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THE USE OF STEM CELLS IN NEUROLOGY

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ABSTRACT

Stem cells, due to their ability to differentiate and self-renew, have found applications in various therapeutic processes, including the treatment of neurological diseases. Because the central nervous system has limited regenerative capacity, neurological disorders remain both a clinical and societal challenge. Clinical studies have shown that regenerative therapy using stem cells produces beneficial effects in the treatment of conditions such as Parkinson's disease, Alzheimer's disease, stroke, and spinal cord injury. However, safety concerns - including the risk of tumor formation, variable cell survival, heterogeneity of cell preparations, and lack of standardized procedures- continue to be analyzed.

This article presents various sources of stem cells - embryonic stem cells (ESC), induced pluripotent stem cells (iPSC), and adult stem cells such as mesenchymal stem cells (MSC) and neural stem cells (NSC). Therapeutic mechanisms and modern technologies, including biomaterials, tissue engineering, and gene therapy, which enhance the effectiveness of cell-based therapies, are also discussed. Current applications of regenerative therapy in selected neurological disorders are presented, with particular emphasis on mechanisms of action, results from preclinical and clinical studies, and ethical and legal issues. The article highlights the need for further clinical research and for advancements enabling controlled cell differentiation.The use of stem cells may transform the understanding and treatment of neurological diseases; however, fully utilizing their potential requires further multidisciplinary research.

KEYWORDS

Stem Cells, Neural Stem Cells (NSC), Mesenchymal Stem Cells (MSC), Induced Pluripotent Stem Cells (iPSC), Cell-Based Therapy, Neuroregeneration, Neuroprotection, Neurodegenerative Diseases

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Introduction

Neurological diseases such as stroke, Parkinson's disease, dementias, multiple sclerosis, and injuries of the nervous system generate significant economic and social costs for patients, their families, and society. They also pose a major challenge for modern neurology due to the growing incidence of these disorders. An additional difficulty is the limited availability of therapeutic interventions, primarily due to the low proliferative capacity of neurons and the complex organization of neuronal microcircuits, whose reconstruction remains a significant clinical challenge (1). Until the mid-20th century, it was believed that neurons did not undergo renewal.

Later scientific discoveries demonstrated the occurrence of neurogenesis in the adult human brain. This breakthrough laid the foundation for the therapeutic use of stem cells in neurological disorders. Owing to their ability to differentiate into specialized neural cells and modulate the inflammatory microenvironment, stem cells represent a potentially groundbreaking tool in treating diseases previously considered incurable (2). Current therapeutic interventions include neural cell transplantation, the use of mesenchymal stem cells, generation of neuronal cells from iPSCs, and hybrid methods combining cells with biomaterials or gene therapy. Although stem cells offer a promising treatment perspective for many neurological diseases, several safety issues remain -such as the risk of teratoma formation, genomic instability in certain cell types, variable therapeutic efficacy, and difficulties integrating transplanted cells into existing neuronal networks (3).Another significant limitation is the small number of clinical trials, which hinders the development of reproducible and widely applicable therapies. Nevertheless, an increasing body of preclinical data highlights the considerable potential of stem cells, particularly in the treatment of elderly patients with neurological disorders. The aim of this article is to present current applications of stem cells in neurology, with emphasis on scientific evidence, new technologies, and clinical outcomes.

Methodology

This article is a systematic review of the literature concerning the use of stem cells in neurology. Publications were analyzed from the following databases: PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. The search included studies published between 2005 and 2025. Only peer-reviewed articles, studies involving the use of stem cells in neurological diseases, reports presenting preclinical or clinical results, and papers describing cellular, molecular, or bioengineering mechanisms related to cell-based therapies were included.

The analysis considered the type of cells used, research model (animal, in vitro, clinical), mechanisms of action, as well as the efficacy and safety of the therapies. Data were summarized narratively, with comparisons of study findings and identification of areas requiring further investigation.

Types of Stem Cells Used in Neurology

The use of stem cells in neurology encompasses various cell populations. Current studies and publications distinguish several types of cells employed in regenerative therapies: embryonic stem cells (ESC), induced pluripotent stem cells (iPSC), neural stem cells (NSC), and mesenchymal stem cells (MSC). Each of these cell types possesses distinct biological properties and potential clinical applications (4, 5).

