Permanent effects on monoaminergic neurotransmitters biosynthesis and metabolism after prenatal and postnatal exposure to Chlordimeform, in female and male rat's prefrontal cortex

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INTRODUCTION

Formamidine pesticides induce permanent sex and region-dependent effects on development of monoaminergic neurotransmitter systems. The mechanisms that induce these effects are not known, but it has been suggested that these effects could be related to monoamine oxidase (MAO) inhibition. However, chlordimeform, a formamidine pesticide, is a very weak MAO inhibitor, which suggests that other mechanism should be involved. In this regard, formamidines, in general and chlordimeform, in particular, may alter the expression of the enzymes that mediate the synthesis and metabolism of monoaminergic neurotransmitters systems. Therefore, an alteration of these enzymes in the brain could mediate the effects observed.

METHODS

In order to confirm that the formamidines produce permanent alterations of the monoamine neurotransmitter systems by alteration of the expression of the enzymes that synthesize and/or metabolize these neurotransmitters, we evaluated, in frontal cortex of male and female rats, the effect on the expression of MAO, COMT, BDH, TH, TRH and AD enzymes at 60 days of age after maternal exposure to chlordimeform (5 mg/kg body weight).

RESULTS

Chlordimeform induced a significant decrease in the expression of the enzymes TRH and TH in both males and females. We determined a bigger increase in the expression of TH [35, 66% (P<0,001)] and TRH [42, 14% (P<0,001)] enzymes in males than in females. Chlordimeform treatment did not alter the expression of MAO, COMT, AD, BDH enzymes.

CONCLUSIONS

The present findings indicate that after maternal exposure to formamidines, in general and chlordimeform, in particular, induces a permanent alteration of monoaminergic neurotransmitters, through alteration of the enzymes that synthetize these neurotransmitters.

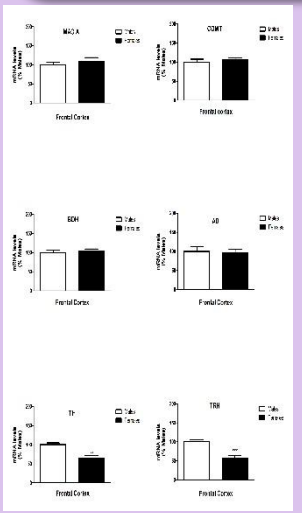

Figure x. Sex difference results from real-time PCR targeting MAO, COMT, BDH, AD, TH y TRH genes after chlordimeform treatment in male and female rats. MAO, COMT, BDH, AD, TH y TRH gene expression was compared to male rats results. Each bar represents mean ± SD of 6 samples. Levels were measured using QPCR. ACTB was used as an internal control. ***p ≤ 0.001, **p ≤ 0.01, significantly different from males.

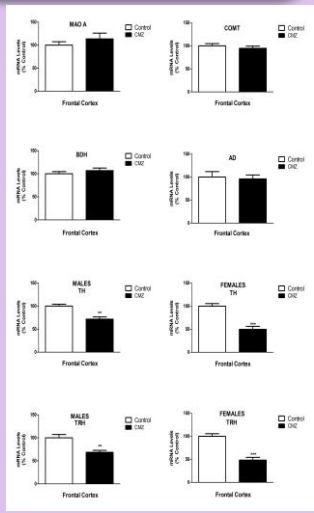

Figure x. Results from real-time PCR targeting MAO, COMT, BDH, AD, TH y TRH genes after chlordimeform treatment in male and female rats. MAO, COMT, BDH, AD, TH y TRH gene expression was compared to controls. Each bar represents mean ± SD of 6 samples. Levels were measured using QPCR. ACTB was used as an internal control. ***p ≤ 0.001, **p ≤ 0.01 significantly different from controls.