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Amitraz changes NE levels mediated by blocking estrogenic action in CNS of male rats

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Amitraz is a formamidine insecticide/acaricide that alters different neurotransmitters levels, among other neurotoxic effects. Oral amitraz exposure (20, 50 and 80 mg/kg bw, 5 days) has been reported to increase norepinephrine (NE) content and to decrease its metabolite and turnover rates in the male rat brain, particularly in the striatum, prefrontal cortex, and hippocampus. However, the mechanisms by which these alterations are produced are not completely understood. Amitraz alters estradiol concentrations in the brain that regulate the enzymes responsible for this neurotransmitter synthesis and metabolism. Thus, alterations in estradiol levels in the brain could mediate the observed effects. To test these hypothesis regarding possible mechanisms, we treated male rats with 20, 50 and 80 mg/kg bw for 5 days with or without tamoxifen (TMX, 1 mg/kg bw), a selective estrogen receptor antagonist, and then isolated tissue from striatum, prefrontal cortex, and hippocampus. We then measured tissue levels of NE neurotransmitter. Amitraz produced a dose-dependent increase of the NE levels in all brain regions studied compared to the control group. The increase of NE ranged from highest to lowest in striatum, hippocampus and prefrontal cortex. Moreover, amitraz induced a dose-dependent decrease of MHPG metabolite content and its turnover rate (MHPG/NE) in all brain regions studied compared to the control group. MHPG decrease ranged from highest to lowest in prefrontal cortex, striatum and hippocampus and turnover rate decrease ranged from highest to lowest in striatum, prefrontal cortex and hippocampus. TMX co-treatment with amitraz partially reversed the change in NE neurotransmitter and its metabolite levels as well as the turnover rates induced by amitraz alone in all brain regions studied. Our present results provide new understanding of the mechanisms contributing to the harmful effects of amitraz.

Biography

Javier Del Pino received his PharmD degree at the University Complutense University of Madrid in 2004. He has two Master's in Sciences degrees 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 Associate 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 got a position as Associate Professor of Toxicology at the Complutense University of Madrid.

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