SESN3 and seizures following brain injury

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Seizures are the most common neurological sequelae following brain injury such as stroke and traumatic brain injury (TBI). The mechanisms of seizure/epilepsy in these acute neurological disorders remain unclear. Recent studies indicated that epilepsy could be mediated by energy metabolism related proteins such as Sestrin3 (SESN3). The present study attempted to reveal the contribution of SESN3 to seizure generation in cerebral ischemia in diabetic condition and TBI. Transient global ischemia was produced in adult rats and mice. Diabetes was induced by i.p. injection of 50 mg/kg streptozotocin (STZ). TBI was induced in mice using the control cortical impact method. The seizure activity was defined by the Racine scale III-V. The neuronal death in the brain was determined by hematoxylin eosin staining. The expression levels of SESN3 were analyzed by western blotting and immunohistochemistry. The neuronal excitability was recorded using electrophysiological approaches. The blood glucose levels was >300 mg/dL in animals one week after STZ injection. The seizure rate was significantly increased after 15 min ischemia. No obvious neuronal damage was observed in hippocampus and cerebral cortex. SESN3 expression in hippocampus was significantly increased in diabetic animals with post-ischemia seizures. The potassium channel expression and currents in hippocampal neurons were decreased and neuronal excitability increased in these animals. The seizure rate was significantly decreased from 60% of wild type mice to 15% of SESN3 knockout mice after 15 min ischemia. In mice with TBI, the seizure was induced by GABAA receptor blocker Pentyleneletrazole (PTZ, 40 mg/Kg, i.p.). One week after TBI, the latency of seizure onset was reduced in SESN3 KO mice; the input resistance of hippocampal neurons decreased and the rheobase increased in these KO animals. These data suggest that SESN3 involved in seizure generation after brain injury by affecting neuronal excitability.

Recent publications:

1. 1. Todd O McKinley, Zhigang Lei, Yannik Kalbas, Fletcher A White, Zhongshan Shi, Fan Wu, Zao C. Xu and Richard B Rodgers (2018) Blood purification by nonselective hemoadsorption prevents death after traumatic brain injury and hemorrhagic shock in rats. J Trauma Acute Care Surg. 85(6):1063-1071.
2. 2. Xia Zhigang Lei, Zhongshan Shi, Dave Guo, Henry Su, Yiwen Ruan and Zao C Xu (2016) Enhanced autophagy signaling in post-ischemia seizures under diabetic conditions. Brain Res. 1643:18-26.
3. 3. Lei Z, Zhang H, Liang Y and Zao C Xu (2016) Reduced expression of IA channels is associated with post-ischemic seizures. Epilepsy Res. 124:40-48.
4. 4. Lei Z, Zhang H, Liang Y, Cui Q, Xu Z and Xu Z C (2014) Reduced expression of IA channels is associated with post-ischemic seizures in hyperglycemic rats. J. Neurosci Res. 92(12):1775-1784.
5. 5. Deng L, Deng P, Ruan Y, Xu Z C, Liu N, Smith G and Xu X M (2013) A novel growth-promoting pathway formed by GDNF-overexpressing schwann cells promotes propriospinal axonal regeneration, synapse formation, and partial recovery of function after spinal cord injury. J. Neurosci. 33(13):5655-5667

Biography

Zao C. Xu is a Professor in Indiana University School of Medicine, USA. He has more than 30 years of experience in Neuroscience research using electrophysiological, morphological and molecular biological approaches. The major research projects in his laboratory are the mechanisms underlying the neuronal injury/survival after cerebral ischemia and traumatic brain injury and the mechanisms of seizure/epilepsy following acute neurological disorders such as stroke and traumatic brain injury.

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