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REVIEW

Mechanisms and Research Progress of Magnetic Nanoparticles in Modulating Neural Plasticity for Neuroregeneration

Yue Liu[1,2], Yizhuo Zhang[2,3], Yingying Huang[2,3], Xia Bi[2]

[1]Sports and Health Institute, Shanghai University of Sport, Shanghai, People's Republic of China; [2]Department of Rehabilitation Medicine, Shanghai University of Medicine & Health Sciences Affiliated Zhoupu Hospital, Shanghai, People's Republic of China; [3]Shanghai University of Medicine & Health Sciences; Shanghai University of Traditional Chinese Medicine, Shanghai, People's Republic of China

Correspondence: Xia Bi, Department of Rehabilitation Medicine, Shanghai University of Medicine & Health Sciences Affiliated Zhoupu Hospital, Shanghai, People's Republic of China, Email bixiash@163.com

Abstract: Magnetic nanoparticles (MNPs), particularly those exhibiting superparamagnetism and biocompatibility, have garnered significant interest in the biomedical field due to their unique physicochemical properties. Recent studies have shown that MNPs can modulate neural plasticity by influencing key signaling pathways such as BDNF (Brain-Derived Neurotrophic Factor) and the PI3K/Akt pathway, critical for neuronal growth, synaptic connectivity, and functional recovery. This review provides a comprehensive analysis of the mechanisms through which MNPs interact with neural tissues, highlighting the diversity of nanoparticle types (eg, iron oxide, gold, and carbon-based nanoparticles) and their applications in neurodegenerative disease treatment and neural regeneration. Despite the immense potential of MNPs in neurodegenerative disease treatment, this review also compares them with traditional interventions, discussing their advantages and limitations. Additionally, it addresses key challenges, particularly the difficulty of overcoming the blood-brain barrier, and issues related to biocompatibility, toxicity, and long-term safety. In clinical applications, ethical concerns, such as patient informed consent and long-term risks, must also be considered alongside efficacy and safety. This review offers insights into these challenges and provides a framework for future research, aiming to accelerate the clinical integration of MNP-based neurotherapies.

Keywords: magnetic nanoparticles, neural plasticity, neural signaling pathways, research progress

Introduction

Neuroplasticity is the brain's ability to reorganize its structure and function in response to experience, learning, and injury, crucial for maintaining function and recovery after injury.[1] After events like a stroke, neuroplasticity helps the brain recover by reorganizing surrounding neurons and forming new connections. This involves molecular, cellular, and structural changes, including synaptic plasticity, neurogenesis, and neural circuit modulation, enabling the brain to adapt to injury, learning, and environmental changes.[2] However, spontaneous neural plasticity has limitations in cases of severe brain injury or chronic neurodegenerative diseases, where traditional interventions like drugs or electrical stimulation may not precisely target specific brain regions.

Recently, MNPs have emerged as promising tools for modulating neuroplasticity. MNPs possess unique properties, including superparamagnetism, biocompatibility, and the ability to be controlled by external magnetic fields, making them ideal for biomedical applications. MNPs can be engineered to interact with biological systems at the molecular level, influencing cellular processes and signaling pathways that regulate neuroplasticity.[3] As shown in Figure 1, after MNPs cross the blood-brain barrier, they sequentially activate intracellular genes at the molecular level, enhance synaptic plasticity at the cellular level, and ultimately achieve the overall remodeling and repair of neural functions at the system level, providing a progressively amplified biological pathway for subsequent intervention strategies. MNPs achieve this by influencing key neural signaling pathways, such as the BDNF and PI3K/Akt pathways, which are crucial for neuronal

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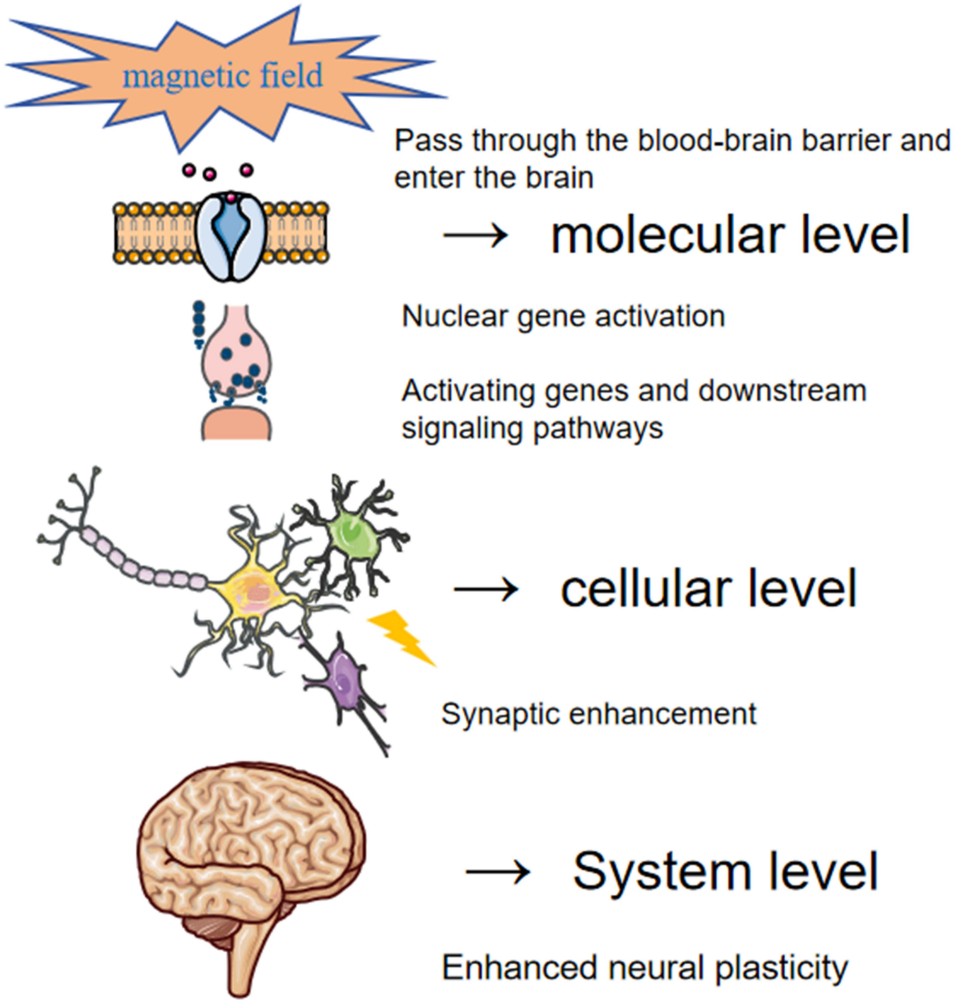

Figure 1 After MNPs cross the blood-brain barrier, they first activate genes and trigger downstream signaling pathways at the molecular level, enhance synaptic plasticity at the cellular level, and ultimately lead to the remodeling and repair of neural functions at the system level, providing a progressively amplified biological pathway to support subsequent intervention strategies.

growth, synaptic plasticity, and recovery after neural injuries. Different types of MNPs, such as iron oxide (Fe_3O_4), gold, and carbon-based nanoparticles, each possess unique characteristics for diverse neurotherapeutic applications. MNPs hold significant potential in neuroscience, offering precise spatial and temporal control over therapeutic agent delivery to targeted brain areas, potentially enhancing treatments that promote neuroplasticity. Incorporating MNPs into neuroplasticity research opens new avenues for therapeutic interventions in neurological disorders, including stroke, traumatic brain injury, and neurodegenerative diseases. Compared to conventional drug therapies, MNPs provide superior targeting precision and spatiotemporal control, enabling more accurate intervention in specific nerve cells and brain regions. Unlike rehabilitation therapies, MNPs can directly intervene in the neuroplasticity process at the molecular and cellular levels. Studies have indicated that MNPs can facilitate the targeted delivery of neuroprotective agents to damaged brain regions, enhancing recovery and promoting plastic changes in neural networks.[4] MNPs offer higher precision, lower energy consumption, and avoid the complexities of light delivery and genetic manipulation compared to optogenetics, electrical stimulation, and viral vector gene delivery.[5–7]

