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• 中文摘要	神經受損部位的嚴重發炎反應, 常刺激周圍的星狀膠細胞(astrocyte) 的聚集, 且大量分泌細胞外間質, 以修補受損的組織, 形成神經膠疤(glial scar). 而過量神經膠疤的形成,影響神經纖維之再生, 並阻隔神經纖維之連結, 影響神經訊號的傳導, 使神經系統組織修復失敗. 細胞外間質爲形成結締組織的重要物質. 主要提供細胞附著並影響細胞的活性,包括增生與分化. 對於組織的修復是必須的物質.神經膠疤中重組後的細胞外間質(matrixremodeling)中富含硫化軟骨蛋白多醣(chondroitin sulfate proteoglycan, CSPG)成分, 是造成抑制神經纖維再生之關鍵物質. 蛋白多醣(proteoglycan) 爲一種同時具有核心蛋白質(core protein) 及一條或多條黏多醣(glycosaminoglycan, GAG)的醣蛋白(glycoprotein).硫化軟骨黏多醣(chondroitin sulfate, CS)對於神經纖維再生可能有抑制的作用. 影響神經細胞的附著及移動, 進而造成神經組織修復的不完整.顯示調控各類蛋白多醣之表現的訊號機轉可能不同且有不同期程, 急性期及慢性期(acute phase vs. chronic phase) 之差異.因此在神經組織修復過程中如何調控細胞外間質的重組, 特別是對於蛋白多醣之表現及調控之機轉將成爲神經組織修復成功與否之關鍵. 本計劃已成功建立模擬受傷後活化之星形膠細胞並觀察其硫化軟骨蛋白多醣之表現,並在脊椎損傷動物模式中得到類似得結果, 此外其可能受到的分子調控機轉亦得到部分證實.
• 英文摘要	Reactive gliosis and inflammation induced by traumatic injury result in pronounced expression of extracellular matrix (ECM) molecules, e.g., chondroitin sulfate proteoglycans (CSPGs), that inhibit neuronal recovery and regeneration. However, the detailed regulatory mechanism of CSPG expression in astrocytes in response to injury remains unclear. Additionally, little is known about the effect of glucocorticoid treatment on CSPG expression after injury. In this study, we used alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionate (AMPA) plus cyclothiazide stimulation to mimic the elevated excitatory condition upon injury, allowing us to study CSPG expression and how it is affected by the glucocorticoid methylprednisolone (MP). Furthermore, astrocyte

media under various culture conditions were collected to culture adult rat dorsal root ganglion (DRG) for neurite outgrowth analyses. The results showed that the expression of glial fibrillary acidic protein (GFAP), an indicator of astrocyte reactivation, was induced by AMPA + cyclothiazide stimulation. Both mRNA and protein levels of the CSPGs neurocan and phosphacan were upregulated in reactivated astrocytes. Pre-treatment with MP downregulated GFAP and CSPG expression. The effect of MP was reversed by addition of RU486, an antagonist of the glucocorticoid receptor. Media from AMPA + cyclothiazide-induced astrocytes inhibited DRG neurite outgrowth. However, the inhibitory effect was reduced dramatically by pretreatment of reactive astrocytes with MP. MP promoted DRG neurite outgrowth as well as treatment with chondroitinase ABC, which removes the inhibitory chondroitin sulfate (CS). These results suggest that the neuroprotective effect of MP is at least partially attributable to its regulation of astrocyte activation and CSPG expression after neurotrauma.