Embryonic stem cells (ESC) are derived from early embryonic development and can differentiate into all three germ layers. They are highly plastic and capable of generating mature neurons, oligodendrocytes, and astrocytes. However, their use is associated with a risk of teratoma formation (6). Induced pluripotent stem cells (iPSC) are created by reprogramming somatic cells into a pluripotent state, enabling the creation of disease models, patient-specific cells, and reducing the risk of immunological rejection (7). At the same time, their use may involve genetic mutations and genomic instability (8). Neural stem cells (NSC) are primarily found in the subventricular zone and the hippocampus and can differentiate into the three major neural lineages. NSC-based therapies are considered relatively safe, but their limited availability and restricted proliferative capacity pose significant challenges (9). Mesenchymal stem cells (MSC), derived from adipose tissue, bone marrow, and umbilical cord blood, are widely used in regenerative therapies. MSCs are multipotent and exert strong paracrine, anti-inflammatory, and neuroprotective effects. They are among the best-studied cells used in neuroregeneration. Their main advantages include modulation of the inflammatory environment, prevention of neuronal apoptosis, and support of angiogenesis (10).

Mechanisms of Action of Cell-Based Therapies

Understanding the mechanisms by which stem cells act on the central nervous system is crucial for developing effective and safe cell-based therapies. These mechanisms are complex and involve both direct regeneration of damaged neural cells and indirect effects on the neural tissue microenvironment. The most important mechanisms include neuronal differentiation, paracrine activity, immune modulation, neuroprotection, promotion of angiogenesis, and enhancement of neuroplasticity (11). Stem cells can differentiate into neurons, astrocytes, and oligodendrocytes and integrate into the existing neuronal network. In Parkinson's disease, this enables the regeneration of dopaminergic neurons, while in spinal cord injury it supports the reconstruction of neural pathways (12). Moreover, stem cells exhibit neuroprotective and immunomodulatory properties: they reduce oxidative stress, limit neuronal apoptosis, and stabilize the blood–brain barrier (13). In multiple sclerosis, stem cells inhibit T-cell activation, which reduces demyelination (14). They also exert paracrine effects by secreting anti-inflammatory cytokines and growth factors such as BDNF, GDNF, and VEGF, thereby reducing neurodegeneration and promoting neuronal repair (15). The application of stem cells in spinal cord injuries is also linked to their ability to enhance neuroplasticity, leading to the formation of new synaptic connections and reorganization of neuronal networks (16). In stroke, the therapeutic benefits result from the induction of angiogenesis, which improves tissue perfusion, facilitates neuronal regeneration, and increases the effectiveness of neurorehabilitation (17).

Application of Stem Cells in Neurological Disorders

Stem cells play an increasingly important role in the treatment of numerous neurological diseases. Their potential applications include stroke, Parkinson's disease, multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), spinal cord injuries, Huntington's disease, cerebral palsy, and Alzheimer's disease. Stroke remains one of the greatest challenges in modern neurology due to the high rate of long-term disability and mortality. Stem cell therapy offers hope for improved outcomes. Transplantation of stem cells into the penumbra -the region at risk of functional loss after stroke-enables cell migration to the injury site, where differentiation occurs, the infarct area is reduced, neuroplasticity is enhanced, and motor functions are restored.

Clinical studies have shown that MSCs can improve neurological function, especially when therapy is introduced during the subacute phase (18). In Parkinson's disease, the transplantation of dopaminergic neurons derived from iPSCs is of particular importance. This therapy has proven especially effective in patients at an early stage of the disease. Implanted iPSC-derived cells differentiate, secrete neurotrophic factors, and contribute to improved motor function. Clinical trials have confirmed the safety and efficacy of such implantations (12). In multiple sclerosis, axonal demyelination results from inflammatory and neurodegenerative processes within the CNS. Stem cells have been shown to promote axonal remyelination and reduce inflammation in animal models. Phase II clinical trials have confirmed the safety of these therapies, although their efficacy requires further investigation (10). Amyotrophic lateral sclerosis (ALS) is characterized by progressive degeneration of motor neurons. Interest in cell-based therapies increased after discovering the link between SOD1 mutations and familial ALS. The therapeutic goal is to slow motor neuron degeneration through the neuroprotective effects of MSCs and NSCs and to reduce microglial activation. Clinical trials have demonstrated a potential to delay disease progression (19). In spinal cord injuries, stem cells support axonal regeneration and remyelination. Combining cell therapies with biomaterials such as hydrogels has resulted in increasingly favorable regenerative outcomes (20).

