

Methyl Parathion Toxicity in Rats is Changed by Pretreatment with the Pesticides Chlordecone, Mirex and Linuron

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Introduction

Methyl parathion administration (MPT) leads to a dose-dependent reduction of acetylcholinesterase activity (Benke and Murphy 1975). The mechanism of action requires activation of methyl paraoxone by the hepatic enzyme system, presumably by cytochrome P-450-mediated metabolism. Phenobarbital, the P-450 inducer, can reduce the toxicity of MPT (Sultatos 1987), whereas some pesticides may change the hepatic enzyme system. The purpose of the present investigation was to elucidate if pretreatment with other pesticides and phenobarbital changed the toxicity of MPT, expressed by the AChE activity in the brain, after a sublethal dose of the organophosphate.

Materials and Methods

Six groups of 10 male Wistar rats each (200-250 g) were injected with 2.5 mg MPT/kg intraperitoneally. One group was not pretreated. A second group was pretreated for 3 days with betanaphthoflavone, 35 mg/kg i.p. The other groups were pretreated for 7 days, one with phenobarbital, 1 mg/ml, in drinking water, *ad libitum*, and the following groups were dosed daily by gavage with the insecticides chlordecone, 1 mg/kg, or mirex, 5 mg/kg, or the herbicide linuron, 35 mg/kg.

Two hours after the MPT injection the rats were decapitated, the brains were removed and homogenized. The AChE activity was assayed by the modified method of Ellman et al (1961), great precaution being taken to avoid temperature changes and to keep the time interval between incubation and measurement constant. Using a spectrophotometer, the enzymatic activity was measured at 410 nm at 37°C. All values presented are means \pm SD.

Results

The AChE activity in brains of the rats given MPT alone was found to be $7.99 \pm 0.41 \mu\text{mol} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$, representing about 20% lower activity than without treatment (data not presented).

When rats were pretreated with phenobarbital, chlordecone or mirex, the inhibition of the AChE following MPT was reduced, the AChE activities measured to 8.53 ± 0.74 , 8.58 ± 0.77 and $8.82 \pm 0.87 \mu\text{mol} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$, respectively. For all three groups these values were significantly different from the MPT only group ($p < 0.05$, two-sided Student's *t*-test).

Pretreatment with linuron had the opposite effect, as the AChE activity was further reduced compared with the MPT only group, the activity being $7.39 \pm 0.55 \mu\text{mol} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$. This is a significant decrease ($p < 0.05$). Betanaphthoflavone did not affect the MPT effect significantly, the AChE activity in this group being 8.12 ± 0.52 .

Conclusion

The AChE activity in the brain following a single dose of MPT was increased after pretreatment with phenobarbital, and the insecticides chlordecone and mirex, which could be interpreted as a reduction of toxicity concerning acetylcholinesterase inhibition. Pretreatment with the herbicide linuron, on the other hand, led to a further decrease in AChE activity than found with MPT alone, representing a sign of increased toxicity. These signs of positive and negative toxic interactions after exposure to more than one pesticide may have consequences for a similar human situation.

References

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