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论著

细胞外信号调节激酶在TPPB促进PC12产生可溶性淀粉样前体蛋白中的作用

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摘要 目的：观察在蛋白激酶C(PKC)激动剂TPPB促进可溶性淀粉样前体蛋白(sAPPα)释放过程中参与的信号转导通路。

方法:以1 μmol/L的TPPB作用于PC12细胞3 h，同时加入信号转导通路的抑制剂，Western印迹法检测上清液内sAPPα的含量和细胞外信号调节激酶(p42/44MAPK)及磷酸化的p42/44MAPK的表达。

结果:1 μmol/L的TPPB作用于PC12细胞3 h可以显著增加上清液内sAPPα的含量，细胞外信号调节激酶抑制剂U0126、c-Jun氨基末端激酶抑制剂SP600125和蛋白酪氨酸激酶抑制剂genistein可以部分消除此作用；而p38MAPK抑制剂SB203580对sAPPα的含量无显著影响。1 μmol/L的TPPB可以使磷酸化的p42/44MAPK表达增加，而对总的p42/44MAPK无显著影响。

结论:细胞外信号调节激酶、c-Jun氨基末端激酶和蛋白酪氨酸激酶可能参与TPPB促进sAPPα生成的过程。

关键词 蛋白激酶C； 淀粉样前体蛋白； 有丝分裂素激活蛋白激酶类； 阿尔茨海默病

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Involvement of extracellular signal regulated kinase in the regulation of amyloid precursor protein processing in PC12 cells by TPPB

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Abstract

<FONT face=Verdana>AIM: To explore the signal transduction pathways involved in the regulation of amyloid precursor protein (APP) processing by protein kinase C (PKC) activator TPPB.
METHODS: PC12 cells were treated with TPPB (PKC activator) for 3 h and various signal transduction inhibitors were added to the conditioned medium to investigate their effects on α-secretase form of soluble amyloid precursor protein (sAPPα) secretion after TPPB treatment via Western blotting. Extracellular signal regulated kinase (ERK, p42/44MAPK) and phospho-p42/44MAPK were also measured after TPPB treatment.
RESULTS: TPPB (1 μmol/L) significantly increased sAPPα secretion as compared with control group. The increase in sAPPα secretion by TPPB was partially blocked by ERK inhibitor U0126, c-Jun N-terminal kinase (JNK) inhibitor SP600125 and protein tyrosine kinase (PTK) inhibitor genistein, but not by p38MAPK inhibitor SB203580. TPPB (1 μmol/L) increased the expression of phospho-p42/44MAPK without altering total p42/44MAPK levels.
CONCLUSION: ERK, JNK and PTK may be involved in the regulation of APP processing by TPPB.</FONT>

Key words Protein kinase C Amyloid precursor protein Mitogen-activated protein kinases Alzheimer disease

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