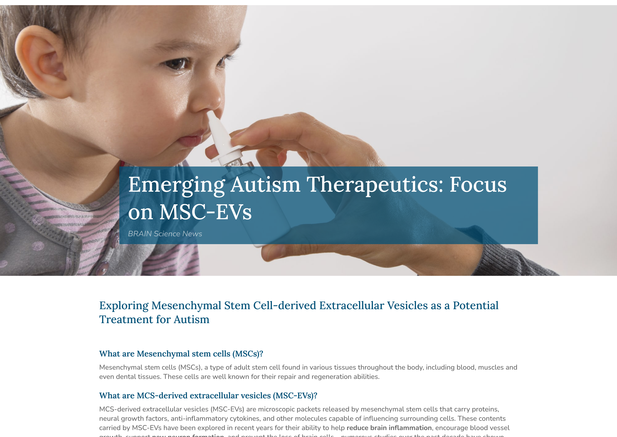


Emerging Autism Therapeutics: Focus on MSC-EVs

BRAIN Science News

Exploring Mesenchymal Stem Cell-derived Extracellular Vesicles as a Potential Treatment for Autism

What are Mesenchymal stem cells (MSCs)?

Mesenchymal stem cells (MSCs), a type of adult stem cell found in various tissues throughout the body, including blood, muscles and even dental tissues. These cells are well known for their repair and regeneration abilities.

What are MCS-derived extracellular vesicles (MSC-EVs)?

MCS-derived extracellular vesicles (MSC-EVs) are microscopic packets released by mesenchymal stem cells that carry proteins, neural growth factors, anti-inflammatory cytokines, and other molecules capable of influencing surrounding cells. These contents carried by MSC-EVs have been explored in recent years for their ability to help **reduce brain inflammation**, encourage blood vessel growth, support **new neuron formation**, and prevent the loss of brain cells – numerous studies over the past decade have shown that MSC-EVs can improve brain function in experimental animals and hold promise for treating conditions like Alzheimer's, Parkinson's, brain injuries, schizophrenia, and autism.

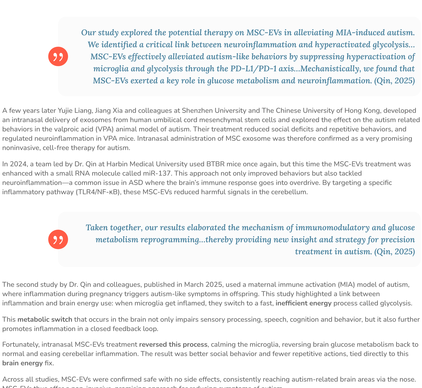
Unlike traditional stem cell therapies, which implant living cells that may integrate into the body, MSC-EVs provide a cell-free alternative, delivering their therapeutic contents without risks like immune rejection or uncontrolled growth, offering a safer and more consistent option.

> *"Since no negative symptoms were detected following intranasal administration…efficacy of this non-invasive therapeutic approach should be further explored in upcoming clinical studies for the amelioration of behavioral symptoms in patients suffering from schizophrenia and Autism Spectrum Disorder" (Harrell, 2021)*

Intranasal Delivery

The intranasal delivery method, via nasal drops or aerosol spray, stands out for brain-related conditions like autism because it **bypasses the blood-brain barrier**—a protective shield around the brain—allowing MSC-EVs to reach critical areas of the brain such as the frontal cortex and cerebellum.

This summary covers three studies that tested MSC-EVs in mouse models of autism, revealing how they address symptoms and underlying issues. Together, these studies demonstrate that MSC-EVs can significantly **reduce autism-related symptoms** in animal experiments, including social difficulties, repetitive behaviors, and communication challenges.



Studies on MSC-EVs in autism models

The first studies, published between 2016-2018 and carried out by Nisim Perets, Stav Hertz, M. London and Daniel Offen at Tel Aviv University and Hebrew University, Jerusalem, used BTBR mice strain, bred to mimic human ASD traits. After delivering MSC-EVs through the nose, the researchers observed improved social interactions, less repetitive grooming, better vocal communication, and enhanced maternal care in female mice. The MSC-EVs reached key brain regions within 96 hours and produced lasting benefits even after clearing from the system. In a later study, published in 2020, the team demonstrated beneficial effect MSC-EVs in a mouse model of autism carrying the Shank3 mutation (Shank3B KO).

