• 系統編號	RN9311-0151
• 計畫中文名稱	糖皮質固醇與興奮性胺基酸之協同性促進感覺神經再生之機轉研究---從分子到系統
• 計畫英文名稱	Study of Synergistic Facilitation of Glucocorticoids and Excitatory Amino Acid Signalings on Sensory Nerve Regeneration---from Molecule to System
• 主管機關	行政院國家科學委員會
• 計畫編號	NSC91-2320-B038-015
• 執行機構	台北醫學大學生理科
• 本期期間	9108 ~ 9207
• 報告頁數	10 頁
• 使用語言	中文
• 研究人員	李怡萱 Lee, Yi-Hsuan
• 中文關鍵字	皮質固酮; 紅藻胺酸; 糖皮質固醇受體; 麩胺酸受體; 蛋白激脢 C; 生長相關蛋白; 神經纖維生長; 背根神經結
• 英文關鍵字	Corticosterone; Kainic Acid; Glucocorticoid Receptor; Glutamate receptor; Protein kinase C; Growth associated protein; Neurite outgrowth; Dorsal Root Ganglion
• 中文摘要	在我們之前的研究中，已發現隸屬於糖皮質固醇類的皮質固酮 corticosterone (CORT) 與興奮性麩胺酸受體催動劑紅藻胺酸 (kainic acid, KA)會協同性地促進背根神經節在軸突切斷後的神經纖維再生。在本計畫中，我們進一步闡明了此一作用的信號路徑機轉。 CORT 會協同性的促進 GAP-43 表現的增加，而此一增加主要在神經纖維與生長點的表現。另一臨床上用來治療脊髓損傷的糖皮質固醇 methylprednisolone 也有與 CORT 相同的作用。 CORT+KA 增加 GAP-43 expression 的作用，會受 protein kinase C 抑制劑 Ro-318220, 糖皮質固醇受體 (GR)拮抗劑 RU486, 及礦皮質固酮受器 (MR)拮抗劑 spironolactone 所抑制。 CORT+KA 促進的神經纖維生長速率則完全被 RU489 及 AMPA/KA receptor 拮抗劑 CNQX 抑制。我們進而發現，在 KA 之前，而非 CORT 之前投予 PKC 抑制劑，也會抑制 CORT+KA 的神經生長促進作用。以上結果顯示 CORT 與 KA 爲活化其個別之受體，且 KA 所活化的 PKC 可能在此協同作用中扮演重要的角色。再者，我們也探討了由髓鞘所釋放的神經生長抑制蛋白 Nogo A receptor (NgR)在 CORT 及 KA 作用下的表現情形。Western blot 結果顯示 CORT+KA 會降低 NgR 的表現。因此，糖皮質固醇與興奮性胺基酸促進神經軸突受損後再生的原因，可能是藉由 protein kinase C 活性而促進 GAP-43 表現，並同時降低 Nogo A Receptor 的表現所致。
• 英文摘要	In the previous study, we demonstrated that a glucocorticoid corticosterone (CORT) and a glutamate receptor agonist kainic acid (KA) promote neurite outgrowth in axotomized rat dorsal root ganglion (AX-DRG) neurons. In this study we further elucidate the possible mechanisms involved

in these synergistic effects. Immunofluorescence staining also revealed that CORT+KA increased GAP-43 immunoreactivities especially along neurites and growth cones of DRG neurons. Another therapeutically used glucocorticoid methylprednisolone also showed profound synergy with KA in increasing GAP-43 expression. In addition, CORT+KA-increased GAP-43 expression was reduced by protein kinase C (PKC) inhibitor RO-318220, glucocorticoid receptor (GR) antagonist RU486, and mineralcorticoid receptor (MR) antagonist spironolactone. The neuite growth rate promoted by the CORT+KA treatment was completely abolished by both RU486 and the AMPA/KA receptor antagonist CNQX, and was partially attenuated by spironolactone. Furthermore, PKC inhibitor attenuated the CORT+KA-increased neurite growth when applied immediately before the KA treatment. We compared the expression of two proteins, growth-associated protein (GAP-43) and a myelin-associated growth inhibitory protein NogoA receptor (NgR) in DRG neurons. Western blot analysis showed that combined treatment of CORT and KA results in increased expression of GAP-43 and decreased expression of NgR in DRG neurons. Taken together, these results suggest that CORT and KA activate their specific receptors to promote neurite growth synergistically, which might involve counterbalanced expressions of GAP-43 and NgR via a PKC-dependent signaling pathway.