DOI: 10.16016/j.1000-5404.1997.04.019

Acute toxic effects of 1, 1-dimethylhydrazine on GABA and Glu in the brain in rats

Long Dongmei, Gao Ning, Cao Bo, Zhao Qing, Hu Ran (Department of Environmental Hygiene, Faculty of Preventive Medicine, Third Military Medical University, Chongqing, 630038)

Abstract Objective: To study the biochemical mechanism of the acute intoxication by 1, 1-dimethylhydrazine (UDMH) through intratracheal infection from the angle of neurotransmitter. Methods: Adult male Wistar rats were randomized into four groups: 1) Normal control group (NCG); 2) Low-dosage group (LDG, 80mg/kg); 3) Middle-dosage group (MDG, 160mg/kg); 4) High-dosage group (HDG, 240mg/kg). The contents of GABA and glu and the activities of GAD and GABA-T were determined at the 30th, 60th and 90th min after the infection. Results: 1) The content of GABA and activity of GAD were significantly lower in LDG, MDG and HDG than in the control ($P < 0.01$). These two indices were in dose-effect and time-effect manners. 2) The activity of GABA-T was significantly lower in HDG than in the control ($P < 0.05$). 3) The content of Glu was remarkably higher in MDG and HDG than in the control ($P < 0.01$). Conclusion: UDMH induces intoxication of the central nervous system through decreasing the activity of GAD to result in the decrease of the content of GABA. It also might be due to the increase Glu content in the brain.

Key words 1, 1-dimethylhydrazine (UDMH); neurotransmitter; neurotoxicity; rat

人 C5aR在大肠杆菌中的功能性表达及 C5a对中性粒细胞及肾小球内皮细胞粘附的影响

Functional expression of human C5a receptor in *Escherichia coli* and the effect of C5a on the properties of adhesion between granulocytes and glomerulus vascular endothelial cells

齐 洁* 朱锡华 (第三军医大学基础医学部免疫学教研室) 重庆, 630038

C5aR具有广泛的分布,除髓样细胞外,还分布于多种脏器的实质细胞. C5aR介导了众多的生物学效应,参与了许多疾病的发生、发展,并在多种病变中起重要作用. 然而 C5a-C5aR系统目前还有许多未知的领域,亟待去深入开拓.

为了获得高质量充足的 C5aR材料来源,满足多方研究的需要,我们用大肠杆菌高密度生长的优势及融合蛋白易纯化的特点,构建了人 C5aR和细菌麦芽糖结合蛋白(MBP)基因融合的表达质粒 C5aR-pmal-p2 通过 PCR调整了 C5aR cDNA阅读框架,改变了原有 cDNA两端的酶切位点,缺失了起始密码并增加了一个细菌偏性的终止子. DNA测序表明 C5aR cDNA与表达载体中的 MBP开放阅读框架一致. 将重组质粒转入 DH5α 菌中,首次在细菌内膜上表达出了具有配体结合活性的 C5aR. Western-Bolt和 IGSS检测表明表达的 C5aR具抗体结合活性并且定位表达于细菌内膜. 表达量占整个细菌蛋白总量的 3.2%. 受体的放射性配体结合实验(RBA)证实 ^{125}I-C5a与完整表达菌的结合可达饱和,每个细菌上 C5aR的含量不低于60个放射性配体结合位点,与 C5a的亲和力接近体内正常细胞的测定值, kd= 3.62nM. 提示细菌内膜上的 C5aR正确折叠,保持了良好的构象.

本研究应用 IGSS技术发现肾小球内皮细胞(GVEC)上分布有 C5aR. 为揭示 GVEC上 C5aR介导的生物学效应,本研究还探讨了 C5a-C5aR对 Paw-GVEC粘附的影响. 用微管吸吮技术率先从生物力学角度直接定量地证实了 C5a对 Paw-GVEC粘附特性的影响,经 2000 ng/ml C5a刺激,粘附力(Fa)达到 0.014 dyn,相对粘附应力(S1)达到 1720 dyn/cm2,与对照组均有非常显著性差异($P < 0.01$). S1结果提示 C5a浓度在 2000ng/ml以下时,参与粘附的分子相对恒定,而当 C5a刺激浓度达 2000ng/ml时, S1显著增加,细胞间粘附的分子机理可能发生变化. PMN的髓过氧化酶(MPO)检测结果表明, PMN与 GVEC粘附的发生依赖于 C5a刺激的剂量. 本研究从不同角度阐明了 C5a对 PMN-GVEC粘附的影响,为深入探讨 C5a和 C5aR在炎症性病变中的重要作用打了下基础,同时为深入研究 C5a和 C5aR提供了有用的实验工具和材料来源,也为其它膜蛋白的表达及探讨外源性膜蛋白在 *E. coli* 蛋白中正确折叠和嵌入细胞膜的机理提供了参考.

关键词 C5a受体; C5a; 大肠杆菌表达; 融合蛋白; 肾小球内皮细胞; 中性粒细胞; 粘附; 微管吸吮

中图法分类号 R392.11

(收稿: 1997-06-20; 修回: 1997-07-11)

(编辑 张大春)

* 齐 洁, 女, 33岁, 讲师, 博士研究生

?1994-2016 China Academic Journal Electronic Publishing House. All rights reserved. http://www.cnki.net