Circuit mechanisms underlying CB1R mediated suppression of dentate granule cell recruitment by cortical input

Yu-Jui Li[1], Chia-Wei Yeh[1], and Cheng-Chang Lien[1,2,*]
李育叡[1], 葉家維[1], 連正章[1,2,*]

[1]Institute of Neuroscience,
[2]Brain Research Center, National Yang Ming Chiao Tung University, Taipei, 112, Taiwan

In the central nervous system, endocannabinoids play an important role in regulating synaptic plasticity, signaling environmental cues, and modulating various functions. The dentate gyrus (DG) as the first station in the hippocampus, is crucial when it comes to receiving multimodal inputs from the cortex and processing the information forward to downstream hippocampal CA regions. In the DG, the cannabinoid type 1 receptors (CB1Rs) are highly expressed in GABAergic cholecystokinin-expressing interneurons (CCK-INs) and glutamatergic hilar mossy cells, and have been implicated in cognition and emotion. However, how the endocannabinoid system modulates the DG input-output transformation remains unclear.

Using electrophysiological and pharmacological approaches, we found that activating endocannabinoid signaling by the CB1R agonist, WIN 55,212-2 (5 μM), attenuated the perforant path (PP)-mediated granule cell population spikes (GC pSpikes) without affecting synaptic transmission of the PP. Moreover, CCK-INs appear to be essential for CB1R-induced suppression of GC activity because either blockade of $GABA_AR$ or chemogenetic inactivation of CCK-INs abolished the reduction of GC pSpikes after CB1R activation. The neural mechanism by which CB1R activation at CCK-INs contributes to the suppression of GC responses to the cortical inputs remains unclear and awaits to be explored in the near future.