

论著

胰岛素样生长因子1对缺血缺氧神经元的保护及其与PI3K信号转导通路的关系

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摘要:

目的: 观察胰岛素样生长因子 1(insulin like growth factor 1, IGF 1)对缺氧缺血神经元的保护作用并探讨其可能的作用机制。方法: 构建体外培养的神经元氧糖剥夺模型 (oxygen and glucose deprivation, OGD), 第7天将培养的神经元分为8组(4组暴露于氧糖剥夺, 另4组非暴露), 分别施加纯化的IGF 1单体, 并观察加入PI3K和MAPK信号通路的特异性阻断剂LY294002和PD98059的效应, 利用MTT法分别观察各组神经元的细胞活性; Western印迹观测不同干预因素下Akt 和 p Akt蛋白的表达情况。结果: 神经元正常组和缺血缺氧模型组, 加入IGF 1后细胞增殖活性均显著升高 (P<0.05); 而同时加入IGF 1和LY294002后, IGF 1促神经元活性的作用被明显抑制 (P<0.05), 反之同时加入IGF 1与PD98059后, IGF 1发挥促神经元存活的作用未被明显阻滞 (P>0.05)。Western印迹结果示IGF 1可显著上调p Akt的表达, 这种上调作用可以被LY294002阻滞。结论: IGF 1有明确的神经保护作用, 其可能是通过PI3K/Akt通路来发挥作用的。

关键词: 胰岛素样生长因子 1; 神经元; 信号通路; 氧糖剥夺模型

Protective effects of IGF 1 on neurons under condition of hypoxia and the role of PI3K signal pathway

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Abstract:

Objective To investigate the protective effects of insulin like growth factor 1(IGF 1) on cortical neurons under condition of hypoxia and the possible mechanism. Methods Cerebral cortical neurons from newborn rats were cultured under the condition of oxygen and glucose deprivation (OGD) . On day 7, neurons were treated with IGF 1 or IGF 1 plus LY294002 or PD98059 under condition of OGD or normal condition. MTT assay was used to analyze the viability of neurons in each group. The expression of total Akt and p Akt were analyzed by Western blot. Results Compared with the control, the neuron viability was significantly higher in IGF 1 treated group under normal or OGD condition (P<0.05). The protective effects of IGF 1 were attenuated in the presence of LY294002 but not PD98059. The result of Western blot showed IGF 1 upregulated the expression of p Akt, which was inhibited by LY294002. Conclusion PI3K pathway may play an important role in neuroprotection afforded by IGF 1.

Keywords: insulin like growth factor 1;neuron;signal pathway;oxygen and glucose deprivation model

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参考文献:

- [1] Popken G J, Hodge R D, Ye P, et al. In vivo effects of insulin like growth factor 1 (IGF 1) on prenatal and early postnatal development of the central nervous system [J] . Eur J Neurosci, 2004,19 (8): 2056-2068.
- [2] Moschos S J, Mantzoros C S. The role of the IGF system in cancer: from basic to clinical studies and clinical applications [J] . Oncology, 2002, 63(4): 317-332.
- [3] Atkinson T, Whitfield J, Chakravarthy B. The phosphatase inhibitor, okadaic acid, strongly protects

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primary rat cortical neurons from lethal oxygen glucose deprivation [J] . Biochem Biophys Res Commun, 2009,378(3):394 398.

[4] Akcakus M, Koklu E, Kurtoglu S, et al. The relationship among intrauterine growth, insulin like growth factor 1 (IGF 1), IGF binding protein 3, and bone mineral status in newborn infants [J] . Am J Perinatol, 2006, 23 (8): 473 480.

[5] Ong K, Kratzsch J, Kiess W, et al. Circulating IGF I levels in childhood are related to both current body composition and early postnatal growth rate [J] . J Clin Endocrinol Metab, 2002, 87(3): 1041 1044.

[6] Cui Q L, Fragoso G, Miron V E, et al. Response of human oligodendrocyte progenitors to growth factors and axon signals [J] . J Neuropathol Exp Neurol, 2010, 69(9):930 944.

[7] Pérez Martín M, Cifuentes M, Grondona J M, et al. IGF I stimulates neurogenesis in the hypothalamus of adult rats [J] . Eur J Neurosci, 2010 , 31(9):1533 1548.

[8] Serbedzija P, Madl J E, Ishii D N. Insulin and IGF I prevent brain atrophy and DNA loss in diabetes [J] . Brain Res, 2009,1303:179 194.

[9] Liu X F, Fawcett J R, Thorne R G, et al. Non invasive intranasal insulin like growth factor I reduces infarct volume and improves neurologic function in rats following middle cerebral artery occlusion [J] . Neurosci Lett, 2001,308(2):91 94.

[10] Lin S, Fan L W, Rhodes P G, et al. Intranasal administration of IGF 1 attenuates hypoxic ischemic brain injury in neonatal rats [J] . Exp Neurol, 2009, 217(2):361 370.

[11] Dudek H, Datta S R, Franke T F, et al. Regulation of neuronal survival by the serinethreonine protein kinase Akt [J] . Science, 1997,275(5300): 661 665.

[12] Sun X, Yao H, Douglas R M, et al. Insulin/PI3K signaling protects dentate neurons from oxygen glucose deprivation in organotypic slice cultures [J] . J Neurochem, 2010, 112(2):377 388.

[13] Peruzzi F, Prisco M, Dews M, et al. Multiple signaling pathways of the insulin like growth factor 1 receptor in protection from apoptosis [J] . Mol Cell Biol, 1999, 19(10): 7203 7215.

[14] Peruzzi F, Prisco M, Morrione A, et al. Anti apoptotic signaling of the IGF I receptor through mitochondrial translocation of c Raf and Nedd4 [J] . J Biol Chem, 2001, 276(28): 25990 25996.

[15] Sun X, Huang L, Zhang M, et al. Insulin like growth factor 1 prevents 1 mentyl 4 phenylpyridinium induced apoptosis in PC12 cells through activation of glycogen synthase kinase 3beta [J] . Toxicology, 2010, 271(1/2):5 12.

[16] Brunet A, Bonni A, Zigmund M J, et al. Akt promotes cell survival by phosphorylating and inhibiting a Forkhead transcription factor [J] . Cell, 1999,96(6): 857 868.

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