Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol11Issue1abst003.pdf

Transient Receptor Potential Vanilloid Subtype 1 (TRPV1) In Alzheimer`S Disease And The Effects Of Cannabinoids

Diana Aguirre-Rueda, Soraya Vallés. University of Valencia, Valencia, Spain

One of the hallmarks in Alzheimer's disease (AD) is accumulation of beta-amyloid (Aβ) around neurons and the glial cell activation, such as astrocytes, occurs after plaques appear in brain damaged, to protect neurons from the toxic attack of Aβ, inducing production of anti-inflammatory molecules to decrease the neuro-inflammatory process. Many lines of evidence have suggested that transient receptor potential (TRP) channels consisting of six main subfamilies termed the TRPC (canonical), TRPV (vanilloid), TRPM (melastatin), TRPP (polycystin), TRPML (mucolipin), and TRPA (ankyrin) are involved in (Ca^{2+}) homeostasis disruption. Thus, emerging evidence of the pathophysiological role of TRP channels has yielded promising candidates for molecular entities mediating (Ca^{2+}) homeostasis disruption in AD. ***(Yamamoto S et al, Biochim Biophys 1772(8):958-67, 2007).*** Abnormalities in calcium (Ca^{2+}) regulation in astrocytes have been documented in studies of experimental models of AD, suggesting contributions of these alterations and neuro-toxic factors including reactive oxygen species (ROS), nitric oxide (NO), and cytokines on neuronal dysfunction and cell death in AD. ***(Mattson MP & Chan SL, Cell Calcium 34(4-5):385-97, 2003).*** TRPV1 is also found in astrocytes and accumulating evidence in the literature indicates that TRPV1 have many functions inside the brain, some neuro-protective or neuro-toxic. TRPV1 and has been implicated in neurodegeneration, because can initiate calcium-dependent apoptosis of neuronal and glial cell types. TRPV1 can are activated by phyto and endo cannabinoids such as THC, CBD, CBN, anandamine, and others including temperatures above 43ºC, low pH, and the active ingredient in hot peppers. ***(Karen W Ho et al, Am J Neurodegener Dis 1(1):1-14, 2012).*** The aim of this work is to determine the potential therapeutic effect of cannabinoids on the TRPV1 affected by Aβ. We incubated astrocytes in primary culture **(Vallés SL et al, Brain Pathol 14(4):365-71, 2004)** of Sprawley Dawley, for 24 hr with 10 μM Aβ40–1 **(C),** 10 μM Aβ1–42 **(Aβ)**, 10 μM WIN 55, 212-2 **(Win)** and 10 μM WIN 55, 212-2+10 μM Aβ1–42 **(Win+Aβ)** for 24 hr. Astrocytes were incubated with Win 24 hr before the addition of Aβ. We measured the protein expression levels of TRPV1 by Western-blot technique. The protein is shown and α-tubuline was used as control amount of protein. The results are (Relative Densitometric Units: RDU): **C:** 0, 91±0, 06; **Aβ:** 1, 31±0, 18 ***P<0, 02**; **Win:** 1, 02±0, 18; **Win+Aβ:** 0, 90±0, 18 **#P<0, 05**. Data are means±SD of four independent experiments. *P<0.05 vs. control sample. #P<0.05 vs. Aβ. Our group has shown these alterations in astrocytes in primary culture comparing Aβ with control cells. Here we determined the action of cannabinoids on TRPV1 in astrocytes in culture. Data show that perturbed cellular calcium homeostasis plays a prominent role in the pathogenesis of AD, suggesting potential benefits of therapeutic strategies that stabilize cellular calcium homeostasis maybe using cannabinoids.