functional improvements in motor and sensory outcomes, particularly in subacute injury stages [40].

3.5.4 Summary of Evidence

- Strong preclinical support exists for the regenerative potential of MSCs, NSCs and iPSC-derived cells in SCI models [28-35].
- Clinical studies confirm safety and suggest meaningful motor recovery in a subset of patients, especially when treatment is initiated in the subacute phase [39, 40].
- Future directions include optimization of delivery techniques, cell combinations and integration with scaffolding biomaterials [38, 41].

3.6 Other Neurodegenerative Disorders

3.6.1 Huntington's Disease (HD)

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder caused by a CAG trinucleotide repeat expansion in the *HTT* gene, resulting in progressive neuronal loss in the striatum and cortex [24]. There is currently no cure for HD and treatment remains symptomatic [24].

Stem cell-based approaches have emerged as promising strategies to replace lost neurons, modulate the disease microenvironment and promote neuroprotection. Preclinical studies using mesenchymal stem cells (MSCs) and neural stem cells (NSCs) have shown improvements in motor coordination, decreased inflammation and delayed neuronal degeneration [25,26].

A 2023 systematic review of 15 preclinical studies confirmed that stem cell transplantation leads to significant improvement in motor performance and histological outcomes in HD animal models [25]. However, clinical evidence remains limited [24,27].

A pilot clinical trial using fetal striatal grafts (NEST-UK project) showed long-term graft survival and potential functional benefit but the ethical and logistical challenges of fetal tissue transplantation limit its widespread applicability [27].

Induced pluripotent stem cells (iPSCs) derived from HD patients have enabled disease modeling and screening of potential therapeutic agents. In the future, autologous gene-corrected iPSC-derived cell transplantation may become a viable strategy [26].

3.6.2 Spinocerebellar Ataxias (SCA)

Spinocerebellar ataxias (SCAs) are a group of inherited neurodegenerative disorders primarily affecting the cerebellum and brainstem. Current therapies are palliative[28].

Several studies have explored the neuroprotective effects of stem cell therapy, especially MSCs in SCA animal models. These studies suggest improvements in motor coordination, reduced neuronal loss and decreased oxidative stress [28,29].

A 2022 systematic review emphasized that intrathecal administration of MSCs showed promise in reducing Purkinje cell degeneration and improving balance as well as gait in preclinical settings [29].

Although clinical data are scarce, early-phase trials in cerebellar ataxias (e.g., SCA3) using allogenic MSCs reported mild functional improvements and no major safety concerns [30].

3.6.3 Prion Diseases

Prion diseases such as Creutzfeldt-Jakob disease (CJD) are rapidly progressive and currently incurable. Stem cell-based therapies remain largely experimental owing to the aggressive disease course [31].

Preclinical studies suggest that stem cells may modulate microglial activation and secrete neurotrophic factors that delay neuronal loss [32]. However, no clinical trials have yet been conducted due to ethical and biosafety concerns related to transmissibility [31].

3.6.4 Frontotemporal Dementia (FTD)

FTD is characterized by progressive degeneration of the frontal and temporal lobes. Stem cell approaches focus on neuroprotection, modulation of neuroinflammation and modeling the disease using iPSCs [33].

Recent studies using patient-derived iPSCs have revealed cellular mechanisms underlying FTD (e.g., TDP-43 pathology), enabling targeted drug screening. Therapeutic transplantation remains hypothetical at this stage [33].

3.6.5 Summary of Evidence

- Stem cell therapies show preclinical promise in rare neurodegenerative disorders such as HD and SCA, particularly in slowing progression as well as improving motor symptoms [24-30].
- Clinical trials are limited but ongoing in selected conditions (e.g., HD, SCA3) [27, 30].
- Disease modeling using iPSCs has revolutionized understanding of monogenic disorders like HD and FTD [26, 34].
- Ethical, technical and disease-specific challenges must be addressed before translation to routine clinical use [27, 31, 33].