However, despite their promising potential, MNPs still require further research and optimization with regard to biodegradability and long-term biological safety. The blood-brain barrier (BBB) poses a critical challenge for central nervous system drug delivery. Studies show that while MNPs offer multiple functions, such as targeted delivery, magnetic imaging, and ferroptosis induction, their ability to cross the BBB in systemic administration is still limited

by factors like particle size and surface modification. Thus, optimizing MNPs to overcome the BBB remains a key challenge.[8] Thus, despite their promising prospects, further clinical research and safety evaluations are required to ensure their effectiveness and facilitate their clinical application.[9]

The impact of MNPs on neuroplasticity is not solely attributed to their physical properties; the surface chemistry and functionalization of these nanoparticles play crucial roles in determining their biological interactions, detection techniques like MRI and MPI enable precise tracking of MNPs in biological systems.[10] By modifying the surface characteristics of MNPs, researchers can improve their biocompatibility and target specificity, which is essential for minimizing potential side effects and maximizing therapeutic benefits.[11] Furthermore, the development of multifunctional MNPs capable of delivering drugs, providing imaging contrast, and enabling therapeutic hyperthermia represents a significant advancement in nanomedicine.[12] In terms of ethical and practical considerations, the study utilized anonymized cerebrospinal fluid samples, adhering strictly to ethical standards and eliminating the need for additional informed consent, thereby ensuring patient privacy. At the same time, taking into account the potential off-target effects of magnetic nanoparticles and patient monitoring concerns, the method demonstrates excellent scalability and cost-effectiveness, making it particularly suitable for resource-limited clinical settings.[13] Research has shown that the synthesis methods, functionalization strategies, and applications of MNPs in microorganism concentration demonstrate their advantages in improving diagnostic sensitivity and accuracy. Additionally, the study discusses challenges such as MNPs' stability, detection strategies, and aggregation effects, providing a theoretical basis for their further application in clinical diagnostics.[14]

While several reviews have explored the biomedical applications of MNPs, most have focused on general drug delivery, imaging, or cancer therapy. Few have systematically examined the role of MNPs in modulating neuroplasticity, in the context of neural signaling pathways, synaptic remodeling, and regenerative mechanisms. This review synthesizes recent advancements in nanotechnology and neurobiology, offering a thorough and critical analysis of how MNPs affect neuroplasticity at the molecular, cellular, and systems levels. It primarily highlights the latest developments in preclinical studies of MNPs for neurotherapeutic applications, exploring their potential for clinical translation, while intentionally excluding a detailed discussion of current human clinical trials.

As our understanding of neuroplasticity deepens, the potential of MNPs as modulators of this process becomes increasingly promising. Future research should aim to uncover the specific mechanisms by which MNPs influence neuroplasticity, particularly their impact on synaptic remodeling, neuroinflammation, and the activation of neurotrophic signaling pathways. Through sustained investigation, MNPs may become key components in therapeutic approaches designed to enhance brain recovery and function.

Characteristics, Synthesis and Detection of Magnetic Nanoparticles

Selection of Core Materials

The selection of core materials is a crucial step in the synthesis of MNPs, as it directly influences their magnetic properties, stability, and suitability for various applications. Among the most commonly utilized core materials are iron oxide nanoparticles, particularly magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3), owing to their superparamagnetic properties, biocompatibility, and ease of functionalization. These materials exhibit high magnetic saturation and can be effectively manipulated under an external magnetic field, making them ideal candidates for a range of biomedical applications, including drug delivery, magnetic resonance imaging (MRI), and hyperthermia treatments for cancer. Although materials such as gold nanoparticles offer greater flexibility in surface modification, they lack inherent magnetism, making it difficult to achieve magnetic field-driven targeted delivery and real-time manipulation.[15]

The choice of core material must also align with the specific requirements of the intended application. In biomedical contexts, for example, it is essential that the core material is biocompatible and non-toxic. Iron oxide nanoparticles satisfy these criteria, as they are generally well-tolerated by biological systems. Furthermore, the size and shape of the nanoparticles can be tailored during synthesis, which is crucial for optimizing both their magnetic properties and their interactions with biological systems. For instance, smaller nanoparticles typically exhibit higher surface-to-volume ratios, thereby enhancing their reactivity and interaction with biological molecules.[16]

In addition to these inherent properties, the magnetic characteristics of the core material can be further enhanced through doping with other metals or by modifying the synthesis conditions. Doping iron oxide nanoparticles with elements such as zinc or cobalt has been shown to improve their magnetic performance and stability.[17] Moreover, the choice of synthesis method plays a significant role in determining the crystallinity and morphology of the nanoparticles, which in turn affect their magnetic behavior. For example, microwave-assisted synthesis has demonstrated the ability to produce nanoparticles with superior magnetic properties due to more precise control over the reaction conditions.[18] As shown in Table 1, several different core materials are presented with their respective characteristics, applications, advantages and disadvantages.

In conclusion, the selection of core materials for magnetic nanoparticles is a complex decision that must consider a range of factors, including the desired magnetic properties, biocompatibility, and application-specific requirements. Ongoing research in this field continues to explore novel materials and innovative synthesis techniques to further enhance the performance of magnetic nanoparticles across diverse applications.

Surface Modification Techniques

Surface modification of magnetic nanoparticles is essential for enhancing their stability, biocompatibility, and functionality for specific applications. In recent years, various methods have been developed to enhance the biocompatibility, stability and catalytic activity of magnetic nanoparticles. Through the application of organic coatings (such as polyvinyl alcohol and chitosan), inorganic coatings (such as silicon and metal oxides), and metal composite materials, these surface functionalization methods have significantly improved the performance of magnetic nanoparticles, making them have broad application prospects in the fields of biomedicine and catalysis.[19] The surface properties of nanoparticles significantly influence their interactions with biological systems, including cellular uptake, biodistribution, and clearance rates. Common surface modification techniques include coating with polymers, silica, or other materials to improve stability and reduce agglomeration. For instance, polyethylene glycol (PEG) is frequently used to create a hydrophilic shell around nanoparticles, which enhances their circulation time in the bloodstream and reduces immunogenicity.[20]

Another important aspect of surface modification is the introduction of functional groups that can facilitate the attachment of targeting ligands, drugs, or imaging agents. For example, the functionalization of iron oxide nanoparticles with folic acid or antibodies can enable targeted delivery to cells, thereby improving therapeutic efficacy while minimizing side effects.[21] Additionally, the use of molecularly imprinted polymers (MIPs) on the surface of magnetic nanoparticles allows for selective binding of specific biomolecules, enhancing their application in biosensing and drug delivery.[22]

The choice of surface modification technique depends on the intended application and desired properties of the nanoparticles. For example, silica coating is often employed to create a stable and biocompatible interface, while polymer coatings can provide additional functionalities such as drug loading or targeting capabilities.[23] Moreover, the use of green

Table 1 Comparison of Characteristics, Applications, Advantages and Disadvantages of Different Core Materials of Magnetic Nanoparticles

Nanomaterial Type	Properties	Applications
Magnetic Nanoparticles	Superparamagnetic properties, small size (up to ~10 nm), high surface area	Biomedical applications such as drug delivery, cancer treatment, magnetic resonance imaging (MRI), hyperthermia[16]
Magnetite Nanoparticles	Ferrimagnetic, tunable sizes (30–200 nm), high saturation magnetization, superparamagnetic behavior	Used in solar energy harvesting, magnetic imaging, photonic materials, OLEDs, and magnetic field sensors[17]
Polymeric Nanocomposites	Nanofillers (eg, nanotubes, graphene) embedded in a polymer matrix	Environmental applications, enhanced mechanical properties, biomedical (drug delivery, wound healing)[16]
Gold Nanoparticles	Biocompatible, easily functionalized, surface plasmon resonance properties	Drug delivery, imaging, cancer therapy, biosensors[17]
Iron Oxide Nanoparticles	Magnetic, biodegradable, and surface functionalized for targeting specific tissues	Cancer therapy, MRI contrast agents, environmental cleanup[17]
Graphene	Exceptional electrical conductivity, mechanical strength, biocompatibility	Electronics, energy storage, biosensors, drug delivery[16]

synthesis methods for surface modification, such as using plant extracts, has gained attention due to their eco-friendliness and potential to create biocompatible nanoparticles.[24]

In conclusion, surface modification techniques play a crucial role in enhancing the performance of magnetic nanoparticles for various applications. Ongoing research aims to develop novel modification strategies that can further improve the functionality and biocompatibility of these nanoparticles, thereby expanding their potential in biomedical and environmental applications.

