Chronic oral exposure to low doses of Chlorpyrifos differentially affects physical and behavioral endpoints in ApoE2, ApoE3 and ApoE4 transgenic mice

Peris F1,2, Reverté I1,2, Cabré M1, Domingo JL1, Sánchez-Santed F3, Colomina MT1,2

(1) Laboratory of Toxicology and Environmental Health, School of Medicine, Rovira i Virgili University, Reus, Spain; (2) Department of Psychology and Research Center in Behavioral Assessment (CRAMC), Rovira i Virgili University, Tarragona, Spain; (3) Department of Neuroscience and Health Sciences, University of Almería, Spain

fiona.peris@urv.cat

Introduction

Chlorpyrifos (CPF) is an organophosphate pesticide widely used over the world in intensive agriculture and livestock. Various studies have demonstrated neurotoxic effects in adult mammals after chronic and acute CPF exposure such as cognitive impairments (1), oxidative stress (2) and neuronal damage (3), which suggest a possible relationship between CPF exposure and Alzheimer’s disease (AD) or cognitive impairment in aged population (4). Genetics, gender or age provide distinct protection or vulnerability to AD. According to this, being carrier of the ε4 allele of the apolipoprotein E (ApoE) gene is a well-established risk factor to develop AD in addition to the neurotoxic effects, recently, several studies have begun to describe metabolic effects resulting from exposure to chlorpyrifos (5). The present study aims to evaluate physical and behavioral endpoints in ApoE transgenic male mice carrying different polymorphisms of human ApoE (ε2, ε3, ε4) after a chronic oral exposure to low doses of CPF.

Materials and Methods

Animals

Adult (3/6 months) ApoE (ε2, ε3, ε4) transgenic male mice. Treatment

Diet exposure using a CPF supplemented food (2mg/kg), or its respective control, throughout thirteen weeks.

Weekly body weight control over the whole treatment period. After it, five additional weekly records were made.

Food intake control during the five post-treatment weeks.

Barnes maze

Spatial reference memory task during the last week of CPF treatment (3 months after the CFF treatment started).

• Acquisition: 5 training days, 2 trials/day
  Maximum time allowed to find the escape box = 180 s
  Time to escape box < 30 s
  Time inter-trial = 30-60 min
• Retention: 1 probe trial, 24 h after the last acquisition session
  Without escape box
  Time of free movement = 120 s

Cholinesterase (Che) activity

Plasma Che levels assessed by the Ellman method using Cobas Mira analyzer in two stages: half of treatment (1.5 months) and the end of it (3 months).

Results and Discussion

Conclusions

Body weight changes

There were no significant differences in food intake among CPF treated subjects and their respective controls, nor between the three different genotypes.

In conclusion, CPF differentially affects physical and behavioral endpoints in ApoE2, ApoE3 and ApoE4 transgenic mice. Further studies are needed to understand the mechanisms of action of CPF on memory and learning processes.

References