IL-1-Src kinase signal pathway in PTZ-induced epileptogenesis and sleep alterations

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Objective: Epilepsy is one of the common neurological disorders and often accompanies with sleep disruptions. Interleukin-1 (IL-1) is a sleep regulatory substance and may participate in pathogenesis of epilepsy. However, the role of IL-1 in the epilepsy-sleep interaction is still unclear. Therefore, this study investigates the IL-1 signaling pathways in the epileptogenesis and sleep alterations induced by pentylenetetrazol (PTZ).

Methods: All mice were genotyped by polymerase chain reaction (PCR) analysis. The spontaneous seizures were induced by PTZ injection (35 mg/kg), the sleep-wake activity was analyzed, and the seizure threshold was determined. The expression of subunit proteins of NMDA receptor, NR1, NR2, and phosphorylated-NR2B were determined in the frontal cortex, hypothalamus and hippocampus by the Western blotting. Activators and inhibitors of Src kinase were administered intracerebroventricularly.

Results: Occurrence of spontaneous seizure was significantly higher in the wildtype treated with PTZ than that in the IL-1 receptor type 1 (IL-1R1) knockout (KO) mice treated with PTZ. Non-rapid eye movement (NREM) sleep decreased in wildtype mice, but not in IL-1R1 KO mice, treated with PTZ. 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 treated with PTZ when comparing to those in the wildtype mice treated with PTZ. Furthermore, administration of Src kinase inhibitor blocked PTZ-induced NMDA activation, and suppressed epileptogenesis and sleep disturbance in wildtype mice. In contrast, activators of Src kinase restored the IL-1 signaling in the IL-1R1 KO mice.

Conclusion: Our results suggest that the IL-1-Src kinase signal pathway and consequence of NMDA activation contribute to the PTZ-induced epileptogenesis and sleep disruption.

中文題目：IL-1-Src kinase 傳遞路徑在癲癇發作與睡眠障礙的機轉

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