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Review Article

Review of Cell Therapy Approaches to Autism: A Review of Clinical Trial

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Abstract

Autism Spectrum Disorders (ASD) are characterized by persistent social communication and interaction difficulties, as well as repetitive behavioral patterns, often accompanied by abnormalities of the immune system and inflammatory reactions. Stem cell-based therapies, particularly those involving stem cells, are being investigated as potential treatments. This review examines cellular and molecular ASD abnormalities, stem cell types, animal models, ongoing clinical trials, and therapy limitations. ASD, a complex neurodevelopmental disorder with early onset social communication challenges and repetitive behaviors, lacks effective treatments. New research links ASD to neuroinflammation, microglia and glucose metabolism. Ten clinical trials of cell therapy show generally positive results. Although cell therapies show promise, extensive research is needed. This abstract discusses the potential of cell therapy for conditions lacking effective treatments, including cerebral palsy and ASD. It acknowledges complexity and incomplete understanding of pathophysiology. Disparate results in ASD cell therapy trials raise concerns about therapeutic targets and approaches, which require refined preclinical studies. Global ASD prevalence has increased, but treatments for core symptoms remain inadequate. Stem cell therapies show potential. Non-pharmacological interventions, such as diet and supplements, can address comorbidities. This brief abstract summarizes the aim, methodology, key results and conclusions of the full article.

This review analyzes the role of miRNAs in ASD onset and progression. It is exploring miRNAs as regulators of neural development, diagnostic biomarkers and therapeutic targets. Findings from in vivo and in vitro models, including induced pluripotent stem cells (iPSCs), highlight the miRNA impact on ASD phenotypes. miRNAs are critical to understanding ASD pathogenesis. This review discusses neural stem cell-derived extracellular vesicles (NSC-EVs) as a treatment for CNS disorders. It highlights the mechanisms, therapeutic roles and advantages of cell-free therapy of NSC-EVs. The prevalence of Neuropsychiatric Disorders (NPD) is increasing globally, without full understanding of pathophysiology and effective treatments. Human induced pluripotent stem cells (hiPSCs) offer patient-specific neuropharmacological study potential. Guidelines and best practices for hiPSC-based NPD studies, with emphasis on donor selection, experimental design, and translational relevance, aim to improve drug discovery and clinical translation.

Keywords: Autism Spectrum Disorder; Clinical trials; Neuroinflammation; Stem cell therapies

Background

Autism Spectrum Disorder (ASD) encompasses various neurodevelopmental challenges, including social interaction difficulties and repetitive behaviors. Abnormalities in the immune system and inflammatory responses in ASD make it a potential candidate for cell-based therapies.

ASD is a heterogeneous neurodevelopmental condition characterized by social interaction challenges, repetitive behaviors, and focused interests. The increasing prevalence of ASD highlights the need for effective treatments. New therapies such as cell therapy are gaining a lot of interest due to the lack of traditional cures. Recent advances in understanding ASD include:

Neuroinflammation: Some studies suggest a link between brain inflammation and ASD.

Microglia: These brain immune cells have attracted interest for their potential role in ASD.

Glucose Metabolism: Evidence suggests disruption of brain glucose metabolism in ASD.

This background sets the stage by presenting existing knowledge. The background recognizes the growing anticipation of cell therapies as treatments for complex, poorly understood conditions such as cerebral palsy and ASD. This section provides context for the research, emphasizing the importance of decision-making tools in monoclonal antibody manufacturing and recent advances in regenerative medicine therapies. It highlights the global prevalence and characteristics of ASD, together with the role of miRNA in its pathogenesis and progression.

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder influenced by genetics and environment. It is characterized by impaired social functioning and stereotypical behaviours. Recent research has highlighted miRNAs as key players in ASD. Diseases of the Central Nervous System (CNS) pose significant health challenges. Neural Stem Cells (NSCs) offer therapeutic potential with some associated risks. This paper focuses on NSC-EV as a potentially safer and more efficient alternative. Neuropsychiatric disorders have a significant impact globally. Despite extensive research, our understanding of their mechanisms is incomplete [1-4].

Method

This review article focuses on stem cell therapies for ASD and uses an approach involving the collection, analysis and synthesis of existing research. The authors review cellular and molecular abnormalities, stem cell types, animal models, and ongoing clinical trials associated with ASD. The authors conducted a comprehensive review of 10 clinical trials investigating cell therapies for ASD patients, covering different methods, participant profiles and outcomes. This review article examines cell therapies in cerebral palsy and ASD, using an approach that involves collecting, analyzing and synthesizing existing research and literature. Although the abstract provides an overview of cell therapy trials in these diseases, it does not describe the selection or analysis methods. The review covers various study types, including animal models, cellular models, necropsy specimens and iPSCs derived from ASD patients, with the aim of demonstrating a comprehensive understanding of the role of miRNAs in ASD.

