1.長期給予 MPTP 對小黑鼠血中促腎上腺皮質素(ACTH)以及促腎上腺皮質釋放激素(CRF)表現的影響

2.長期給予 MPTP 對小黑鼠腦中 NMDA 受體多亞型蛋白以及細胞骨架蛋白(spectrin) 表現的影響

1.The effect of chronic treatment of 1-methyl-4-phenyl-1,2,3,6-tetrahdro-pyridine (MPTP) on the plasma concentration of adrenocoricotrophic hormone (ACTH) and corticotropin- releasing factor (CRF) in C57BL/6J mice. 2.The effect of chronic treatm

中文摘要

我們研究長期給予 1-甲基-4-酚基-1,2,3,6,-四氫嘌呤(1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, MPTP)此種會選擇性導致 dopa-minergic neuron 退化的藥物，想知道此藥物是否會對下視 CRF 及 ACTH 調控路徑產生影響？因此，我們連續 7 天給予 C57BL/6J mice MPTP，在停止給藥後之第一天、第三天、第七天、第十四天以及第三十天犧牲老鼠取其週邊血，分別利用酵素免疫分析(Enzyme-linked-immuno sorbent assay, ELISA) 及放射免疫分析法 (Radio-immunoassay, RIA) 的方法分別偵測小黑鼠血中的促腎上皮質釋放激素及 ACTH 的濃度。我們發現長期給予 MPTP 並不會影響血中 CRF 的澧度，但在停藥後第一天會短暫性增加 ACTH 在血中的濃度。因此，由此結果可知，在 MPTP 的打藥過程中，有可能也會影響到 CRF 的表現，因而導致停藥後 ACTH 仍然會有短暫性上升。接下來，我們爲了要偵測 MPTP 給藥後對神經細胞造成的損傷，是否會影響到 NMDA 受體的表現?因此，我們利用西方點墨法，在連續 7 天給予動物 MPTP 後，分別在停藥後第 1、3、7、14、30 天，去偵測大腦皮質、海馬迴、紋狀體、下視丘上的 NMDA 各種受體多亞型蛋白。結果我們發現，MPTP 給藥後，所引起各種 NMDA 受體的變化十分複雜，但與過去本實驗室以[3H]TCP ligand binding，所偵到會有短暫性抑制 NMDA 受體的數目結果並不一致。另外，我們亦偵測酪胺酸羥化酵素(Tyrosine hydroxylase,TH)、細胞骨架蛋白(spectrin)在腦中的含量，利用此兩種蛋白質的表現量，來看長期給予 MPTP 對多巴胺神經元所造成毒性的存在。我們發現，在停藥後的 30 天內，TH 在紋狀體有慢慢回復的情形，配合 spectrin 在細胞膜上的表現，我們也發現 spectrin 也有逐漸回復的情形。不過，我們在海馬迴中並未偵測到 TH 的表現量，而其 spectrin 在細胞膜上的表現量亦無降低的情形。終其這些結果，我們發現，長期給予 MPTP 對紋狀體系統會有很明顯的生化損傷，表現在 TH 及 spectrin 上。但 MPTP 給藥後，對 NMDA 受體的表現，其結果尚無法得到一個結論。

英文摘要

We have determined the effect of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) on the releasing corticotropin releasing factor (CRF) and adrenocoricotrophic hormone (ACTH) by quantifying the plasma level CRF and ACTH using radioimmuno-assay (RIA) and enzyme-linked-immuno sorbent assay (ELISA) in the C57BL/6J mice with 7 days treatment of MPTP. We found that MPTP treatment did not affect the plasma level of CRF, but transiently increase in the plasma level of ACTH at 1st day after continuation MPTP treatment. This result suggested that chronic MPTP treatment might affect CRF-ACTH pathway and degenerate the dopaminergic system. However, this effect might occur before continuation of MPTP treatment. We also determine the NMDA subunits expression with cortex, hippocampus, striatum and hypothalamus after continuation MPTP treatment. We found very complicated fluctuation of NMDA receptor subunits expression in different brain region. However, there was no change of NMDA receptor subunits in the cortex. In the hippocampus, most of subunits were unevenly increased. There was complicated fluctuation on the NMDA receptor subunits expression in the striatum and hypothalamus. We also determined the neurotoxity of MPTP on the neuronal cells by examining the expression of tyrosine hydroxylase (TH) and neurodentritic spectrin on membrane and its degradation product. We found that in the striatum, there was gradually reverse of the TH after continuous MPTP treatment. The level of the TH on the 30th days after MPTP treatment was not significantly different to that of control group in the cortex. In the striatum, accompanied with this phenomena, the expression of spectrin on the membrane, there was a transit decrease at the 1st, 3th day after MPTP treatment but than become no signification to control group 7 day after MPTP treatment. This result indicated that MPTP treatment could induce striatum neuron degernation.