Synthesis Methods and Characterization

The synthesis of magnetic nanoparticles involves various methods, each with its advantages and limitations. Common synthesis techniques include co-precipitation, thermal decomposition, hydrothermal synthesis, and microwave-assisted synthesis. Co-precipitation is one of the most widely used methods due to its simplicity, cost-effectiveness, and ability to produce nanoparticles with controlled size and morphology. In this method, iron salts are precipitated in an alkaline medium, resulting in the formation of magnetite or maghemite nanoparticles.[21]

Thermal decomposition involves the heating of iron precursors in organic solvents, leading to the formation of nanoparticles with high crystallinity and uniform size. This method allows for better control over the size and shape of the nanoparticles, which is crucial for optimizing their magnetic properties.[16] Hydrothermal synthesis, on the other hand, utilizes high-pressure and high-temperature conditions to facilitate the growth of nanoparticles, often resulting in well-defined shapes and sizes. Inductive heating technology has demonstrated significant advantages in the synthesis of magnetic nanoparticles. Studies have shown that inductive heating can be used to synthesize core-shell nanoparticles starting from magnetic cores, facilitating the synthesis of Iron-Nickel ($FeNi_3$) supported on Molybdenum (Mo) and Iron Carbide ($Fe_{2.2}C$) supported on Molybdenum (Mo) nanoparticles with high molybdenum content. Compared to traditional heating methods, inductive heating leads to the deposition of significantly more molybdenum on the nanoparticle surface.[25] This technique not only enhances synthesis efficiency but also enables precise control over the structure and composition of the nanoparticles, opening up new possibilities for the application of magnetic nanoparticles in catalysis and other fields.

Microwave-assisted synthesis has emerged as a promising technique that offers rapid and uniform heating, leading to the production of nanoparticles with enhanced magnetic properties. This method allows for precise control over the reaction parameters, resulting in high reproducibility and scalability of nanoparticle production.[26]

Characterization of synthesized magnetic nanoparticles is essential to assess their size, shape, crystallinity, and magnetic properties. Techniques such as transmission electron microscopy (TEM), scanning electron microscopy (SEM), dynamic light scattering (DLS), and X-ray diffraction (XRD) are commonly employed for morphological and structural analysis. Magnetic properties are typically characterized using vibrating sample magnetometry (VSM) or superconducting quantum interference device (SQUID) magnetometry. For instance, Transmission Electron Microscopy (TEM) can elucidate the lattice structure and particle morphology of nanoparticles, helping researchers understand crystallinity and interactions, while SEM provides detailed information on surface morphology, including surface roughness and shape distribution, and spectroscopic techniques such as Ultraviolet-Visible Absorption Spectroscopy and Infrared Spectroscopy offer crucial data on optical properties, surface modification, and functionalization of magnetic nanoparticles, enabling comprehensive characterization for their optimization and application.[17] These technologies provide researchers with more accurate characterization methods, assisting them in optimizing synthesis methods, improving the morphology, size distribution and surface functionalization of magnetic nanoparticles, thereby designing new types of magnetic nanoparticles with superior performance and enhancing their applications in fields such as medicine, nano-optics and drug delivery. Figures 2 and 3 illustrate the synthesis and surface modification processes of nanoparticles.

In summary, the synthesis methods and characterization techniques for magnetic nanoparticles are critical for tailoring their properties for specific applications. Ongoing advancements in synthesis techniques and characterization methods continue to enhance our understanding of magnetic nanoparticles, paving the way for their successful integration into various fields, including biomedicine, environmental remediation, and electronics.

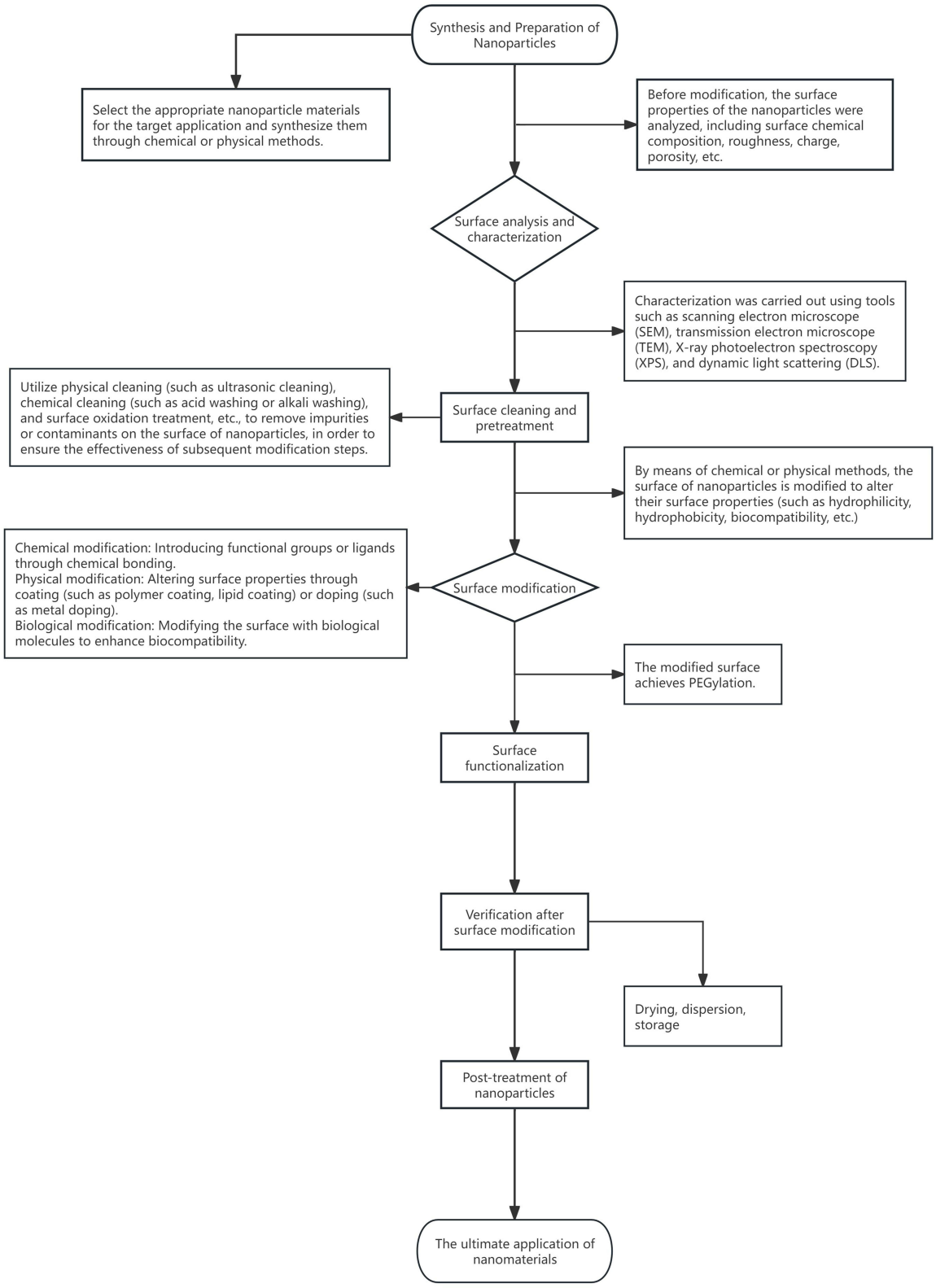

Figure 2 Surface modification of nanoparticles: From synthesis to functionalization and application.

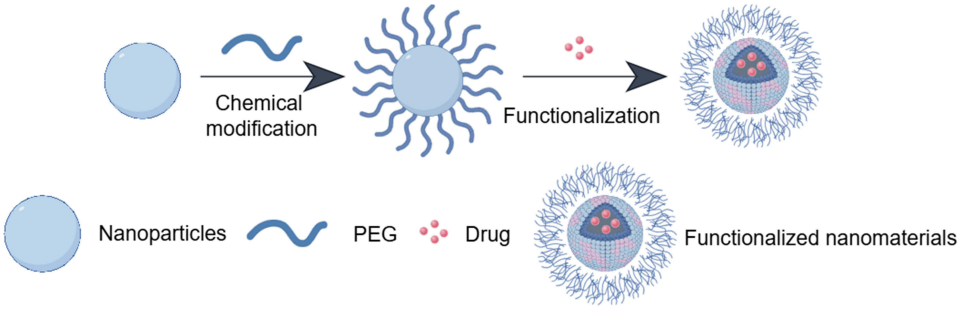

Figure 3 Schematic Diagram of Nano-material Synthesis.