Technologies Supporting Cell-Based Therapies

Cell-based therapies are increasingly supported by modern biomedical technologies that enhance their safety and efficacy, although their application still requires further standardization and research. The most important technologies include tissue engineering, biomaterials, gene therapy, cell delivery systems, and 3D modeling (21). Biomaterials such as hyaluronic acid, fibronectin, and alginate enable precise delivery of cells and create an environment conducive to regeneration. When combined with MSCs or NSCs, they improve the integration of transplanted cells and reduce inflammation (22). Tissue engineering — including the use of 3D scaffolds, hydrogels, and collagen matrices -can guide neuronal regeneration and stabilize transplanted cells (23). Gene therapy supports stem cell-based treatments by modifying cells to increase the production of neuroprotective factors or modulate immune processes.

Combining iPSCs with CRISPR/Cas9 gene editing represents a highly promising direction in regenerative medicine (24). Exosomes and microvesicles constitute an alternative to classical cell-based therapies, offering similar paracrine effects with a lower risk of oncogenesis (25).

Status of Clinical Research and Future Directions

Clinical research on the application of stem cells in neurology is rapidly expanding, with a large number of ongoing studies. Most trials focus on conditions such as stroke, multiple sclerosis, spinal cord injuries, and Parkinson's disease (26). Currently, ongoing studies evaluating MSCs in multiple sclerosis suggest a reduction in inflammatory activity and improvements in neurological function, although these trials remain in early stages (27). Likewise, clinical studies using iPSC-derived dopaminergic neurons in Parkinson's disease have demonstrated stable integration of transplanted cells into the nervous system and improved motor function (28).

Stem cell therapies show particularly strong potential in treating spinal cord injuries. Research results indicate improved neural conduction and partial regeneration of spinal pathways (29). However, most studies remain in early phases, and large, placebo-controlled randomized trials are still lacking -a necessary step before implementing these therapies into routine clinical practice. Despite promising results, significant limitations and dilemmas remain. Evidence confirming long-term therapeutic efficacy is insufficient, and many studies involve small patient cohorts, limiting the generalizability of findings (30). The variability in cell types, doses, delivery methods, and outcome measures makes it difficult to compare results between centers (26). Another major challenge is the lack of standardized clinical protocols regarding patient qualification, cell preparation, efficacy assessment, and monitoring of transplanted cell survival. Despite advances in imaging techniques such as MRI and PET, full visualization of cell fate remains difficult (31). Future developments may rely on genetically modified stem cells, such as those carrying corrected mutations responsible for neurodegenerative diseases, paving the way for personalized therapies. Enhancing patient safety remains a priority, as stem cell therapies carry risks of tumor formation, aberrant cell migration, immune reactions, and lack of durable clinical effects (30). Further research is needed to reduce oncogenic risk and immunogenicity, particularly in allogeneic therapies. Accessibility also remains a major challenge -these therapies are costly, often still experimental, and available only in specialized centers, which may lead to inequalities in access to advanced treatment options (32).

Summary

Stem cell–based medicine opens new therapeutic possibilities for neurological diseases for which effective treatments have been lacking. Stem cells can support regeneration, modulate the immune response, and replace damaged neural cells. Clinical studies confirm their potential in the treatment of conditions such as stroke, Parkinson's disease, multiple sclerosis, Alzheimer's disease, and Huntington's disease. However, the use of cell-based therapies comes with significant limitations, including the lack of standardized procedures, technical challenges related to controlling the fate of transplanted cells, and inconsistent results from clinical trials. Concerns regarding the risk of tumor formation also remain. At the same time, ethical, regulatory, and societal issues associated with the development of such therapies must be considered.

Further research -both preclinical and clinical - is essential to enable the standardization and personalization of regenerative therapies. Cell-based treatments in neurology continue to be one of the most important directions in the development of regenerative medicine, and their clinical potential suggests that research in this area will intensify in the coming years. There is also a genuine need to implement safe and effective cell therapies into everyday clinical practice.

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