E-Poster

EP-991

Intranasal and Intracerebroventricular Administration of Metabolic Glycoengineered NSCs After Cardiac Arrest

Topic: Miscellaneous

Xiaofeng Jia[1], Xiao Liu[2], Subash Marasini[2]

[1]*Neurosurgery, Orthopaedics; Anatomy & Neurobiology, University of Maryland School of Medicine, Baltimore, United States*
[2]*Neurosurgery, University of Maryland School of Medicine, United States*

BACKGROUND

Cardiac arrest (CA)-induced global cerebral ischemia is a leading cause of neurological deficits with limited effective therapies. Transplantation of neural stem cells (NSCs) holds potential as a promising therapeutic strategy. Unfortunately, this potential is hindered by a lack of optimal and consistent delivery methods as well as by limited functionality of the cells following *in vivo* transplantation. Recent advances in metabolic glycoengineering (MGE) improve cell viability and ultimately boost the therapeutic effectiveness of transplanted NSCs through modifying their glycans. This report compared the effects of different delivery routes for this innovative approach of using MGE modified NSCs (MGE-NSCs) to treat ischemic brain injury post-CA.

METHODS

MGE-NSC therapy was used to treat rats with 9 min- or 11 min-asphyxia CA, representing severe and very severe brain injury after CA, by comparing randomly selected intranasal and intracerebroventricular (ICV) delivery administered 3 h after resuscitation. Neurological deficit scores (NDS), and neurobehavior tests were compared 3 d and 4 w after CA. Cresyl violet staining was utilized to measure neuron ischemia. Tracking of transplanted MGE-NSCs was evaluated by immunofluorescence staining.

RESULTS

The ICV administration route exhibited superior outcomes in the early phase of recovery compared to intranasal route, showing better NDSs shortly after resuscitation. Three days post-resuscitation, the transplanted MGE-NSCs predominantly migrated to the cortex and hippocampus, with a higher percentage of MGE-NSCs observed in the ICV group compared to intranasal administration. However, intranasal administration surpassed the ICV route in late stage recovery. Specifically, at four weeks, rats treated with intranasal-NSCs showed superior locomotor function and reduced anxiety-/depression-related behaviors compared to those treated with ICV-NSC therapy. A greater number of MGE-NSCs survived in the intranasal group, with a predominant distribution to additional regions such as cerebellum and brainstem at week 4 along with decreased microglia recruitment. Both intranasal and ICV administration of MGE-NSCs promoted neuron differentiation, vascular angiogenesis, and synaptic plasticity. Notably, intranasal-NSC therapy generally exhibited comparable or superior effectiveness to ICV-NSCs at a later stage, as indicated by these histological measurements.

CONCLUSION

Our study showcased the remarkable advantages of administering MGE-NSCs through ICV in short-term effects and intranasal routes in long-term effects for brain injury after CA. These findings underscore the efficacy of MGE-NSC therapy in enhancing recovery following CA, highlighting the tailored treatment approaches for different phases of post-resuscitation care.

Statement of Disclosures

This work was partially supported by R01NS125232 and R01NS110387 from the National Institute of Neurological Disorders and Stroke, and 2024-MSCRFD-6401 from Maryland Stem Cell Research Fund (all to Xiaofeng Jia).

Doi: 10.5606/archisprm.2026.EP-991

Corresponding Author:
Xiaofeng Jia
Neurosurgery, Orthopaedics; Anatomy & Neurobiology, University of Maryland School of Medicine, Baltimore, United States
Email: xjia@som.umaryland.edu