4. Discussion

The translation of stem cell therapies from preclinical models to clinical practice in the treatment of neurodegenerative diseases remains a significant scientific and ethical challenge. Although preclinical evidence has demonstrated considerable potential for neuroprotection, neuroregeneration and functional improvement, clinical application is still in its infancy [3,6,7,12-14,18,24].

4.1 Current Clinical Trials and Therapeutic Applications

To date, most clinical applications of stem cells in neurodegenerative diseases have focused on safety and feasibility [5,11,15,16,23,26]. Early-phase trials using mesenchymal stem cells (MSCs), neural stem cells (NSCs) and induced pluripotent stem cells (iPSCs) have been initiated for several conditions including Parkinson's disease, amyotrophic lateral sclerosis (ALS), spinal cord injury (SCI) and Huntington's disease [6-11,18-21, 24-26, 28].

In Parkinson's disease, open-label phase I/II trials have demonstrated that transplantation of dopaminergic neurons derived from fetal tissue or pluripotent stem cells can be safe and may improve motor function [9-11,30,34]. Similarly, intrathecal administration of autologous bone marrow-derived MSCs in ALS has shown favorable safety profiles and potential slowing of disease progression [18-23].

For spinal cord injury, several trials using MSCs or NSCs have reported partial functional recovery in sensory and motor domains, particularly in patients with incomplete injury. However, variability in outcome measures and small sample sizes limit the strength of conclusions [24-28].

4.2 Efficacy and Safety Considerations

While safety data from early trials are encouraging, long-term efficacy remains uncertain [5,8,15-17,22,26,29]. Many studies report modest clinical improvements without clear evidence of structural regeneration. Furthermore, functional benefits are often temporary or limited in scope [24,26-28].

Potential risks associated with stem cell therapies include:

- **Tumorigenicity**: particularly with pluripotent cells (e.g., iPSCs, ESCs) owing to the risk of teratoma formation [10, 11, 33, 35].
- **Immune rejection**: despite the relatively low immunogenicity of MSCs, allogeneic transplantation may elicit immune responses [5, 18, 21].
- **Aberrant differentiation**: improperly controlled cell fate may result in unintended tissue formation or ectopic growth [11, 35].
- **Delivery challenges**: accurate targeting and engraftment into the CNS remain technically demanding [24-27, 32].

4.3 Regulatory and Ethical Challenges

Ethical concerns persist regarding the use of embryonic or fetal tissue, particularly in jurisdictions with strict bioethical frameworks. Additionally, global discrepancies in regulatory standards have led to the proliferation of unregulated"stem cell clinics" offering unproven therapies [36, 41].

Clinical-grade stem cell products must meet Good Manufacturing Practice (GMP) standards and trials must comply with rigorous protocols to ensure safety, reproducibility and transparency [37].

4.4 Future Directions in Clinical Translation

To advance stem cell therapies toward routine clinical application, future research must address:

- **Optimization of cell types and sources**, including standardized protocols for differentiation and quality control [30-33, 35].
- **Improved delivery systems** such as biomaterials, scaffolds or targeted microinjection [25, 26, 28, 32].
- **Combination therapies**, integrating stem cells with gene editing (e.g., CRISPR) or pharmacological agents [34, 40].
- **Large-scale randomized controlled trials (RCTs)** to generate high-quality evidence for safety and efficacy [6, 11, 17, 27].

A personalized approach—tailoring cell type, delivery method and dosing to individual patient characteristics—may enhance therapeutic outcomes [11,30,34]. Moreover, regulatory harmonization and international collaboration will be critical to ensure responsible and ethical progress [37,39].

The landscape of stem cell research in the context of neurodegenerative diseases is rapidly evolving. Although clinical application remains limited, technological and conceptual advances are expanding the therapeutic horizon. Future progress will depend on the integration of stem cell science with genetics, bioengineering and personalized medicine [37,39].

4.5 Emerging Technologies

Gene editing technologies such as CRISPR-Cas9, open new avenues for correcting genetic mutations in patient-derived iPSCs prior to transplantation. This approach may be particularly beneficial in monogenic neurodegenerative disorders like Huntington's disease or certain hereditary ataxias [33,34,40].

