MicroRNA-29a-5p Protects Against Cerebral Ischemia and Reperfusion Injury After Endovascular Thrombectomy in Acute Stroke

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Introduction

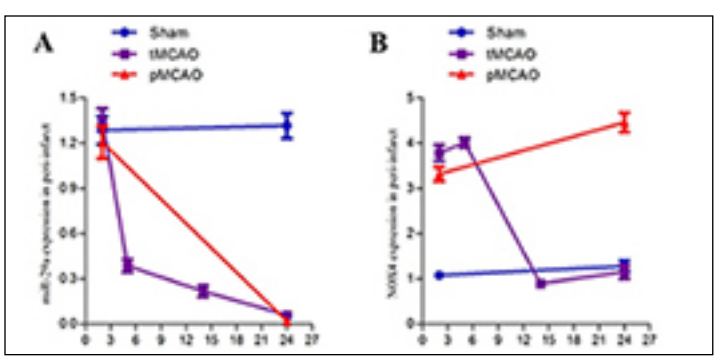
Cerebral ischemia and reperfusion (I/R) injury occurs after endovascular mechanical thrombectomy for patients with acute ischemic stroke. MicroRNA-29a (miR-29a) is involved in regulating cerebral ischemia process, but its underlying mechanism is unclear. This study investigated the role of miR-29a in cerebral I/R injury after mechanical reperfusion in transient middle cerebral artery occlusion (tMCAO) model.

Methods

The intraluminal filament tMCAO model was established in male rats with 2 hour ischemia followed by reperfusion. The expression of miR-29a in the infarction core and peri-infarct cortex and whole blood were quantified at 0, 3, 12, and 24 hour after reperfusion. Permanent MCAO model was also evaluated. Intravenous miR-29a-5p agomir was delivered immediately after reperfusion or before reperfusion. Infarct volume, brain water content, neurological score and blood-brain barrier damage, and the expression of miR-29a-5p, NADPH oxidase (NOX4), aquaporin-4 and caspase-3 were determined at 24-hour after ischemia.

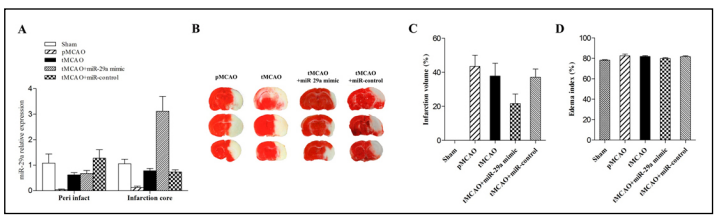
Results

MiR-29a-5p levels in the infarction core and peri-infarct cortex were significantly decreased at 3 hours after reperfusion in tMCAO group. The decreased levels of miR-29a-5p in brain tissue and whole blood lasted for 24 hours after ischemia.

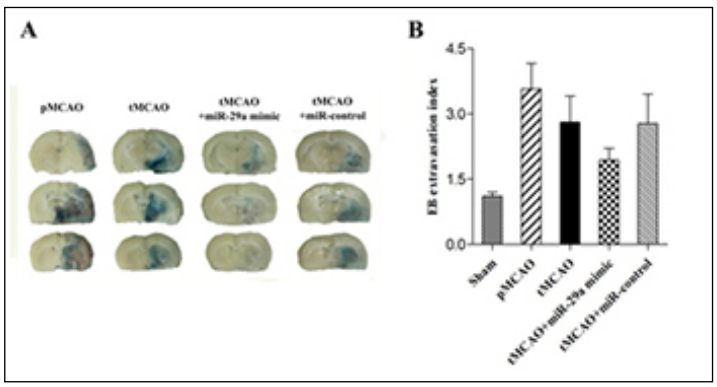


Results

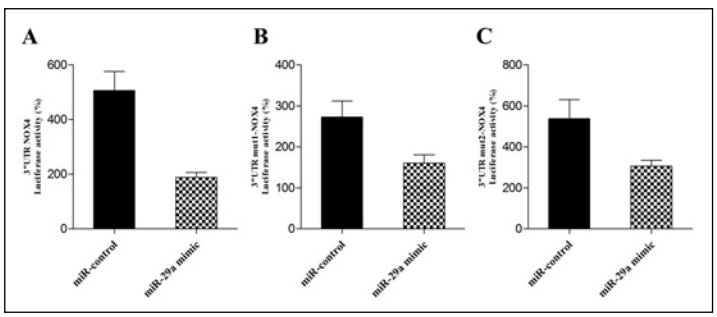
Intravenous miR-29a-5p agomir reduced infarct volume ($p<0.01$) at 24-hour after ischemia compared to the tMCAO group.



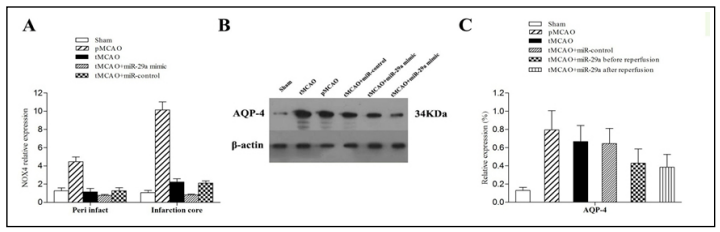
MiR-29a-5p agomir attenuated brain edema and reduced reperfusion-induced blood-brain barrier breakdown, resulting in improved neurological outcome ($p<0.05$).



Dual-luciferase reporter system showed that NOX4 was the direct target gene of miR-29a-5p.



Intravenous miR-29a-5p agomir increased the expression of miR-29a-5p and suppressed the up-regulation of NOX4, AQP4, caspase-3 in both the infarction core and peri-infarct cortex compared with the tMCAO group ($p<0.05$).



Conclusions

MiR-29a-5p overexpression protects against cerebral I/R injury via downregulating NOX 4. Infusion of miR-29a-5p agomir immediately after reperfusion and before reperfusion represents a novel adjunctive therapeutic strategy to improve outcome after mechanical reperfusion for acute stroke.

References

Ouyang YB, Xu L, Lu Y, et al. Astrocyte-enriched miR-29a targets PUMA and reduces neuronal vulnerability to forebrain ischemia. Glia 2013;61:1784-94.
Wang Y, Huang J, Ma Y, et al. MicroRNA-29b is a therapeutic target in cerebral ischemia associated with aquaporin 4. J Cereb Blood Flow Metab. 2015;35:1977-1984.

Learning Objectives

By the conclusion of this session, participants are able to: 1) Describe the role of miR-29a-5p in cerebral ischemia and reperfusion injury after mechanical reperfusion in transient middle cerebral artery occlusion animal model. 2) Discuss the mechanism of miR-29a-5p as a potential neuroprotective target. 3) Identify an effective treatment by intravenous infusion of miR-29a-5p agomir immediately after reperfusion and before reperfusion to improve outcome after mechanical reperfusion for acute stroke in rat models.