Detection Method

MNPs have found extensive use in biomedical applications, various techniques have been developed for detecting MNPs in vivo. Among the traditional detection methods, Magnetic Resonance Imaging (MRI) and Positron Emission Tomography-Computed Tomography (PET-CT) are widely utilized for in vivo tracking and quantification of MNPs. The combination of PET-CT provides a real-time monitoring method for the biodistribution and targeted accumulation of magnetic nanoparticles, enabling precise tracking of the MNPs location and movement within the body.[27]

In recent years, Magnetic Particle Imaging (MPI), an emerging technology, has demonstrated advantages in the detection of MNPs. Unlike traditional MRI, MPI directly measures the magnetic response of superparamagnetic iron oxide particles, offering higher temporal and spatial resolution without the negative contrast issues commonly associated with MRI.[28,29] MPI has been used for long-term in vivo tracking of magnetic nanoparticles, providing precise quantification of their distribution, accumulation, and clearance in the body.[28] This technology shows great promise in evaluating drug delivery systems and monitoring disease progression, with particularly significant applications in joint diseases and tumor-targeted therapies.[28,29]

Magnetic Nanoparticles and Interaction with Neural Cells

Mechanisms of Cellular Uptake

MNPs have emerged as pivotal tools in biomedical applications, particularly in the context of neural cell interactions, where their internalization mechanisms are crucial for their efficacy in both therapeutic and diagnostic contexts. Research indicates that MNPs can be designed for targeted drug delivery, cell labeling and magnetic hyperthermia therapy to neural cells through surface modification and magnetic response. The surface properties and magnetism of MNPs are crucial for their interaction with neural cells. Surface modification can alter their charge and protein corona, affecting uptake efficiency and intracellular distribution; magnetic response enables them to generate thermal effects under external magnetic fields, which is beneficial for the treatment of neurodegenerative diseases. Moreover, the interaction between MNPs and neural cells is also influenced by factors such as cell type, concentration, exposure time and magnetic field stimulation, which jointly determine the effects of MNPs on the viability, apoptosis, differentiation and neurite growth of neural cells. Precise regulation of the physical and chemical properties of MNPs is of great significance for optimizing their application in neuroscientific research and treatment.[30] Additionally, numerous investigations have revealed that the uptake of MNPs predominantly occurs through endocytosis, involving various pathways such as clathrin-mediated endocytosis and macropinocytosis, which play integral roles in nanoparticle internalization. For instance, one study found that the uptake of 10 nm silver nanoparticles by embryonic zebrafish cells predominantly occurred through macropinocytosis, while larger nanoparticles utilized clathrin-mediated pathways.[31] As shown in Figure 4, the process of nanoparticles entering cells through endocytosis is illustrated. This indicates a size-dependent mechanism for nanoparticle uptake, which is critical for optimizing the design of MNPs for specific cellular targets. Furthermore, the presence of specific surface modifications on nanoparticles can significantly enhance their uptake efficiency. For example, the functionalization of MNPs with targeting ligands, such as antibodies or peptides, can facilitate specific binding to receptors on neural cells, thereby promoting their internalization.[32]

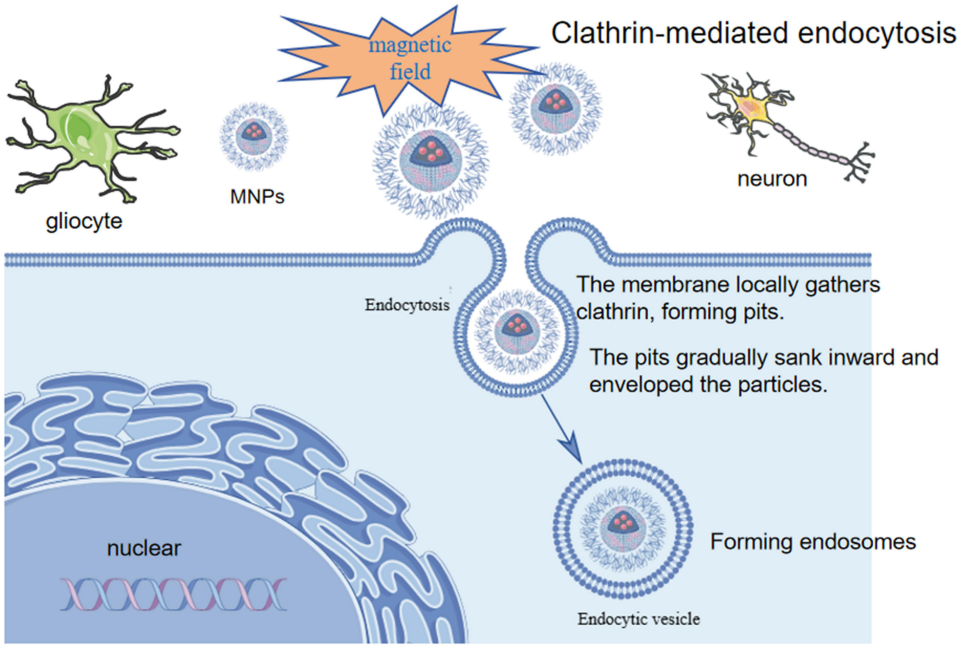

Figure 4 Schematic illustration of magnetic nanoparticles entering neural cells via endocytosis under the influence of a magnetic field.

Moreover, the physicochemical properties of MNPs, such as size, shape, and surface charge, play a pivotal role in determining their cellular uptake efficiency. Smaller nanoparticles tend to exhibit higher cellular uptake due to their ability to evade immune detection and penetrate cellular membranes more effectively.[33] Additionally, the interaction of MNPs with the cellular membrane can induce membrane curvature, facilitating endocytosis. This phenomenon has been observed with silica nanoparticles, where their uptake was influenced by the membrane's mechanical properties and the presence of specific receptors.[34]

Understanding these mechanisms is crucial for the development of MNPs that can effectively target neural cells for therapeutic purposes, such as drug delivery or gene therapy. The ability to manipulate these uptake pathways through nanoparticle design can enhance the efficacy of treatments for neurodegenerative diseases and other neurological disorders. Table 2 summarizes the primary uptake routes and corresponding key evidence for different types of MNPs based on their surface coatings and size, highlighting the influence of specific inhibitors on cellular internalization mechanisms. After understanding the mechanism of cellular uptake of magnetic nanoparticles, we further explored their effects on neural cell pathways.

Table 2 This Table Summarizes the Application of Different Types of Magnetic Nanoparticles in the Internalization Mechanisms and Neural Differentiation Processes of Neural Cells

MNPs Type	Cell Type	Endocytosis Mechanism	Key Findings
Fe3O4 MNPs (from bacteria)	Human Embryonic Stem Cells (hESCs)	Endocytosis via lipid bilayer, magnetized cells separated by magnets	MNPs were incorporated into hESCs, forming 3D aggregates (hEBs). MNPs enhanced neural induction in hEBs under neural induction medium (NIM).[35]
Magnetoelectric MNPs	Rat Hippocampal Neurons	Cell membrane interaction via electric field conversion	MNPs influenced neural activity by converting magnetic fields into electric fields, affecting action potentials and neuromodulation.[36]
Iron oxide (IONPs)	Neural Cells (primary culture)	Endocytosis by neural cells; particles retained in vesicles	IONPs enhanced cell viability and differentiation in magnetic hydrogels, boosting neuronal network formation under AMF stimulation.[37]

Impact on Cellular Signaling Pathways

The interaction of magnetic nanoparticles with neural cells also has profound implications for cellular signaling pathways. The application of magnetic nanoparticles holds great potential in cell signaling research. Studies have demonstrated that magnetic nanoparticles can bind to cell surface receptors through the surface coating of specific ligands. Under the influence of an external magnetic field, these nanoparticles apply nanoscale forces on the ligand-receptor bonds, thereby activating mechanotransduction pathways in cells.[38] This technology allows for precise control of mechanical stimuli to cells, providing a powerful tool for studying mechanosensitive structures and signaling pathways in cells. MNPs can modulate various signaling cascades that are essential for maintaining cellular homeostasis and facilitating responses to environmental stimuli. For instance, Iron oxide magnetic nanoparticles accumulate in the brain, induce reactive oxygen species production, raise 8-hydroxy-2′-deoxyguanosine levels, and activate pro-inflammatory factors such as tumor necrosis factor-alpha and interleukin-6, leading to sustained neuroinflammation that down-regulates brain-derived neurotrophic factor and disrupts the synaptic plasticity and neural recovery it mediates.[39] Furthermore, Under an electromagnetic field, MNPs cause a moderate increase in intracellular reactive oxygen species, activate the epidermal growth factor receptor, and subsequently induce phosphorylation of CREB at serine-133 via the PI3K/Akt and MAPK/ERK cascades, and the activated CREB translocates into the nucleus, binds to cAMP-response elements in the promoters of neuro-differentiation genes, and initiates transcriptional programs including NeuroD1, Neurogenin1, and BDNF, thereby driving stem-cell differentiation toward the neuronal lineage.[40]