The review compiles data from different studies on NSC-EVs, including animal models and in vitro research, indicating their potential in CNS diseases [5]. It also covers iPSC-derived NSCs and their advantages. This article reviews current practices for using hiPSCs for neuropharmacological and neuropsychiatric research. It describes patient recruitment guidelines, including detailed donor profiles that include demographic, clinical, medical, diagnostic, and genetic data. It covers control group selection, experimental design and overall hiPSC-based study methodology [6].

Result

Over the past decade, there has been significant progress in the field of cellular therapies for Autism Spectrum Disorders (ASD). This review consolidates results from multiple studies to provide an updated overview of the therapeutic potential, mechanisms and challenges associated with these therapies.

Effectiveness and Mechanisms

Preclinical data: Preclinical studies have shown benefits for cellular therapy in ASD. Stem cells, instead of replacing cells, appear to support damaged tissue, especially in the brain, by acting as chasers. Clinical Trials: Although limited, some clinical trials have shown promising results in reducing ASD symptoms. Of these, only five have been completed, each with distinct variations, making standard conclusions difficult. Safety: In all studies reviewed, no significant adverse events were reported, suggesting that cellular therapies for ASD are generally well tolerated. Cellular therapies explored: Various cellular therapies, including cord blood cells, bone marrow mononuclear cells, and mesenchymal stromal cells, have been mentioned. In particular, their transplantation showed gap junction-mediated interactions with the cerebral endothelium, suggesting a possible mechanism underlying their therapeutic benefits.

The Role of miRNAs and NSC-EVs

miRNAs in ASD: miRNAs have been shown to significantly regulate the translation of vital mRNAs in neural development,

which affects ASD onset and progression. In addition, emerging miRNA-based therapeutic strategies are now being evaluated in preclinical settings. Potential of NSC-EVs: Extracellular vesicles derived from Neural Stem Cells (NSC-EVs) hold promise for modulating both the local nervous system microenvironment and remote neuronal functions. These vesicles, rich in miRNAs and proteins, are known for their roles in neuroprotection, anti-apoptosis, and Blood-Brain Barrier (BBB) repair. In the context of ASD, miR-1290 plays a central role.

Insights into hiPSCs in NPD research

Detailed guidelines and recommendations have been provided concerning the use of human induced pluripotent stem cells (hiPSCs) to study Neuropsychiatric Disorders (NPDs). Great emphasis is placed on ensuring the reproducibility, statistical rigor and translational potential of these in vitro models.

Discussion

Autism Spectrum Disorders (ASD) represent a complex web of neurodevelopmental challenges characterized by diverse impairments spanning communication, cognition and emotion regulation. Given the diversity and inherent heterogeneity, the development of standardized therapeutic strategies is daunting. But recent advances in cellular therapies, particularly stem cell transplantation, have rekindled hope. This discussion brings together insights from various studies and highlights the potential of these therapies, their challenges and areas for future exploration [7-9].

Understanding ASD and its Complexities

Neurophysiological features: The multifaceted impairments in ASD, encompassing challenges in perception, motor, executive function, and theory of mind, underscore the need for tailored therapeutic interventions. Immune pathology: Links between ASD and neuroinflammation, microglial activation, cytokine imbalances, and oxidative stress suggest that targeting these pathways may have therapeutic dividends.

Glucose metabolism: New evidence of altered glucose metabolism in ASD points to another potential therapeutic target.

Cellular Therapies: A Beacon of Hope with Caveats

Stem Cell Transplantation: Contrary to earlier beliefs about cell replacement, new findings indicate stem cells primarily support damaged tissue. Stem cell transplantation is emerging as a vanguard of cellular therapies, but the primary outcome remains safety focused. Security vs. Efficacy: While current studies champion the safety of their methods, it is imperative to understand that a large portion of drugs falter in clinical trials, primarily due to deficiencies in safety or efficacy. Stem cell therapies, in their experimental infancy, may not guarantee success. miRNA regulatory mechanisms: miRNAs, crucial in regulating ASD phenotypes, constitute a therapeutic avenue, with early evaluations in preclinical settings promising but requiring further validation. Neural Stem Cell-Derived Extracellular Vesicles (NSC-EVs): Despite their potential in Central Nervous System (CNS) disorders, difficulties in the regulation of brain development via NSC-EVs remain elusive. A deeper understanding, especially of engineered EVs, is critical to improving their applicability. Human induced pluripotent stem cells (hiPSCs): While promising for deciphering neuropsychiatric disorders (NPD) and fast-tracking drug discovery, hiPSCs come with challenges such as the need for standardization and translation of in vitro findings to clinical areas.

