Cannabinoids as Therapeutics
Edited by R. Mechoulam

Cannabinoids in neurodegeneration and neuroprotection

Javier Fernández-Ruiz[1], Sara González[1], Julián Romero[2] and José Antonio Ramos[1]

[1] *Departamento de Bioquímica y Biología Molecular, Facultad de Medicina, Universidad Complutense, 28040-Madrid, Spain*
[2] *Laboratorio de Apoyo a la Investigación, Fundación Hospital Alcorcón, 28922-Alcorcón, Madrid, Spain*

Introduction

Among a variety of cellular and tissue functions, it has been suggested that the endocannabinoid system might also exert an important function in the cellular decision about death or survival (for review see [1–3]). This finding has derived from several experimental observations indicating that cannabinoids combine at the same time neuroprotective [4–6] and anti-proliferative [1, 3] properties. Thus, over the last decade, a considerable volume of work has accumulated evidence to assume that the endocannabinoid system plays a role in the protection against acute or chronic brain damage [4–6]. This fact is particularly relevant considering the postmitotic characteristics of neuronal cells, which makes repair processes after several types of brain injury extremely difficult. For instance, plant-derived, synthetic and/or endogenous cannabinoids provide neuroprotection in *in vitro* and *in vivo* models that replicate cytotoxic events, mainly energy failure and excitotoxicity, occurring during several types of accidental brain injury (i.e. ischemia and head trauma), that acutely trigger degeneration (see [4–6] for recent reviews). In addition, cannabinoids are also neuroprotective in several chronic neurodegenerative pathologies that also involve the occurrence of excitotoxicity, mitochondrial dysfunction, inflammation and/or oxidative stress, such as Parkinson's disease (PD), Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), Alzheimer's disease (AD) and multiple sclerosis (MS); see [4, 7] for review.

On the other hand, the activation of different elements of the endocannabinoid system, as part of an endogenous protectant response, has been documented in different experimental paradigms of neurodegeneration, although with variable results, depending on age, species, type and severity of injury, and mechanism(s) activated for cell death (reviewed in [5, 8, 9]). Thus, several studies have demonstrated that neuronal damage is accompanied by an increase in the production of endocannabinoids (see [5, 8] for recent reviews), although