Additionally, the mechanical forces generated by MNPs under the influence of external magnetic fields can lead to significant alterations in cellular signaling. These forces can induce changes in the cytoskeletal structure of neural cells, which in turn affect the activation of mechanotransduction pathways. For example, the application of magnetic forces on MNP-loaded cells has been shown to enhance the expression of genes related to neuronal differentiation and synaptic plasticity.[41] This highlights the potential of using MNPs not only as passive carriers but also as active modulators of cellular signaling.

Moreover, the interaction of MNPs with cellular membranes can lead to the activation of signaling pathways that are critical for cellular responses to stress and injury. The presence of MNPs can influence the release of reactive oxygen species (ROS) and other signaling molecules that play a role in inflammatory responses and cellular repair mechanisms.[35]

In conclusion, the impact of magnetic nanoparticles on cellular signaling pathways is a critical area of research that holds promise for developing novel therapeutic strategies for neurological disorders. By understanding how MNPs influence these pathways, researchers can design more effective treatments that leverage the unique properties of nanoparticles to enhance neural cell function and promote recovery from injury or disease.

Effects of Nanoparticles on Neural Cell Function

Relevant studies have shown that microglial cells in the central nervous system (CNS) are capable of rapidly and extensively internalizing MNPs under baseline conditions.[42] However, this uptake characteristic remains largely unchanged upon cellular activation. Moreover, the interaction of magnetic nanoparticles with neural cells extends beyond simple uptake; it also exerts a profound impact on various cellular functions. Research indicates that magnetic nanoparticles (such as DMSA@Fe_3O_4) can guide neural stem cells (NSCs) to differentiate into functional neurons through external static magnetic fields (SMF). Specifically, after nanoparticles are taken up by NSCs, they can promote the differentiation of neurons under the action of SMF and enhance neuroprotection by activating the PI3K/AKT/mTOR signaling pathway. Moreover, the magnetic field can also guide axon regeneration, myelin sheath reconstruction, and promote neural regeneration, thereby improving functional recovery. These findings provide a new perspective for the potential application of magnetic nanoparticles in the repair of neural injuries.[43] In addition, MNPs can influence various aspects of neural cell behavior, including proliferation, differentiation, and synaptic connectivity. For instance, one study demonstrated that the incorporation of iron oxide nanoparticles into neural stem cells enhanced their differentiation into neurons while also promoting neurite outgrowth and synaptic formation.[37] This suggests that MNPs can serve as effective scaffolds that not only facilitate the physical growth of neural cells but also enhance their functional capabilities.

Furthermore, the application of alternating magnetic fields to MNPs has been shown to induce localized heating, which can further stimulate neural cell activity and promote differentiation. This method, known as magnetic hyperthermia therapy, has been explored as a means to enhance the therapeutic effects of neural stem cell transplantation in models of spinal cord injury.[35] The localized heating generated by MNPs can activate cellular signaling pathways that are critical for neurogenesis, thereby improving the outcomes of regenerative therapies.

However, the effects of MNPs on neural cells are not universally positive. Some studies have reported that high concentrations of MNPs can lead to cytotoxic effects, including oxidative stress and apoptosis.[36] This underscores the importance of carefully optimizing the dosage and surface characteristics of MNPs to minimize adverse effects while maximizing therapeutic benefits.

In summary, the influence of magnetic nanoparticles on neural cell function is multifaceted, with potential applications in enhancing neural regeneration and function. Continued research in this area is essential to fully harness the therapeutic potential of MNPs while mitigating any associated risks.

Magnetic Nanoparticles Enter the Brain

Recent advances in MNPs-based neuroengineering have demonstrated their unique capacity to modulate neuroplasticity while overcoming the BBB. By integrating external SMF with ligand-driven targeting, gold-coated superparamagnetic iron-oxide nanoparticles (SPIO-Au-PEG) engineered with insulin ligands increased the brain-to-blood distribution coefficient from 2.86% to 3.72% and simultaneously elevated local magnetic flux density, thereby promoting actin-mediated cytoskeletal rearrangements in neurons and enhancing synaptic plasticity-related signaling cascades.[8] Complementarily, a dual-magnetic strategy that sequentially applies an external magnetic field (EMF) for endothelial docking and an alternating magnetic field (AMF) for hyperthermia-triggered tight-junction opening has been shown to transiently raise brain-tissue temperature to ~40 °C; this reversible thermal perturbation elevated MNP transmigration across an in-vitro BBB model from 37% to 63% and was corroborated by in-vivo ICP-MS data revealing a two-fold enrichment of Fe in cortical regions, indicating a direct, magnetically tunable influence on regional neuroplasticity.[44]

To further refine brain specificity, biomimetic and small-sized zwitterionic platforms have been merged with magnetic guidance. T807-conjugated erythrocyte-membrane-coated human-serum-albumin nanoparticles (T807-ETm/HSA NPs) exploit the high lipophilicity and positive surface charge of the tau-selective ligand to target neuronal populations, achieving a 12% transport efficiency across a triple-culture BBB model and a six-fold higher fluorescence signal in murine hippocampus compared with untargeted controls, thereby positioning magnetically assisted constructs as precision tools for activity-dependent plasticity modulation.[45] Likewise, cross-linked carboxybetaine-functionalized hyperbranched polycarbonate micelles (MCB(S)) with a hydrodynamic diameter <10 nm prolonged systemic circulation ($t_{1/2\beta}$ = 6.2 h) and exploited BGT-1 transporter overexpression on brain endothelium; when loaded with IR780 and paclitaxel, NIR-triggered photothermal release suppressed orthotopic glioblastoma growth while preserving perilesional neurons, illustrating that magneto-chemical synergy can spatially constrain neuroplastic changes to pathological foci.[46] Collectively, these studies establish that rationally designed MNPs can couple magnetic navigation with molecular targeting to traverse the BBB, focally modulate neuroplasticity, and deliver therapeutics with unprecedented spatial resolution.

Magnetic Nanoparticles Regulating Mechanisms of Neural Plasticity

MNPs have emerged as a promising tool in neuroscience, particularly due to their potential to modulate neural plasticity. This modulation plays a crucial role in various neurological processes, including neurotransmitter release, synaptic plasticity, and neuronal regeneration. The unique properties of MNPs, such as their biocompatibility and responsiveness to external magnetic fields, enable precise and controlled interventions within neural tissues. This section will examine the mechanisms by which MNPs influence neural plasticity, with a focus on their regulation of neurotransmitter release, alterations in synaptic plasticity, and their capacity to promote neuronal regeneration.

Regulation of Neurotransmitter Release

The release of neurotransmitters is a fundamental process in neuronal communication, and MNPs have been shown to influence this process through several mechanisms. Studies indicate that MNPs can enhance the release of neurotransmitters

such as dopamine and glutamate by modulating calcium signaling pathways within neurons. The application of an external magnetic field can induce mechanical stress on the MNPs, which in turn can affect the dynamics of calcium ion channels in neuronal membranes.[47] This modulation can lead to an increase in intracellular calcium levels, promoting the exocytosis of SMF magnetic hyperthermia neurotransmitter-containing vesicles.

