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Amitraz changes 5-HT levels mediated by alterations in estradiol content 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 Dopamine (DA) content and to decrease its metabolites 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 DA neurotransmitter. Amitraz produced a dose-dependent increase of the DA levels in all brain regions studied compared to the control group. The increase in DA ranged from highest to lowest in prefrontal cortex, striatum and hippocampus. Moreover, amitraz induced a dose-dependent decrease of DOPAC and HVA metabolites content and turnover rate (DOPAC+HVA/DA) in all brain regions studied compared to the control group. There were no differences between the decrease in the DOPAC and HVA content in the hippocampus, but the decrease in the DOPAC content was higher than the decrease in the HVA content in the striatum and the decrease in the HVA content was higher than the decrease in the DOPAC content in prefrontal cortex. The decrease of DA turnover rate (DOPAC+HVA/DA) ranged from highest to lowest in prefrontal cortex, hippocampus and striatum. TMX co-treatment with amitraz partially reversed the change in DA neurotransmitter and its metabolites 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 has completed his Doctor of Pharmacy degree from the Complutense University of Madrid in 2004. He has completed his Master's degree in Science, specialized in Neurotoxicology and Neurodevelopmental Toxicology and has completed his PhD in Toxicology. He has worked in the Institute of Health Carlos III from the National Center of Environmental Health. 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 got a position as Associated Professor of Toxicology at the Complutense University of Madrid.

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