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• 計畫英文名稱	The Allosteric Effect of Neurosteroid on the N-Methyl-D-Aspartate Receptor in CNS.		
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• 中文關鍵字	中樞神經系統；神經性類固醇；NMDA 受體；海馬； 異位作用		
• 英文關鍵字	Central nervous system；Neurosteroid；NMDA receptor；Hippocampus； Allosteric interaction		
• 中文摘要	最近研究顯示,興奮性胺基酸接受器亞型之一的 N-methyl-D-aspartate(NMDA)接受器會受到一種中樞神經分泌產生的類固醇,即 Pregnenolone sulfate(PS)的調節。PS 可以 NMDA agonist 刺激所引發的細胞內向電流。爲了進一步了解 PS 此促進作用的機制。我測定 PS 對海馬迴細胞膜上的 NMDA 接受器的 Ligand binding site 的影響。所使用的放射性 Ligand 包括:/sup 3/H-Glutamate 乃是結合在 NMDA agonist binding site; /sup 3/H-glycine 乃是結合在 Strychnine-insensitive glycine binding site; /sup 3/H-TCP 乃是結合在 NMDA 離子通道內。PS 明顯的增強未均衡(Non-equilibrium) /sup 3/H-TCP binding 但對已達均衡的/sup 3/H-TCP binding 無作用。其 EC/sub 50/爲 85.plmin.23.mu.M。PS 促進 TCP 的結合(Association)及解離(Dissociation)速率。但對 TCP binding site 的數目及親和力無作用。PS 可增強 NMDA-displaced /sup 3/H-glutamate binding 的親和力,但對/sup 3/H-glycine binding 毫無作用。綜合此實驗結果,PS 極可能藉由促進 NMDA agonist 結合的親和力來增強 NMDA 離子通道的開關速率,進而促進 NMDA agonist 所引發的反應。		
• 英文摘要	N-methyl-D-aspartate (NMDA) receptor, one of the glutamate receptor subtypes, takes a very critical role in inducing various neurophysiological (brain development, learning and memory) and neuropathological (epilepsy, ischemia-hypoxia neurotoxicity) conditions. Recent investigation has demonstrated that pregnenolone sulfate (PS), a local synthetic steroid in brain (also termed neurosteroid), specifically potentiates NMDA-evoked current in neuronal cell cultures. It is possible that this steroid produces the potentiating effect by interacting with the ligand binding sites on the NMDA receptor/channel complex. To test this possibility, I examined the effect of PS and other steroid analogues on the ligand binding to three distinct sites on the NMDA receptor/channel complex of rat hippocampal membranes. [/sup 3/H] glycine is used to examine the effect of PS on ligand binding to strychnine-insensitive glycine binding		

sites on the NMDA receptor. [/sup 3/H] glutamate is used to examine the effect of PS on ligand binding to the NMDA recognition sites. [/sup 3/H] N-[1-(2-thienyl)cyclohexyl] -piperidine (TCP) is used to examine the effect of PS on activation of the NMDA receptor-gated ion channel and on ligand binding to the phencyclidine binding site. PS potentiated /sup 3/H-TCP binding under non-equilibrium condition but did not affect pre-equilibrated TCP binding. The EC50 is 85+23.mu.M. Corresponding to this finding is that PS increase both the association and dissociation rate of TCP but did not have effect on the number or affinity of TCP binding sites. Paralleling with the potentiating effect on TCP binding is that PS increase the affinity of H/sup 3/-glutamate binding to the NMDA binding sites but has no effect on H/sup 3/-glycine binding. These finding suggest that PS increases the NMDA agonists-elicited response by enhancing the affinity of NMDA binding to its binding sites the NMDA receptor.