THE NEUROPROTECTIVE IMPACT OF CB1 CANNABINOID RECEPTOR AGONIST IN A RAT MODEL OF ALZHEIMER DISEASE

M. Janahmadi¹, M. Haghani², M. Javan³

¹Neuroscience Centre and Dept. of Physiology, Neuroscience Centre and Dept. of Physiology, Medical School, Shahid Beheshti Medical Sciences University, ²Neuroscience Research Center and Dept. of Physiology, Medical School, Shahid Beheshti Medical Sciences University, ³Dept. of Physiology, School of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Introduction: There is increasing evidence suggesting that cannabinoid receptor agonists are neuroprotective in several experimental models of neurological disease, such as Alzheimer’s disease. However, the cellular mechanism underlying this neuroprotection is not fully understood.

Aims: The present work explored the intrinsic electrophysiological alterations in CA1 neurons in an animal model of Alzheimer’s disease (AD). Furthermore, neuroprotective effect of ACEA, a CB1 receptor agonist, against Aβ neurotoxicity was studied.

Methods: AD model was produced by bilateral injections of Amyloid β (Aβ 1-42) into the prefrontal cortex and behavioural assessment tests and whole cell patch clamp recording under current clamp conditions were used to explore the possible protective effect of ACEA, a selective CB1 receptor agonist, against Aβ-induced toxicity in CA1 neurons. ACEA was injected 6h after amyloid β injection and continued daily for 12 days.

Results: ACEA treatment improved the learning memory behaviour compared to AD group. Aβ injected rats demonstrated irregular firing with significantly increase in the CV (p< 0.05) and a decrease in firing frequency compared to control rats, while ACEA treatment restored the regular firing pattern and normal excitability of CA1 neurons. Aβ was also resulted in a significant increase in the amplitude of after hyperpolarization potential (AHP), which play an important role in regulating the firing behaviour, and the duration of action potential (AP). In contrast, ACEA returned both amplitude of AHP and AP duration to control levels.

Conclusions: CB1 receptor activation causes neuroprotection in a rat model of AD by preserving normal neuronal intrinsic excitability.