• 系統編號	RN9607-3573
• 計畫中文名稱	以大白鼠大腦皮質初級神經細胞培養探討血清素及其接受器對 NMDA 接受器引神經分化及細胞毒性的影響(II)
• 計畫英文名稱	The Role of Serotonin and Its Receptor on the NMDA Receptor-Mediated Neuronal Differentiation and Neurotoxicity in the Rat Primary Cortical Neuronal Culture (II)
• 主管機關	行政院國家科學委員會
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• 中文關鍵字	血清素接受器; NMDA 接受器; 大腦皮質初級神經細胞培養; 血清素接受器拮抗劑
• 英文關鍵字	Serotonin receptor; NMDA receptor; Primary cortical culture; 5-HT receptor antagonist
• 中文摘要	血清素接受器在中樞神經功能發育過程的調控中扮演一個重要的角色。在本研究中，我們探討在大白鼠大腦皮質初級神經細胞培養中，以血清素接受器的拮抗劑長期壓抑其活性，是否會對 NMDA 接受器一種興奮性胺基酸的受體的表現造成影響。我們由培養的第三天開始，在大腦皮質初級神經細胞培養中加入 1 μM 非選擇性血清素接受器拮抗劑 methysergide maleate 或 dihydroergocristine mesylate、5-HT1 接受器之選擇性拮抗劑 pindolol、或 5-HT2 接受器之選擇性拮抗劑 cyproheptadine hydrochloride，持續培養 9 天。這些拮抗劑的處理並不會對細胞造成明顯的毒害，但降低了 NMDA 接受器在引發和細胞死亡以及細胞內鈣離子蓄積方面的效力，同時也提高了 NR2B 選擇性拮抗劑 ifenprodil 在抑制細胞內鈣離子蓄積方面的效力，並降低了 NMDA 接受器非選擇性拮抗劑 MK-801 在抑制細胞內鈣離子蓄積方面的效力。此外，免疫轉漬法的結果也顯示，NMDA 接受器次單元 NR1A 和 NR2A 的表現量降低，但 NR2B 則否。以上結果顯示，長期壓抑血清素接受器的活性，可能會降低大腦皮質神經細胞中 NMDA 接受器特定次單元的表現，並進而影響 NMDA 接受器所調節的神經傳導。
• 英文摘要	Serotonin (5-HT) receptor is an important receptor system regulating the development of neuronal function in the CNS. In the present study we determined whether long-term suppression of the activity of serotonin receptor by serotonin receptor antagonist would affect the expression of

N-methyl-D-aspartate (NMDA) receptor, one subtype receptor of excitatory amino acid, in rat primary cortical cell culture. The cultured cells were incubated with 1 .mu.M of non-selective 5-HT receptor antagonist, methysergide maleate or dihydroergocristine mesylate, or 5-HT1 selective antagonist, pindolol, or 5-HT2 selective antagonist, cyproheptadine hydrochloride, for 9 consecutive days since the third days after cells were plated. Treatment of these antagonists did 3 not produce significant cell toxicity but decreased the potency of NMDA in inducing cell death and intracellular 45Ca2+ accumulation. Associating with these change are an increase in the potency of NR2B-selective antagonist, ifenprodil, and a decrease in the potency of MK-801, a non-selective NMDA receptor antagonist, in inhibiting NMDA-induced intracellular accumulation of 45Ca2+. Furthermore, immunoblotting assay showed a decrease in the expression of NMDA receptor subunit protein NR1A and NR2A, but not the NR2B. These results indicated that long-term suppression of the activity of 5-HT receptor, probably the 5-HT1 and 5-HT2 receptor, could result into a subunit-specific down-regulation of NMDA receptor in cortical neurons, which further alters the NMDA receptor-mediated neurotransmission.