

6th Global Summit on

Toxicology & Applied Pharmacology

October 17-19, 2016 Houston, USA

Neuroprotective or neurotoxic effects of 4-aminopyridine mediated by KChIP1 regulation in primary hippocampal cells

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4-Aminopyridine (4-AP) is a potassium channel blocker used for the treatment of neuromuscular disorders. Otherwise, it has been described to produce a large number of adverse effects among them cell death mediated mainly by blockage of K⁺ channels. Specifically, 4-AP has been reported to produce cell death in central nervous system on hippocampal cells. However, a protective effect against cell death has also been described. On the other hand, Kv channel interacting protein 1 (KChIP1) is a neuronal calcium sensor protein that is predominantly expressed at GABAergic synapses and it has been related with modulation of K⁺ channels, GABAergic transmission and cell death. According to this KChIP1 could play a key role in the protective or toxic effects induced by 4-AP. We evaluated, in wild type and KChIP1 silenced primary hippocampal neurons, the effect of 4-AP (0.25mM to 2mM) with or without semicarbazide (0.3 M) co-treatment after 24 h and after 14 days 4-AP alone exposure on cell viability. 4-AP induced cell death after 24 h (from 1mM) and after 14 days treatment, which was modulated by KChIP1 through GABAergic transmission. These data might help to explain protective and toxic effects observed after overdose and long term exposure.

Biography

Javier Del Pino received his PharmD degree at the University Complutense University of Madrid in 2004. He has two Masters in Sciences 2009 and 2010. He specialized in neurotoxicology and neurodevelopmental toxicology and received his PhD in Toxicology in 2009. In 2010 he worked in Institute of Health Carlos III in the National Center of Environmental Health. From 2010 to 2012 he was Associated Researcher at University of Massachusetts (UMASS) working in Sandra Petersen's Lab in a National Institute of Health (NIH) project on developmental effects of TCDD endocrine disruptor on sexual differentiation. In 2016 he has obtained a position as Associated Professor of Toxicology at the Complutense University of Madrid.

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