MNPs, particularly superparamagnetic iron oxide nanoparticles (SPIONs), have shown significant promise in modulating neurotransmitter release. These nanoparticles, when conjugated with neurotransmitter analogs and engineered binding proteins, can be used to detect neurotransmitter interactions through changes in their magnetic properties, such as T2-weighted MRI signals. This approach allows for minimally invasive and highly specific mapping of neurochemical dynamics, providing useful insights into neurotransmitter regulation.[48]

Moreover, MNPs can interact with the cytoskeleton of neurons, which plays a crucial role in the transport of vesicles to the synaptic cleft. The mechanical forces generated by MNPs under magnetic stimulation can enhance the movement of these vesicles, facilitating a more efficient release of neurotransmitters.[49] This effect is particularly relevant in the context of neurodegenerative diseases, where impaired neurotransmitter release is a common feature. By enhancing neurotransmitter release, MNPs may offer a therapeutic strategy for restoring synaptic function in conditions such as Parkinson's disease and Alzheimer's disease.[50]

In addition to enhancing neurotransmitter release, MNPs can also modulate the release of neurotrophic factors that support neuronal health and plasticity. For instance, the application of magnetic fields has been shown to increase the secretion of BDNF, which is essential for synaptic plasticity and the survival of neurons.[51] This dual role of MNPs in regulating both neurotransmitter and neurotrophic factor release highlights their potential as a multifaceted approach to enhancing neural plasticity.

Changes in Synaptic Plasticity

Synaptic plasticity, the ability of synapses to strengthen or weaken over time, is crucial for learning and memory. MNPs have been shown to induce changes in synaptic plasticity through their effects on intracellular signaling pathways. The application of magnetic fields can activate mechanotransduction pathways that lead to the phosphorylation of key proteins involved in synaptic plasticity, such as cyclic AMP response element-binding protein (CREB).[52] This activation can enhance the expression of genes associated with synaptic strengthening, thereby promoting long-term potentiation (LTP), a cellular mechanism underlying learning and memory.

Furthermore, MNPs can influence the morphology of dendritic spines, the small protrusions on neurons where synapses are formed. Changes in spine morphology are closely linked to synaptic plasticity; for instance, the formation of new spines is associated with LTP. Studies have demonstrated that MNPs can promote the growth of dendritic spines in response to magnetic stimulation, thereby enhancing synaptic connectivity.[53] This effect is particularly important in the context of neurodevelopmental disorders, where altered synaptic connectivity is a hallmark feature. Recent studies indicate that MNPs can be used to deliver therapeutic agents that promote synaptic regeneration and neuronal function. For instance, magnetic nanoparticle formulations of BDNF have been shown to revive spine density reduction caused by HIV infection and morphine exposure.[54]

Moreover, the ability of MNPs to modulate synaptic plasticity extends to their role in the regulation of inhibitory and excitatory neurotransmitter balance. By influencing the release of GABA (gamma-aminobutyric acid), the primary inhibitory neurotransmitter, MNPs can help restore the excitatory-inhibitory balance that is often disrupted in various neurological conditions.[55] This balance is crucial for maintaining proper neural circuit function and preventing excitotoxicity, which can lead to neuronal damage.

Promotion of Neuronal Regeneration

The regenerative capacity of neurons is limited, particularly in the CNS. However, recent studies have shown that MNPs can enhance neuronal regeneration through various mechanisms. One of the primary ways MNPs promote regeneration is by providing mechanical stimulation to neurons. The application of an external magnetic field can generate forces that stimulate axonal growth and guidance.[56] This mechanical stimulation can activate intracellular signaling pathways that are essential for neuronal growth, such as the RAS signaling cascade, which promotes axon elongation and branching. MNPs, when incorporated into collagen-based hydrogels, have shown significant promise in promoting neuronal regeneration. These

nanoparticles can be oriented in three-dimensional scaffolds under an external magnetic field, facilitating the creation of aligned collagen fibers that provide directional cues for neuronal growth. This method has been demonstrated to enhance the regenerative capabilities of neuronal tissues, as neurons grown in these aligned hydrogels exhibited elongated and co-oriented growth patterns, aiding in more effective neuronal pathfinding and regeneration.[57]

Additionally, MNPs can be used as delivery vehicles for neurotrophic factors that support neuronal survival and regeneration. By functionalizing MNPs with neurotrophic factors such as nerve growth factor (NGF) or BDNF, researchers have been able to enhance the regenerative response of neurons following injury.[52] The targeted delivery of these factors to the site of injury can significantly improve the outcomes of regenerative therapies, offering a promising avenue for treating conditions such as spinal cord injuries and peripheral nerve damage.

Furthermore, MNPs can facilitate the recruitment of endogenous stem cells to sites of injury. The application of magnetic fields can enhance the migration of stem cells, promoting their differentiation into neurons and glial cells that are essential for repair.[43] This approach not only enhances the regenerative capacity of the nervous system but also helps to create a supportive microenvironment for neuronal growth.

In conclusion, the modulation of neural plasticity by magnetic nanoparticles represents a promising frontier in neuroscience. Through their effects on neurotransmitter release, synaptic plasticity, and neuronal regeneration, MNPs offer a multifaceted approach to enhancing neural function and promoting recovery from injury. As research continues to elucidate the mechanisms underlying these effects, MNPs may pave the way for novel therapeutic strategies in the treatment of neurodegenerative diseases and nerve injuries.

Immune Interactions in the Liver

MNPs are extensively researched for their biomedical potential, including targeted drug delivery. Once injected into the bloodstream, MNPs are mainly processed by the liver's mononuclear phagocyte system (MPS), particularly Kupffer cells, which are the liver's resident macrophages.[58] These cells play a crucial role in clearing nanoparticles from circulation, especially those with surface characteristics or sizes that favor phagocytosis.[59] Recent studies have shown that surface modifications, such as PEGylation, can reduce the uptake of MNPs by Kupffer cells, thereby enhancing their circulation time and increasing their potential for disease targeting.[60] Moreover, MNPs engineered with specific biomimetic features, like those resembling natural magnetosomes, have been shown to effectively avoid immune detection while still being internalized by Kupffer cells.[58] This selective uptake is essential in developing nanoparticles that can efficiently target liver diseases while minimizing adverse immune responses.[61]

Additionally, the role of glutathione (GSH) in modulating the biotransformation of nanoparticles within the liver is well understood. For instance, bimetallic nanoparticles undergo rapid transformation in hepatic sinusoids due to GSH interactions, affecting their sequestration by Kupffer cells.[60,61] This transformation not only influences the retention of nanoparticles in the liver but also alters their elimination pathways, indicating that managing this process could optimize nanoparticle performance in therapeutic settings.[59]

Research Progress in Animal Models

Application of Magnetic Nanoparticles in Various Neurological Diseases

MNPs have emerged as a promising tool in the treatment and understanding of various neurological diseases, including Alzheimer's disease (AD) and Parkinson's disease (PD). These nanoparticles, particularly those based on iron oxides, exhibit unique properties that allow for targeted drug delivery and imaging, making them invaluable in both therapeutic and diagnostic applications. For instance, studies have demonstrated that magnetoelectric nanoparticles can dissociate stable β-amyloid aggregates associated with Alzheimer's disease when exposed to low-frequency magnetic fields, thus presenting a novel therapeutic strategy to mitigate the toxic effects of amyloid plaques, as shown in Figure 5.[62] Furthermore, the use of MNPs in conjunction with stem cell therapy has shown potential in animal models of PD. Human adipose-derived stem cells (hADSCs) labeled with magnetic nanoparticles were tracked in vivo, revealing significant recovery of motor functions in PD models.[63] This targeted approach not only enhances the delivery of therapeutic agents but also minimizes systemic side effects, a common challenge in traditional drug therapies.