Organoids and 3D bioprinting enable the creation of complex neural tissue architectures for disease modeling, drug screening and potentially for reconstructive transplantation. Brain and spinal cord organoids derived from stem cells can simulate patient-specific pathophysiology and facilitate personalized drug testing [10,32,34].

Biomaterial scaffolds and hydrogel matrices are also being developed to improve stem cell survival, engraftment and guided differentiation after transplantation. These platforms might serve as supportive microenvironments mimicking the extracellular matrix (ECM) of the central nervous system [25,27,32].

4.6 Toward Personalized Stem Cell Therapy

Personalized medicine aims to tailor stem cell therapies based on individual genetic, epigenetic and immunological profiles [11,30,33]. Patient-derived iPSCs offer immunocompatibility and the possibility of autologous transplantation, minimizing the risk of immune rejection [9-11,34].

Integration with **omics technologies**—genomics, transcriptomics, proteomics—will allow deeper stratification of patients and identification of responders to specific cell therapies. Machine learning approaches are also being explored to predict optimal treatment strategies and outcomes [34,40].

4.7 Overcoming Clinical and Regulatory Barriers

Long-term success of stem cell therapies will require:

- **Standardization of clinical protocols** including unified criteria for patient selection, dosing, delivery routes and outcome assessment [5, 16, 17, 27, 37].
- **Multicenter randomized controlled trials** with extended follow-up to establish durable efficacy and safety [6, 11, 26, 27].
- **International regulatory harmonization**, especially in ethical oversight, product approval and manufacturing practices [36, 37, 39].

Additionally, public and scientific education is essential to counteract misinformation and unethical commercialization of unproven treatments [36,41].

4.8 Ethical and Socioeconomic Considerations

Equitable access to stem cell therapies is a growing concern. High development costs and individualized production processes may limit availability to high-income settings [36,40]. Public funding and healthcare system integration will be necessary to ensure broader accessibility [36,39].

Ethical debates concerning embryonic stem cells, donor consent and data privacy in personalized applications must be addressed with transparency and adherence to international guidelines [36,38,39].

4.9 Clinical Perspectives

In the next decade, stem cell therapies might become adjunctive or even frontline treatments for selected neurodegenerative diseases [5,6,11,15,27,34]. A combined approach, integrating cell therapy with neuroprotective drugs, neuromodulation or gene therapy, may provide synergistic benefits [5,33,34,40].

Clinical translation will depend on continuous collaboration between neuroscientists, stem cell biologists, clinicians and bioethicists [36,37,39]. The ultimate goal remains the restoration of neural function and improvement of quality of life for patients suffering from currently incurable conditions [5,6,11,15].

5. Conclusions

Stem cell-based therapies represent one of the most promising frontiers in the treatment of neurodegenerative diseases. Over the past two decades, remarkable progress has been made in understanding stem cell biology, developing differentiation protocols and exploring clinical applications. Multiple stem cell types including embryonic stem cells, mesenchymal stem cells and induced pluripotent stem cells have demonstrated therapeutic potential in preclinical models of Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, spinal cord injury and other neurodegenerative conditions.

In spite of significant advances, the translation of stem cell therapies from bench to bedside remains challenging. Safety concerns such as tumorigenesis, immune rejection and improper differentiation must be addressed through rigorous quality control and also long-term clinical monitoring. Ethical considerations and regulatory heterogeneity across countries further complicate clinical implementation.

Ongoing and future clinical trials are critical for validating efficacy and safety, identifying patient subgroups most likely to benefit and optimizing treatment protocols. Emerging technologies like gene editing, organoids as well as personalized cell therapy are expected to accelerate clinical translation and improve therapeutic outcomes. Interdisciplinary collaboration and standardization of research methodologies will be key to ensuring reproducibility and progress.

To sum up, while stem cell therapy is not yet a routine clinical option for neurodegenerative diseases, it holds substantial promise. Continued investment in research, ethical governance and international cooperation will be essential to unlock the full therapeutic potential of stem cells and ultimately improve the quality of life for patients affected by these debilitating disorders.

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