Hippocampal astrogliosis facilitates NR2B phosphorylation via IL-1R1–Src signaling during the early onset of seizure-related sleep disruption

Yu-Ju Minnie Chou[1], Machi Kuroda[2], Takuma Oshima[2], Pei-Lu Yi[3], Takashi Matsuwaki[2], and Fang-Chia Chang[1,4,5*]

1 Department of Veterinary Medicine, School of Veterinary Medicine, National Taiwan University, Taipei, Taiwan

2 Department of Veterinary Medical Sciences, University of Tokyo, Tokyo, Japan

3 Department of Sport Management, College of Tourism, Leisure and Sports, Aletheia University, New Taipei City, Taiwan

4 Graduate Institute of Brain & Mind Sciences, College of Medicine, National Taiwan University, Taipei, Taiwan

5 Graduate Institute of Acupuncture Science, College of Chinese Medicine, China Medical University, Taichung, Taiwan

Objective

Sleep disturbances are a debilitating hallmark of epilepsy, yet their underlying mechanisms remain poorly understood. This study aimed to elucidate the role of interleukin-1 receptor type-1 (IL-1R1) signaling in seizure-related sleep disruption through hippocampal neuroinflammatory pathways.

Methods

We utilized IL-1R1 knockout (KO) mice and wild-type controls to examine seizure recurrence, hippocampal NR2B phosphorylation, and neuronal activation in CA3 and dentate gyrus (DG). Sleep parameters (NREM and REM) were assessed at different zeitgeber times (ZT). Src signaling activation was used to evaluate its regulatory effect on NR2B phosphorylation in IL-1R1 KO mice.

Results

IL-1R1 KO mice exhibited significantly fewer recurrent seizures, reduced hippocampal NR2B phosphorylation at ZT24, and decreased neuronal activation in CA3 and DG, without notable changes in NREM or REM sleep. Src activation in IL-1R1 KO mice restored NR2B phosphorylation at ZT24, increased seizure frequency, and disrupted NREM sleep during the light period. Pronounced astrogliosis and elevated IL-1β release in the DG at ZT24 identified astrogliosis as the trigger of IL-1β-mediated NR2B phosphorylation via Src signaling.

Conclusion

These findings establish a novel mechanistic link between hippocampal astrogliosis, seizure activity, and sleep disruption. IL-1R1 signaling represents a promising therapeutic target for epilepsy-associated sleep disturbances.

中文題目：海馬星形膠質增生透過 IL-1R1–Src 訊號調控 NR2B 磷酸化並參與癲癇早期睡眠障礙

作　　者：Yu-Ju Minnie Chou*, Machi Kuroda, Takuma Oshima, Pei-Lu Yi, Takashi Matsuwaki, and Fang-Chia Chang

(報告者請以*表示， 如許美鈴*　)

服務單位：National Taiwan University