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论著

抗抑郁新化合物SIPI-C和SIPI-F对PC12细胞内游离钙离子浓度的影响

周慧[1], 汪溪洁[1], 翁志洁[2], 李建其[2], 马璟[1]
1. 上海医药工业研究院国家上海新药安全评价研究中心, 上海 201203;
2. 上海医药工业研究院 化学制药新技术中心, 上海 200040

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摘要 目的 研究抗抑郁新化合物SIPI-C和SIPI-F对PC12细胞内游离钙离子浓度($[Ca^{2+}]_i$)的影响, 初步探讨其神经毒性的机制。方法 接种PC12细胞于经胶原Ⅰ包被的培养皿, 加入钙离子荧光探针Fluo-3/AM染色后, 用激光共聚焦显微镜分别记录1 有钙外液中, 10 μmol·L^{-1}的SIPI-A, B, C和F对PC12细胞$[Ca^{2+}]_i$的影响;2 有钙外液中, 1, 10和100 μmol·L^{-1}的SIPI-C和SIPI-F对$[Ca^{2+}]_i$的影响;3 有钙外液中, 硝苯地平10 μmol·L^{-1}对10 μmol·L^{-1}的SIPI-C或SIPI-F作用的影响;4 无钙细胞外液中, 10 μmol·L^{-1} SIPI-C和SIPI-F对$[Ca^{2+}]_i$的影响。结果 有钙外液中, SIPI-A 10 μmol·L^{-1}给药后$[Ca^{2+}]_i$下降, 10 μmol·L^{-1}的SIPI-B, SIPI-C和SIPI-F分别使$[Ca^{2+}]_i$增加27% ($P<0.05$), 84% ($P<0.05$)和87% ($P<0.01$);SIPI-C和SIPI-F明显升高$[Ca^{2+}]_i$;同时给予SIPI-C 10 μmol·L^{-1}和硝苯地平10 μmol·L^{-1}或SIPI-F 10 μmol·L^{-1}和硝苯地平10 μmol·L^{-1}, 给药后荧光强度立即上升达到峰值, 随后下降, $[Ca^{2+}]_i$分别增加24%和15% ($P<0.05$)。在无钙外液中, SIPI-C和SIPI-F 10 μmol·L^{-1}分别使$[Ca^{2+}]_i$增加16%和18% ($P<0.01$)。结论 抗抑郁化合物SIPI-C和SIPI-F可以引起PC12细胞中$[Ca^{2+}]_i$显著增加, 此影响可能与其神经毒性有关。

关键词 抗抑郁药物 烷醇哌嗪衍生物 SIPI-C SIPI-F PC12细胞 细胞内钙离子浓度
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Effect of new antidepressants SIPI-C and SIPI-F on cytosolic free Ca^{2+} concentration in PC12 cells

ZHOU Hui[1], WANG Xi-jie[1], WENG Zhi-jie[2], LI Jian-qi[2], MA Jing[1]

1. National Shanghai Center for New Drug Safety Evaluation & Research, Shanghai Institute of Pharmaceutical Industry, Shanghai 201203, China;
2. Novel Technology Center of Pharmaceutical Chemistry, Shanghai Institute of Pharmaceutical Industry, Shanghai 200040, China

Abstract

OBJECTIVE To investigate the effect of SIPI-C and SIPI-F on cytosolic free Ca^{2+} concentration ($[Ca^{2+}]_i$) in PC12 cells. **METHODS** PC12 cells were cultured in culture dish coated with collagen Ⅰ. After incubation at 37℃ for 40-50 min in 10 μmol·L^{-1} Fluo-3/AM enriched media, the $[Ca^{2+}]_i$ changes were continuously measured by the confocal laser scanning microscope: 1 effect of SIPI-A, B, C and F 10 μmol·L^{-1} on $[Ca^{2+}]_i$ in normal extracellular fluid; 2 effect of SIPI-C and SIPI-F 1, 10 and 100 μmol·L^{-1} on $[Ca^{2+}]_i$ in normal extracellular fluid; 3 effect of nifedipine 10 μmol·L^{-1} on effects of SIPI-C or SIPI-F 10 μmol·L^{-1} in normal extracellular fluid; 4 effect of 10 μmol·L^{-1} SIPI-C or SIPI-F on $[Ca^{2+}]_i$ in non-calcium extracellular fluid. **RESULTS** SIPI-A 10 μmol·L^{-1} decreased $[Ca^{2+}]^i$ while SIPI-B, SIPI-C and SIPI-F 10 μmol·L^{-1} resulted in the elevation of intracellular calcium by 27%, 84% and 87% in normal extracellular fluid. In SIPI-C or SIPI-F 10 μmol·L^{-1} combined with nifedipine 10 μmol·L^{-1} group, $[Ca^{2+}]_i$ was elevated by 24% and 15% after application of compounds. At the same concentration, SIPI-C and SIPI-F resulted in the elevation of $[Ca^{2+}]_i$ by 16% and 18% in non-calcium extracellular fluid. **CONCLUSION** SIPI-C and SIPI-F increase $[Ca^{2+}]_i$ which could be related to SIPI-C and SIPI-F induced neurotoxicity.

Key words antidepressive drugs aryl alkanol piperazine derivatives SIPI-C SIPI-F PC12 cells cytosolic Ca^{2+} concentration

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通讯作者 马璟,E-mail:jma@ncdser.com,Tel:(021)50800333-101;李建其,E-mail:li.jianqi@sipi.com.cn,Tel:(021)55514600-288 jma@ncdser.com;li.jianqi@sipi.com.cn