Silencing miR-181a produces neuroprotection against hippocampus neuron cell apoptosis post-status epilepticus in a rat model and in children with temporal lobe epilepsy

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Received October 10, 2015
Accepted December 12, 2015
Published February 19, 2016
DOI http://dx.doi.org/10.4238/gmr.15017798

ABSTRACT. Epilepsy is one of the most frequent neurological disorders. Recently, the regulation of microRNAs was found to be associated with epilepsy, but the molecular mechanism by which microRNA influences epilepsy process remains to be unveiled and the development of microRNA-based therapy requires more intensive research. In this study, five microRNAs with potential relevance to epilepsy were initially chosen: miR-132, miR-146a, miR-181a, miR-34a, and miR-124. Twenty-five children who were patients with epilepsy were selected as subjects to obtain tissue samples for the study. The miRNA-181a, which represented the most increased fold-changes in clinical samples, were then selected for further function study in mouse model. The temporal lobe epilepsy (TLE) model, along with lithium-pilocarpine-induced status epilepticus (SE), was established in Sprague-Dawley rats. The antagomir of miR-181a was used to determine the role of miR-181a in cell apoptosis. Analyses
were conducted to determine the expression levels of miR-181a, neuronal apoptosis in post-SE, and activated caspase-3. We found evidence of significant time dependent up-regulation of miR-181a amongst post-SE rats and TLE on 24 h (4.47 ± 0.35), 7 days (4.85 ± 0.53), and 2 weeks (5.66 ± 0.64). Experiments with the miR-181a antagomir showed that this particular miRNA led to the inhibition of the protein expression of caspase-3, and was up-regulated in the course of seizure-induced neuronal apoptosis. This study provided evidence that targeting miR-181a leads to a neuroprotective response and is linked to an increase in the activation of the caspase-3 protein. These findings suggest that miR-181a may serve as a promising therapeutic target for epilepsy.

**Key words:** MicroRNA; Epilepsy; Hippocampus; Apoptosis; Status epilepticus