# 1.探討 Pentylenetetrazol 所引起的抽搐對未成熟老鼠腦中 c-fos , c-jun , bax , bcl-2 , cystatin B 及 p53 基因表現之影響 2.探討低濃度 Arachidonic acid 對大白鼠腎上腺髓質嗜鉻腫瘤細胞神經發育之影響

# The effect of pentylenetetrazol-induced seizure on the expression of c-fos , c-jun , bax , bcl-2 , cystatin B and p53 gene in the brain of developing rats2.The effect of low concentration arachidonic acid on neuronal differentiation in rat Pheochromocyto


## 中文摘要

Pentylenetetrazol（PTZ）是一種痙攣劑，它會阻斷 r-aminobutyric acid 接受體（GABAA receptor）的神經性傳導抑制作用，而引起成熟與未成熟動物的抽搐行為。過去已經知道 PTZ 作用在成鼠身上時，會導致腦部細胞死亡，推測其原因可能與 apoptosis 的產生有相關。所以在本實驗中，我們在未成熟的老鼠身上施打 PTZ 後，以 Northern blotting 的方法來定量在 cortex, hippocampus, striatum 與 cerebellum 腦區中 c-fos, c-jun, bax, bcl-2, cystatin B 與 p53 這些與 apoptosis 相關基因的表現，並且用 N-methyl-D-aspartate（NMDA）接受體的非競爭性拮抗劑 MK-801 來阻斷 PTZ 所引起之抽搐行為與其相關之基因表現。由實驗的結果發現，PTZ 會使 7、14 及 30 天大的老鼠產生明顯的 generalized seizure，但若先在老鼠身上施打 MK-801，則可以完全抑制 seizure 的產生。而 Northern blotting 的結果顯示，PTZ 會使所有腦區的 c-fos 表現增加，且其表現與年齡及腦區有密切的關係；而施打 MK-801 也可以有效抑制住因 PTZ 所產生 c-fos。這樣的結果顯示，PTZ 會引發 immediate early gene 的表現，且需要 NMDA receptor的活化。至於 c-fos 的表現是否意謂著會走向 apoptosis 的路徑，還有待更進一步的了解。

## 英文摘要

Pentylenetetrazole (PTZ), a convulsant agent, induces seizure in both mature and developing animals by blocking the r-aminobutyric acid type (GABAA) receptor-mediated inhibitory neurotransmission. The PTZ-induced seizure has been found to produce brain injury in adult rats, partly attributed to the generation of apoptosis. In the present study, I determined whether PTZ could induce apoptosis in the developing rats by quantifying the expression of apoptosis associated genes, namely, c-fos, c-jun, bax, bcl-2, cystatin B and p53 gene in the cortex, hippocampus, striatum and cerebellum of rats received single injection of PTZ using Northern

blotting assay. I also determined whether PTZ-induced seizure and associated gene expression could be blocked by addition of a noncompetitive antagonist of N-methyl-D-aspartate (NMDA) receptor, the MK-801. The result showed that PTZ induced generalized profound seizure on rats with age of 7, 14, and 30 days. Pre-injection of MK-801 completely abolished the seizure. Northern blotting assay showed that injection of PTZ only induced apparent expression of c-fos in all examined brain regions but with an age- and region-specific manner. Injection of MK-801 abolished PTZ-induced expression of c-fos. This result indicates that PTZ is able to trigger the immediate early gene expression and this action requires activation of the NMDA receptor. Whether the expression of c-fos alone means the ongoing of apoptosis or other effect unrelated to apoptosis remains to be elucidate.