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论文

糖基化终末产物对SH-SY5Y细胞氧化应激及凋亡的影响

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摘要：

目的 研究糖基化终末产物（AGEs）对人神经母细胞瘤细胞（SH SY5Y）凋亡的影响，探讨AGEs与阿尔茨海默病（AD）发病机制的关系。方法 分别以不同浓度糖基化修饰的牛血清白蛋白（AGE-BSA）处理SH-SY5Y细胞48h，选取AGE BSA敏感浓度(200μg/mL)处理细胞不同时间，流式细胞仪（FCM）检测细胞凋亡率，确定AGE BSA诱导SH-SY5Y凋亡最佳浓度及时间。将细胞随机分为对照组、牛血清白蛋白（BSA）对照组、AGE BSA组、AGE-BSA+抗RAGE中和抗体组、AGE-BSA+α 硫辛酸组、AGE BSA+DPI (NADPH氧化酶抑制剂)组。FCM检测细胞凋亡率变化，Hoechst 33258染色观察细胞形态改变，应用活性氧荧光探针DCFH-DA检测活性氧 (ROS) 水平，Western blot测定Caspase-12 的表达。结果 细胞凋亡率随AGE BSA浓度增加及作用时间延长而升高，200μg/mL AGE-BSA作用48h细胞凋亡率从对照组的（2.23±0.08）%增加到 (16.8±1.27) % (P<0.05)，同时，Hoechst染核后可见典型凋亡形态改变，细胞内ROS水平显著增高，Caspase-12 蛋白表达明显上调，与对照组相比差异显著(P＜0.05），而分别用抗RAGE中和抗体、α 硫辛酸、DPI预处理后再加入AGE-BSA, 各组与AGE BSA组比较，凋亡率明显下降，ROS水平、Caspase-12 蛋白表达均明显降低(P＜0.05）。结论 糖基化终末产物可刺激SH SY5Y细胞产生大量ROS及活化Caspase-12 介导细胞凋亡，通过阻断其与特异性受体RAGE结合或减少细胞内ROS可减轻细胞凋亡的发生。

关键词： 阿尔茨海默病；糖基化终产物，高级；活性氧；Caspase-12；细胞凋亡

Effect of advanced glycation end products on oxidative stress andapoptosis of SH-SY5Y cells

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Abstract:

Objective To investigate the effect of advanced glycation end products (AGEs) on apoptosis of SH SY5Y cells, and to further explore the relationship between AGEs and the mechanism of Alzheimer disease. Methods SH-SY5Y cells were treated with different concentrations of AGE-BSA for 48h, or with AGE-BSA (200μg/mL) for different times. Cell apoptosis was detected by flow cytometry (FCM) to determine the best concentration and time of AGE-BSA . SH-SY5Y cells were randomly divided into six groups: the normal control group, the BSA control group, the AGE-BSA group, the AGE-BSA+RAGE antibody group, the AG-BSA+Alpha lipoic acid (ALA) group, and the AGE-BSA+diphenyleneiodonium (DPI) group. Cell apoptosis was detected by FCM and Hoechst staining, the level of ROS was evaluated by the 2′, 7′-dichlorofluorescein diacetate (DCFH-DA) method, and expression of Caspase-12 was analyzed by Western blot. Results AGE-BSA induced SH-SY5Y cells apoptosis in a time-and concentration-dependent manner. After treatment with 200μg/mL of AGE-BSA for 48 hours, apoptosis of SH-SY5Y cells was significantly increased to (16.8±1.27) % from (2.23±0.08)%(P<0.05). Apoptosis-like cells could be found after Hoechst stained nuclei, the level of ROS and expression of Caspase-12 statistically increased compared with the normal group (P<0.05). Compared with the AGE BSA group, apoptosis of cells, level of ROS and expression of Caspase-12 in the AGE BSA+RAGE Ab group, the AGE-BSA + ALA group and the AGE BSA + DPI group were significantly decreased (P＜0.05). Conclusion AGEs could induce the production of ROS and activation of Caspase-12, which may be involved in apoptosis of SH SY5Y cells induced by AGEs. Blocking the combination of AGEs and its receptor(RAGE) or reducing production of ROS may protect against AGEs-induced SH-SY5Y apoptosis.

Keywords: Alzheimer disease; Glycosylation end products, advanced; Reactive oxygen species; Caspase-12; Apoptosis

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