Challenges, Limitations and Ethical Considerations

Current knowledge gaps combined with ASD's inherent heterogeneity make evaluations challenging. Unrealistic expectations exacerbate these challenges. Some studies suffer from limited sample sizes, questioning the generalizability of outcomes and underscoring the need for expansive, structured clinical trials. Continuing unregulated studies may border on unethical, especially when the primary goal should be rigorous placebo-controlled studies.

Conclusion and Future Directions: While cellular therapies, particularly stem cell transplantation, shine as potential therapeutic strategies, a confluence of challenges muddy the waters. It is important to approach this field with cautious optimism, grounding efforts in rigorous, standardized and ethically grounded research. The hope lies in bridging existing knowledge gaps, fine-tuning methods, and eagerly exploring the role of cellular therapies in transforming the ASD treatment landscape.

Conclusion

The dynamic field of cellular therapies, spearheaded by stem cell transplantation, stands as a beacon of potential for managing Autism Spectrum Disorders (ASD). However, our journey into this therapeutic space is interspersed with challenges, both scientific and ethical. Central to these therapeutic advances is the underlying pathophysiology of ASD, an understanding of which continues to advance. The preliminary advances in cell therapies have raised hope, suggesting a shift from conventional behavioral interventions to pathways that can directly modify the disease. The landscape of clinical trials exploring stem cell treatments for ASD is still embryonic. A sparse number of studies, each characterized by its unique methodology, makes it difficult to draw firm conclusions. The urgency for more expansive, standardized research is palpable. Bias, a silent subverter of scientific rigour, can sneak into reviews through selective study inclusion or interpretation. It underlines the necessity of methodological review and open reporting in such articles. MiRNAs have emerged as promising candidates both as diagnostic biomarkers and therapeutic interventions in ASD. Their

role in regulating ASD phenotypes offers a glimpse of therapeutic potential. Nevertheless, the transition from preclinical promise to clinically approved miRNA-based interventions is a bridge that has yet to be crossed. Neural Stem Cell-Derived Extracellular Vesicles (NSC-EVs) are opening a new frontier for addressing Central Nervous System (CNS) diseases. Their multifaceted roles, from being therapeutic agents to potential biomarkers, paint a hopeful picture. In addition, the synergy between iPSC technology and NSC-EVs may reshape the therapeutic strategies for complex CNS disorders such as ASD. But the fervor surrounding these cellular therapies is tempered with caution. Many trials involve children, a demographic that relies on guardians for informed consent. The ethical weight of such decisions, especially given the uncertainty surrounding efficacy and safety, is colossal. Finally, human induced pluripotent stem cells (hiPSCs) stand as proof of innovation in studying Neuropsychiatric Disorders (NPDs). However, their translation from the lab to the clinic requires rigorous standardization, emphasizing the guidelines highlighted in various reviews. In conclusion, cell therapies hold a torch of hope for ASD, but the path forward requires a delicate dance of optimism, rigorous research, and ethical considerations. Only with a co-evolution in understanding ASD and refining cell therapies can we truly realize their potential to transform the ASD treatment paradigm.

Limitation

The growing interest in cellular therapies, particularly stem cell transplantation for autism spectrum disorders (ASD), has generated enthusiasm and scrutiny. Reviews highlight the promise of these therapies but reveal common problems and limitations that call for a cautious approach:

Limited clinical trials: Few trials with different designs, participants, cell types, administration methods and outcomes prevent comprehensive conclusions.

Methodological variability: Different study methods prevent definitive insights.

Lack of robust preclinical models: Inadequate models pose challenges and can introduce bias into human studies.

Heterogeneity of conditions: Understanding the diverse nature of cerebral palsy and ASD is critical to effective therapeutic development.

Ethical considerations: Ethical considerations, particularly regarding the participation of children in uncontrolled studies, are crucial.

Potential bias: Selective inclusion and focus on positive results may introduce bias and publication bias.

Overlooking molecular factors: Simple focus on miRNAs may neglect critical molecular factors in ASD.

Safety Concerns: Long-term safety of neural stem cell-derived extracellular vesicles (NSC-EV) requires caution.

Lack of Empirical Evidence: Reviews, especially those discussing human induced pluripotent stem cells (hiPSCs), often lack empirically validated data to support recommendations.

Language and publication exclusions: Restrictive search criteria might overlook relevant studies.

In conclusion, although cellular therapies hold promise for ASD, acknowledging and addressing these limitations is critical to evidence-based research and ethical progress in the field.

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