Neurochemistry and Neuropharmacology

P252. Nano-Formulated Anandamide Decreases Neuroinflammatory Markers in Spontaneously Hypertensive Rats

Feres José Mocayar Marón[1], Virna Margarita Martín Giménez[2], Luciana Matzzei[1], Emiliano Diez[3], Sebastián García[4], Manuel Guevara[1], Diego Enrique Kassuha[2], Roberto Yunes[4] and Walter Manucha[1]

[1]Laboratorio de Farmacología Experimental Básica y Traslacional, Área de Farmacología, Departamento de Patología, Facultad de Ciencias Médicas, Universidad Nacional de Cuyo (IMBECU-CONICET), Mendoza, Argentina
[2]Instituto de Investigación en Ciencias Químicas, Facultad de Ciencias Químicas y Tecnológicas, Universidad Católica de Cuyo, Sede San Juan, Argentina
[3]Instituto de Fisiología, Facultad de Ciencias Médicas, Universidad Nacional de Cuyo, Mendoza, Argentina
[4]Instituto de Investigaciones Biomédicas (INBIOMED)-IMBECU-CONICET, Universidad de Mendoza, Argentina
Presenting author: Feres José Mocayar Marón, fmocayar@gmail.com

Essential hypertension is responsible for almost 95% of all cases of hypertension. Frequently of neurogenic origin, it is linked with an over-excitation of brainstem centers, sympathetic hyperactivation, and imbalance in the levels of pro- and anti-inflammatory cytokines. Spontaneously hypertensive rats (SHRs) is a validated model of hypertension plus several neurocognitive deficits. Since endocannabinoid anandamide (AEA) protects neurons from the inflammatory damage, and cannabinoid signaling decreases in brains of hypertensive animals, we applied a nano-formulated AEA in SHR. We used adult male rats ($n = 7$) of 250 to 300 g normotensive (WKY) and hypertensive (SHR), treated or not with nano-formulated AEA in polycaprolactone (AEA/PCL), at a weekly dose of 5 mg/kg IP, for 4 weeks. Regarding WKY, the SHR showed elevated inflammatory markers (IL-1, IL-6, FNTα, ultrasensitive PCR, and plasma Hsp70, $p < .05$) and oxidative stress markers (NADPH oxidase and nitrites). Protein expression of WT1, AT-1, and iNOS decreased after treatment, while Hsp70 increased within the cerebral cortex ($p < .01$). On the other hand, SHR treatment with AEA/PCL returned values to normal, including abnormal behaviors. These preliminary results suggest anti-inflammatory properties of nano-formulated anandamide, both peripherally and at the level of the central nervous system, specifically within the cerebral cortex.

Neurochemistry and Neuropharmacology

P253. Withdrawn Abstract

Neurochemistry and Neuropharmacology

P254. Allosteric Modulation of α7 Nicotinic Receptors by Flavonoids

Beatriz Elizabeth Nielsen[1], Isabel Bermudez[2] and Cecilia Bouzat[1]

[1]Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB), Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina
[2]Department of Medical and Biological Sciences, Oxford Brookes University, UK
Presenting author: Beatriz Elizabeth Nielsen, nielsenbeatriz@gmail.com

Plants have emerged as a valuable source for neuroprotective compounds like flavonoids. These polyphenolic compounds decrease neurotoxicity and the development of neurodegeneration. Potentiation of α7 nicotinic receptor, which is involved in cognition and memory, is a potential therapeutic strategy in neurodegenerative disorders. In particular, positive allosteric modulators (PAMs) are emerging as the best therapeutic tools. Some flavonoids have been reported as ligands for α7, but the molecular mechanisms underlying this interaction remain unknown. Our main goal is to unravel the molecular basis of flavonoid action at α7 by electrophysiological techniques. We analyzed the effects of prototypes of distinct classes of flavonoids: quercetin, genistein, and 7-dihydroxy-4-phenylcoumarin (neoflavonoid) on α7 activity. At the macroscopic level, the three compounds increased the peak current elicited by acetylcholine with minimal effects on desensitization, indicating that they behave as type I PAMs. At the single-channel level, they increased, with different efficacies, the duration of the open state. By analyzing the effects of flavonoids on mutant and chimeric α7 receptors, we found that they share the transmembrane structural determinants of potentiation known for other PAMs. We conclude that, in addition to the well-known effects as antioxidants, the unique properties of flavonoids as natural α7 PAMs make them candidate compounds for the treatment of neurodegenerative disorders.