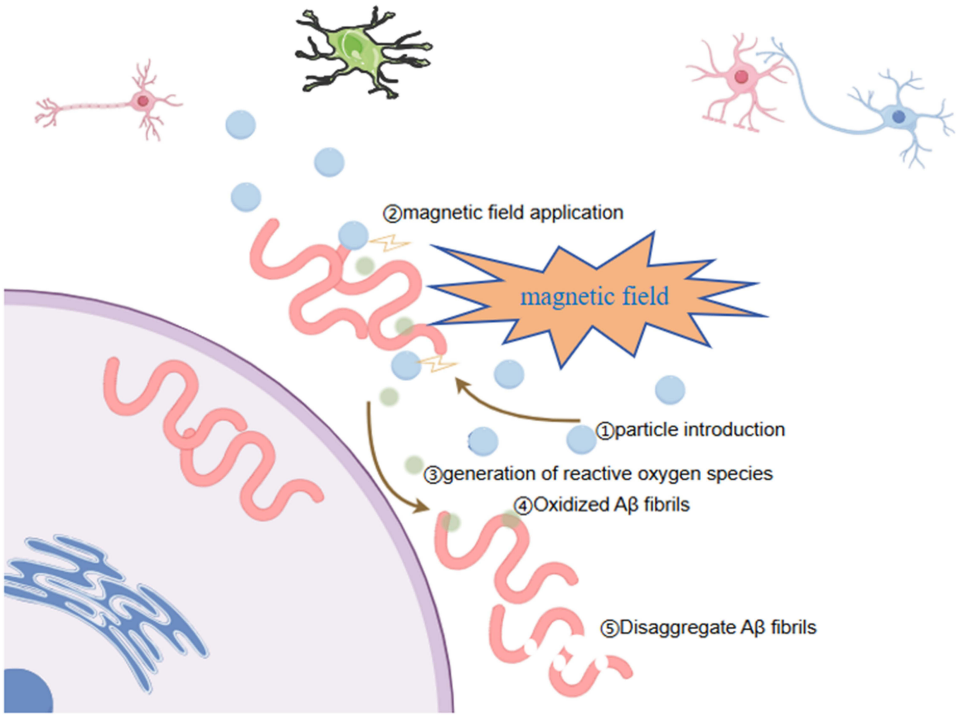

Figure 5 Schematic diagram of magnetic nanoparticles dissociating Aβ fibrils in Alzheimer's disease.

Moreover, the application of MNPs extends to the modulation of calcium signaling pathways in endothelial cells, which is crucial for neurovascular coupling and overall brain health. By applying magnetic fields, researchers have been able to influence calcium ion channel activity, thus opening new avenues for treating vascular dysfunctions associated with neurodegenerative disorders.[47] MNPs have shown great potential in the treatment of neurological diseases by enabling precise drug delivery within the CNS. Recent advancements in intrathecal magnetic drug targeting (IT-MDT) have demonstrated that MNPs can be localized at specific spinal sites using external magnetic fields. This technique has been successfully applied in animal models, resulting in targeted drug delivery with minimal systemic toxicity.[64] The ability to manipulate biological processes through external magnetic fields highlights the versatility of MNPs in addressing complex neurological conditions. Additionally, the integration of MNPs with advanced imaging techniques such as magnetic resonance imaging (MRI) allows for real-time monitoring of disease progression and treatment efficacy, further enhancing the clinical utility of these nanoparticles in neurological research.[65]

Behavioral Experimental Results

The behavioral outcomes of animal models treated with magnetic nanoparticles have provided significant insights into their therapeutic potential in neurodegenerative diseases. In studies involving PD models, the transplantation of magnetic nanoparticle-labeled human adipose-derived stem cells resulted in notable improvements in motor functions, as evidenced by behavioral tests such as the rotarod performance and apomorphine-induced rotation tests.[63] These behavioral assessments indicate that the targeted delivery of stem cells via magnetic guidance not only enhances their viability and integration into the host tissue but also leads to functional recovery in motor activities, a critical aspect of PD management.

Similarly, in models of Alzheimer's disease, the application of magnetoelectric nanoparticles has been shown to significantly reduce amyloid plaque levels and associated neurotoxicity, which correlates with improved cognitive performance in behavioral tasks.[62] The ability to dissociate amyloid aggregates under magnetic stimulation suggests a dual role for these nanoparticles in both therapeutic intervention and monitoring disease progression. Behavioral assessments in these models have underscored the importance of integrating objective measures of function with biochemical analyses, providing a comprehensive understanding of treatment efficacy.

Additionally, the use of magnetic nanoparticles in hyperthermia treatments has demonstrated significant behavioral outcomes in various cancer models. The application of alternating magnetic fields to induce localized heating in tumors has been shown to enhance the therapeutic response, leading to reduced tumor growth and improved survival rates in treated animals.[66] These findings highlight the multifaceted role of magnetic nanoparticles not only in neurodegenerative disease models but also in cancer therapy, showcasing their potential as a versatile platform for improving treatment outcomes across various pathological conditions.

Latest Advances in Mechanistic Research

Recent mechanistic studies involving magnetic nanoparticles have elucidated their diverse roles in modulating cellular processes relevant to neurodegenerative diseases. One significant advancement is the understanding of how magnetic fields can influence cellular signaling pathways. For instance, research has shown that applying a magnetic field can modulate calcium signaling in endothelial cells, which is critical for maintaining neurovascular integrity and function.[47] This modulation is particularly relevant in the context of aging and neurodegenerative disorders, where calcium dysregulation is a common feature.

Furthermore, the use of magnetic nanoparticles to activate specific signaling pathways has been explored in the context of stem cell differentiation. Studies have demonstrated that magnetic nanoparticles can be employed to remotely activate Wnt signaling pathways in neuronal precursor cells, promoting dopaminergic differentiation.[67] This innovative approach highlights the potential of using MNPs not just for drug delivery but also as tools for precise control over cellular behavior, which could revolutionize regenerative medicine strategies for neurodegenerative diseases.

In addition to cellular signaling, the interaction of magnetic nanoparticles with pathological proteins has been a focal point of recent research. The ability of magnetoelectric nanoparticles to dissociate amyloid aggregates in Alzheimer's disease models under magnetic stimulation has opened new avenues for therapeutic intervention.[62] Understanding the underlying mechanisms of these interactions is crucial for developing effective treatments that target the root causes of neurodegenerative diseases rather than merely alleviating symptoms.

Overall, the integration of magnetic nanoparticles in animal models has provided valuable insights into their therapeutic mechanisms, behavioral outcomes, and potential applications in treating complex neurological disorders. As research continues to evolve, the promise of MNPs in enhancing drug delivery, modulating cellular processes, and improving patient outcomes in neurodegenerative diseases becomes increasingly evident. As shown in Table 3, the application of magnetic

Table 3 This Table Summarizes the Applications of Magnetic Nanoparticles in Animal Models of Neurodegenerative Diseases and Cancer, Focusing on Signaling Pathway Activation and Pathological Protein Clearance

Application Area	Animal Model	Type of Magnetic Nanoparticles	Experimental Method	Results and Effects
Parkinson's Disease (PD)	Mouse model (6-OHDA-induced)	Magnetic nanoparticle-labeled human adipose-derived stem cells (hASCs)	MRI imaging and behavioral tests	Magnetic nanoparticles enhanced the targeted delivery of hASCs to the mouse brain, significantly recovering motor functions, including rotation and rotarod performance.[63]
Glioblastoma (GBM)	Rat model (C6 cell-induced glioblastoma)	Aminosilane-coated superparamagnetic iron oxide nanoparticles (SPIONsAmin)	Magnetic hyperthermia and bioluminescence imaging	Magnetic hyperthermia significantly increased tumor cell death in the glioblastoma model, showing the potential of SPIONsAmin for cancer treatment.[66]
Alzheimer's Disease (AD)	Mouse model	Magnetoelectric nanoparticles (BCFO, BiFeO3-coated CoFe2O4 nanoparticles)	Magnetoelectric effect and low-frequency magnetic field treatment	BCFO nanoparticles successfully dissociated β-amyloid aggregates under a low-frequency magnetic field, alleviating Aβ-associated neurotoxicity, showing potential for AD treatment.[62]
Parkinson's Disease Neural Differentiation	Mouse model (SH-SY5Y cells)	Magnetic nanoparticles-labeled neural precursor cells	Magnetic field stimulation and Wnt signaling pathway activation	Remote activation of the Wnt signaling pathway led to enhanced dopaminergic marker expression in precursor cells, promoting differentiation.[67]

nanoparticles in neurodegenerative disease models is not limited to the activation of signaling pathways but also involves the clearance of pathological proteins, demonstrating their potential in the treatment of various neurological disorders.