> *Our study explored the potential therapy on MSC-EVs in alleviating MIA-induced autism. We identified a critical link between neuroinflammation and hyperactivated glycolysis… MSC-EVs effectively alleviated autism-like behaviors by suppressing hyperactivation of microglia and glycolysis through the PD-L1/PD-1 axis…Mechanistically, we found that MSC-EVs exerted a key role in glucose metabolism and neuroinflammation. (Qin, 2025)*

A few years later Yujie Liang, Jiang Xia and colleagues at Shenzhen University and The Chinese University of Hong Kong, developed an intranasal delivery of exosomes from human umbilical cord mesenchymal stem cells and explored the effect on the autism related behaviors in the valproic acid (VPA) animal model of autism. Their treatment reduced social deficits and repetitive behaviors, and regulated neuroinflammation in VPA mice. Intranasal administration of MSC exosome was therefore confirmed as a very promising noninvasive, cell-free therapy for autism.

In 2024, a team led by Dr. Qin at Harbin Medical University used BTBR mice once again, but this time the MSC-EVs treatment was enhanced with a small RNA molecule called miR-137. This approach not only improved behaviors but also tackled neuroinflammation—a common issue in ASD where the brain's immune response goes into overdrive. By targeting a specific inflammatory pathway (TLR4/NF-κB), these MSC-EVs reduced harmful signals in the cerebellum.

> *Taken together, our results elaborated the mechanism of immunomodulatory and glucose metabolism reprogramming…thereby providing new insight and strategy for precision treatment in autism. (Qin, 2025)*

The second study by Dr. Qin and colleagues, published in March 2025, used a maternal immune activation (MIA) model of autism, where inflammation during pregnancy triggers autism-like symptoms in offspring. This study highlighted a link between inflammation and brain energy use: when microglia get inflamed, they switch to a fast, **inefficient energy** process called glycolysis.

This **metabolic switch** that occurs in the brain not only impairs sensory processing, speech, cognition and behavior, but it also further promotes inflammation in a closed feedback loop.

Fortunately, intranasal MSC-EVs treatment **reversed this process**, calming the microglia, reversing brain glucose metabolism back to normal and easing cerebellar inflammation. The result was better social behavior and fewer repetitive actions, tied directly to this **brain energy** fix.

Across all studies, MSC-EVs were confirmed safe with no side effects, consistently reaching autism-related brain areas via the nose. MSC-EVs thus offer a non-invasive, promising approach for reducing symptoms of autism.

Future perspectives

Intranasal administration of stem cell-derived exosomes shows promise for treating neurological diseases due to their non-invasive nature and high brain infiltration. However, challenges remain, including the need for efficient methods to collect sufficient exosomes, as current techniques yield limited amounts. A clear quality control standard and optimal patient dosage are also needed, along with effective tracking methods. Additionally, the potential adverse effects of exosomes require further study. Extensive research and large-scale trials are essential for advancing exosome therapy.

We are hopeful that the encouraging findings from animal studies, as well as human trials currently exploring their benefits of this therapy in disorders such as epilepsy and dementia, will pave the way for human autism studies.

For more potential therapeutics for autism see our database on Drug Repurposing for Autism

KEY HIGHLIGHTS

- **What MSC-EVs Are**: Tiny vesicles from stem cells carrying bioactive molecules, safer than live cell injections.
- **Why Intranasal Delivery**: Bypasses the blood-brain barrier, targeting brain areas like the cortex and cerebellum.
- **2016-2024 Findings**: MSC-EVs improved social skills, reduced repetitive behavior, and enhanced communication in three different models of autism (BTBR, VAP, SHANK3b KO), reaching key brain regions such as frontal cortex and cerebellum, and reducing inflammation.
- **2025 Findings**: In a MIA mice model MSC-EVs corrected microglial metabolic switch (glycolysis) that was causing impaired energy utilization and neuroinflammation. The reprogramming of glucose metabolism by MSC-EVs led to improvement in symptoms.
- **Safety and Potential**: No known adverse effects; effective brain delivery suggests a practical ASD treatment.
- **Human Progress**: Trials, including an epilepsy study ending in 2025, are testing intranasally delivered EVs in humans.

Citations

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