快了细胞凋亡。

本研究发现,在 PTZ 点燃 SE 后激活了抗凋亡蛋白 XIAP 及 XIAP mRNA 在海马神经元中的表达;rHuEPO 干预后上调了 XIAP、XIAP mRNA 的表达,减少了神经元的凋亡,提示:rHuEPO 可以调控 XIAP 的表达,借以发挥抗凋亡的神经保护作用。有实验证明,EPO 也能够通过 JAK/STAT 信号、PKC、NF-κB 等[12,13]途径发挥保护作用。故本实验用 PI3K 抑制剂 LY294002 进一步验证 rHuEPO 对 XIAP 的调控是否通过了 PI3K/Akt 通路。结果显示给予 LY294002 进行阻断后,增加了海马神经元的凋亡,海马神经元内 XIAP、XIAP mRNA 表达显著减少,进一步佐证了 rHuEPO 通过 PI3K/Akt 途径对线粒体凋亡途经的相关调控因子 XIAP 进行了调控,进而介导线粒体凋亡途经,PI3K/Akt 途径是 rHuEPO 发挥神经保护作用的途径之一。但是 Akt 活化后是通过直接磷酸化 XIAP 的 Ser87 位点,还是通过 Akt-IIK-NF-κB-XIAP 途径,亦或是通过 Caspase-9 和第二个线粒体源性 caspase 激活剂(second mitochondrial derived Activa-tor of caspase, Smac/DIABLO)在 XIAP 发挥作用时起到了主要的调节作用等还有待进一步实验验证。

参考文献:

[1] Spandou E, Soubasi V, Papoutsopoulou S, *et al*. Erythropoietin prevents hypoxia/ischemia-induced DNA fragmentation in an experimental model of perinatal asphyxia[J]. Neurosci Lett, 2004,366(1): 24 - 28.

[2] Kaptanoglu E, Solaroglu I, Okutan O, *et al*. Erythropoietin exerts neuroprotection after acute spinal cord injury in rats: effect on lipid peroxidation and early ultrastructural findings[J]. Neurosurg Rev, 2004,27(2): 113 - 120.

[3] Yatsiv I, Grigoriadis N, Simeonidou C, *et al*. Erythropoietin is neuroprotective, improves functional recovery, and reduces neuronal apoptosis and inflammation in a rodent model of experimental closed head injury[J]. FASEB J, 2005,19(12): 1701 - 1703.

[4] Motte J E, da-Silva-Fernandes M J, Marescaux C, *et al*. Effects of pentylenetetrazol-induced status epilepticus on c-Fos and HSP72 immunoreactivity in the immature rat brain[J]. Brain Res Mol Brain Res, 1997,50(1 - 2):79 - 84.

[5] Nadam J, Navarro F,Sanchez P, *et al*. Neuroprotective effects of erythropoietin in the rat hippocampus after pilocarpine-induced status epilepticus[J]. Neurobiol Dis, 2007,25(2):412 - 426.

[6] Qu H, Eloqayli H, Sonnewald U. Pentylenetetrazole affects metabolism of astrocytes in culture[J]. J Neurosci Res, 2005,79(1 - 2):48 - 54.

[7] Cherian L,Goodman J C,Robertson C. Neuroprotection with erythropoietin administration following controlled cortical impact injury in rats[J]. J Pharmacol Exp Ther,2007, 322(2): 789 - 794.

[8] Brines M L, Ghezzi P, Keenan S, *et al*. Erythropoietin crosses the blood-brain barrier to protect against experimental brain injury[J]. Proc Natl Acad Sci U S A, 2000, 97(19):10526 - 10531.

[9] Yano S, Morioka M, Fukunaga K, *et al*. Activation of Akt/protein kinase B contributes to induction of ischemic tolerance in the CA1 subfield of gerbil hippocampu[J]. J Cereb Blood Flow Metab, 2001, 21(4): 351 - 360.

[10] Kilic E, Kilic U, Soliz J, *et al*. Brain-derived erythropoietin protects from focal cerebral ischemia by dual activation of ERK-1/-2 and Akt pathways[J]. FASEB J, 2005, 19(14): 2026 - 2028.

[11] Dan H C, Sun M, Kaneko S, *et al*. Akt phosphorylation and stabilization of X-linked inhibitor of apoptosis protein (XIAP)[J]. J Biol Chem, 2004, 279(7): 5405 - 5412.

[12] Rafiee P, Shi Y, Su J, *et al*. Erythropoietin protects the infant heart against ischemia-reperfusion injury by triggering multiple signaling pathways[J]. Basic Res Cardiol, 2005, 100(3): 187 - 197.

[13] Xu B, Dong G H, Liu H, *et al*. Recombinant human erythropoietin pretreatment attenuates myocardial infarct size: a possible mechanism involves heat shock Protein 70 and attenuation of nuclear factor-kappaB[J]. Ann Clin Lab Sci, 2005, 35(2):161 - 168.

(编辑　吴培红)

《军医大学学报》(英文版)欢迎投稿

Journal of Medical Colleges of PLA 是由 3 所军医大学和南方医科大学共同主办的、国内外公开发行的综合性医学学术类英文期刊,是中国英文版科技论文统计源期刊,并被纳入中文科技期刊数据库、中国期刊网、万方数据库、重庆维普数据库。从 2007 年开始,本刊电子版由全球著名的科技出版集团爱思唯尔(Elsevier)负责海外发行,全文已进入 ScienceDirect 全文数据库,期刊网址 http://www.elsevier.com/locate/jmcpla。国内统一刊号:CN31 - 1002/R,国际标准刊号:ISSN 1000 - 1948。双月刊。设有论著、技术与方法、个案报道、交流等栏目。若无彩图,无需缴纳版面费;亦不收取审稿费;无稿酬。投稿要求:中(或大摘要)、英文稿各 1 份,照片提供 3 份。电子投稿 E-mail:gangela@mail.tmmu.com.cn。照片需以附件形式单独提供 JPG 或 TIF 格式。电子投稿请注明英文版。

联系地址:重庆市沙坪坝区高滩岩第三军医大学学报编辑部(400038)　　**电话**:(023)68752782