Toxicity Leads to Cell Damage

MNPs are increasingly used in biomedical applications, but their toxicity has raised significant concerns. Studies have shown that iron oxide nanoparticles (IONPs), due to their unique magnetic, catalytic properties and nanoscale size, can induce severe oxidative stress in vivo, leading to cellular damage and organ dysfunction.[39,68] Particularly, ultrasmall iron oxide nanoparticles (eg, 2.3 and 4.2 nm) exhibit significant toxicity by generating reactive oxygen species (ROS), such as hydroxyl radicals (·OH), which exacerbate oxidative damage within cells.[69] This oxidative stress leads to cellular damage primarily through lipid peroxidation, DNA damage, and mitochondrial dysfunction, ultimately resulting in cell death.[70] For example, in mouse experiments, intravenously injected 2.3 and 4.2 nm ultrasmall iron oxide nanoparticles induced acute oxidative stress in multiple organs, particularly the heart, which showed significant ·OH generation, associated with acute cardiac failure and death.[69]

Furthermore, the toxicity of iron oxide nanoparticles is not only related to the release of iron ions but also closely associated with their size, surface properties, and dosage. Research has found that, at the same dose, ultrasmall iron oxide nanoparticles are more likely to induce severe toxic reactions compared to larger particles, with toxicity strongly linked to the accelerated release of Fe^2+ and the Fenton reaction.[69,70] Additionally, iron oxide nanoparticles have been shown to cause significant oxidative stress in aquatic organisms, disrupting their metabolic processes and leading to cellular damage and tissue injury.[71]

In conclusion, while iron oxide nanoparticles hold great promise for medical imaging and therapy, their associated toxicity, particularly cell damage induced through oxidative stress and ferroptosis, remains a critical issue that requires urgent attention.[39,71]

Clinical Translation and Prospects

Although MNPs and static EMF offer an appealing "contact-free" lever for remote neural commitment, the current literature is split along a three-dimensional axis of dose, exposure window and cell source. Marcus et al reported that uncoated maghemite at 0.25 mg mL^{-1} induces no acute cytotoxicity yet shortens PC12 neurite length by 30% and depolarises mitochondrial membranes.[72] Semeano et al observed that 0.5 wt % MNP enhances neuro-migration, whereas ≥2 wt % triggers Reactive Oxygen Species (ROS) overload and cell-cycle arrest, indicating a razor-thin margin between pro-maturation and pro-oxidative outcomes.[73] More critically, the same group showed that 0.4 T EMF expands βIII-tubulin+ progenitors during Embryonic Stem Cell (ESC) neural induction, but switches to a 2-fold up-regulation of the astrocytic marker GFAP and concomitant neuronal suppression once cells become adherent—a "stage-dependent fate shift". In human induced Pluripotent Stem Cell (hiPSC) derived dopaminergic neurons, identical field conditions alkalinise lysosomes, raise ROS by 58% and depolarise membrane potential, implying a selective vulnerability of dopaminergic sub-populations.[73] Divergent laboratories have reached opposite conclusions ("completely safe" vs "functionally compromised") within the 0.1–0.4 T range, and most studies omit systematic comparisons of field orientation, exposure timing and particle aggregation state, undermining reproducibility. These controversies underscore the urgent need for a standardised framework that integrates real-time oxidative-stress and electrophysiological readouts before magnetic neuromodulation can progress from proof-of-concept to clinical translation.

The translation of innovative medical technologies from the laboratory to clinical practice faces numerous challenges that can impede their successful implementation. A significant barrier is the complexity of integrating new technologies into existing healthcare systems, which often involves navigating a maze of regulatory requirements, reimbursement policies, and clinical workflows. For instance, precision medicine, which relies on genomic data to tailor treatments, requires the integration of diverse data sources, including clinical, imaging, and biobank data. This integration is not only technically challenging but also raises ethical concerns regarding patient privacy and data security.[74] Moreover, the need for user-friendly decision support tools for both patients and healthcare providers is critical, as these tools can facilitate informed decision-making and improve patient outcomes. However, developing such tools involves significant investment in research and development, which may not always be feasible for smaller institutions or startups.[74]

Another challenge is the variability in patient responses to new therapies, which can complicate clinical trials and the subsequent adoption of these therapies. For example, immunomodulatory therapies, which have shown promise in treating cancers and autoimmune diseases, face hurdles related to precision dosing and off-target effects that can lead to adverse reactions.[75] Furthermore, the manufacturing processes for these therapies must be scalable and reproducible, ensuring that they meet the stringent quality standards required for clinical use. This is particularly pertinent in the case of cell-based therapies and biologics, where the complexity of the products can lead to variability in efficacy and safety.[76]

The clinical translation of nanomedicines also presents unique challenges, including the need for comprehensive preclinical and clinical evaluations to establish safety and efficacy profiles.[76] The regulatory landscape for nanomedicines is still evolving, and there is a need for clear guidelines that address the specific characteristics and risks associated with these novel therapies. Additionally, the high costs associated with developing and bringing new therapies to market can be a deterrent for researchers and companies, particularly in the context of funding constraints and the uncertain reimbursement landscape.[76]

Lastly, the rapid pace of technological advancement in the field of medicine necessitates continuous education and training for healthcare professionals. As new technologies emerge, there is a pressing need for healthcare providers to stay abreast of these developments to ensure they can effectively utilize them in patient care. This requires investment in training programs and resources, which may not always be prioritized within healthcare institutions.[77]

The future of clinical research is poised to be shaped by several key trends that reflect the evolving landscape of healthcare. One promising direction is the increasing emphasis on personalized medicine, which aims to tailor treatments to individual patient characteristics, including genetic, environmental, and lifestyle factors. This approach has the potential to enhance treatment efficacy and reduce adverse effects, ultimately leading to better patient outcomes. Ongoing research in genomics and biotechnology is expected to yield new biomarkers that can guide therapeutic decisions, particularly in oncology and rare diseases.[78]

Another important area of focus is the integration of artificial intelligence (AI) and machine learning into clinical practice. These technologies hold the promise of revolutionizing diagnostics, treatment planning, and patient monitoring by enabling the analysis of vast amounts of clinical data to identify patterns and predict outcomes. For instance, AI algorithms can assist in the interpretation of imaging studies, improving the accuracy of diagnoses and facilitating timely interventions.[79]

The prospects for technological development in healthcare are promising, driven by rapid advancements in various fields, including biotechnology, information technology, and materials science. One of the most significant trends is the growing adoption of digital health technologies, which encompass telemedicine, mobile health applications, and wearable devices. These technologies have the potential to enhance patient engagement, improve access to care, and facilitate remote monitoring of chronic conditions.[79]

In the realm of therapeutics, the development of advanced drug delivery systems, such as nanocarriers and targeted delivery mechanisms, is expected to enhance the efficacy and safety of treatments. For example, the use of nanoparticles for targeted drug delivery can improve therapeutic outcomes while minimizing side effects, particularly in cancer therapy.[33] Ongoing research in this area will focus on optimizing the design and functionality of these delivery systems to ensure their successful translation into clinical practice.

In conclusion, the landscape of clinical translation and technological development is rapidly evolving, with numerous opportunities and challenges ahead. By addressing the barriers to clinical application, focusing on innovative research directions, and embracing technological advancements, the healthcare sector can improve patient outcomes and enhance the overall quality of care.

Conclusion

In conclusion, MNPs have shown tremendous potential in modulating neuroplasticity and promoting neural regeneration, particularly in the treatment of neurodegenerative diseases such as AD and PD. This review discussed the mechanisms by which MNPs enhance neural repair and functional recovery, including synaptic remodeling, neurotrophic signaling, and

cellular endocytosis. Furthermore, the review highlighted how surface modifications of MNPs can improve their compatibility with neural cells, enhancing their delivery efficiency and therapeutic efficacy.

While current studies suggest that MNPs can significantly enhance neuronal growth and synaptic connectivity, concerns regarding cytotoxicity, immune reactions, and crossing the blood-brain barrier remain major obstacles. For instance, low doses of MNPs have been found to promote neuronal growth, while higher doses may lead to cytotoxicity. Thus, careful dose selection will be crucial in future applications. Current limitations include the reliance on animal models and the early stage of clinical trials. Specifically, achieving a balance between therapeutic efficacy and safety, as well as ensuring long-term therapeutic outcomes, are critical issues that require further investigation for clinical translation.

Future research should focus on addressing these challenges, particularly in preclinical trials, by establishing standardized evaluation systems to better understand the safety and efficacy of MNPs for neurotherapeutic purposes. Moreover, interdisciplinary collaboration—especially between neurologists, materials scientists, and toxicologists—will be essential in advancing the clinical translation of MNP-based neurotherapies. Unlike existing reviews, this review explores not only the potential of magnetic nanoparticles in neural plasticity but also integrates recent mechanistic and translational advancements, with a particular focus on overcoming the blood-brain barrier and improving cell-specific delivery, offering new perspectives for future clinical applications. By synthesizing recent mechanistic and translational advancements, this review provides a timely framework for future research, helping to drive the clinical integration of magnetic nanoparticle-based neurotherapies.

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Disclosure

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