

2nd International Conference on Clinical Trials and Therapeutic Drug Monitoring

August 22-24, 2016 Philadelphia, USA

Cadmium induces cell death in SN56 cholinergic neurons from basal forebrain mediated by acetylcholinesterase variants altered expression

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Cadmium is a neurotoxin compound which induces cognitive alterations similar to those produced by Alzheimer's disease (AD). However, the mechanism through which cadmium induces this effect remains unknown. In this regard, we described in a previous work that cadmium induces a more pronounced cell death on cholinergic neurons from basal forebrain. Degeneration of basal forebrain cholinergic neurons, as happens in AD, results in memory deficits attributable to the loss of cholinergic modulation of hippocampal synaptic circuits. Moreover, cadmium induces acetylcholinesterase (AChE) overexpression, which has been related to cell death induction. Moreover, AChE variants alteration has been reported to mediate apoptotic and necrotic cell loss induction of basal forebrain cholinergic neurons and development of AD. According to all above, we hypothesized that cadmium induces the more pronounced cell death on basal forebrain cholinergic neurons through alteration of AChE variants expression alteration. The present study is aimed at researching the mechanisms of cell death induced by cadmium on basal forebrain cholinergic neurons. For this purpose, we evaluated, in SN56 cholinergic murine septal cell line from basal forebrain region, the cadmium toxic effects on neuronal viability through AChE splice variants. This study proves that cadmium induces cell death on cholinergic neurons through overexpression of tetrameric AChE-S and down-regulation of monomeric AChE-R. Our present results provide new understanding of the mechanisms contributing to the harmful effects of cadmium on cholinergic neurons and suggest that cadmium could mediate this effect through AChE splices altered expression.

Biography

Javier del Pino has received his PharmD degree from the University Complutense University of Madrid in the year 2004. He has done two Master's in Sciences in the year 2009 and 2010. He did his Specialization in Neurotoxicology and Neurodevelopmental Toxicology and received his PhD in Toxicology in the year 2009. In 2010, he worked at Institute of Health Carlos III in the National Center of Environmental Health. From 2010 to 2012, he was an Associated Researcher at University of Massachusetts (UMASS), working at 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 became an Associate Professor of Toxicology at the Complutense University of Madrid, Spain

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