The Role of IL-1 Signal and NMDA Receptor in PTZ-induced Epilepsy and Sleep Disruption

National Taiwan University

Yu-Ju Chou*, Pei-Lu Yi, Fang-Chia Chang

Objective: To determine the relationship between IL-1 and NMDA receptors in epileptogenesis and epilepsy-induced sleep disruption using the IL-1R1 knockout (KO) mice.

Methods: All mice were genotyped by polymerase chain reaction (PCR) analysis of genomic DNA with the specific primers for transgene constructs. The spontaneously generalized seizures were induced by intraperitoneal injection of pentylenetetrazol (PTZ), the sleep-wake activity was analyzed, and the seizure threshold was determined in both the wildtype and IL-1R1 KO mice. The expression of subunit proteins, NR1 and phosphorylated-NR2B (at Tyr1472) were determined in the frontal cortex, hypothalamus and hippocampus by the Western blotting.

Results: We found that the occurrence of spontaneous seizure was higher in the wildtype treated with PTZ than that in the IL-1R1 KO mice treated with PTZ. Furthermore, non-rapid eye movement (NREM) sleep was decreased in wildtype mice treated with PTZ, but it was not altered in IL-1R1 KO mice. These results indicate the role of IL-1 signal in both epileptogenesis and sleep disturbance. The expression of NR1 subunit protein and the phosphorylation of NR2B at Tyr1472 in the hippocampus and the hypothalamus were significantly lower in the IL-1R1 KO mice when comparing to those in the wildtype mice. In contrast, the expression of NR1 and the phosphorylated-NR2B in the frontal cortex were significantly higher in the IL-1R1 KO mice treated with PTZ when comparing to those in the wildtype mice. These findings suggest that the epileptogenesis is attributed to the up-regulation of NMDA receptors, which is mediated by the IL-1 signal.

Conclusion: Our results indicate that the increase of NMDA receptor activity by the IL-1 signal contributes to the PTZ-induced epileptogenesis and the epilepsy-induced sleep disruption.

中文題目 ：NMDA 受體在 PTZ 誘發癲癇及睡眠上所扮演的角色

作　　者 ：周于茹[1*] 尹珮璐[2] 張芳嘉[1]

服務單位 ：[1]國立臺灣大學獸醫學系研究所　[2]真理大學運動管理學系