Effects of prenatal and postnatal exposure to chlordimeform on serotonin levels in brain regions of adult's male and female rats.

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INTRODUCTION

Formamidines pesticides have been described to induce permanent effects on development of monoaminergic neurotransmitters systems. The mechanisms that induce these effects are not known but it has been suggested that these effects could be related to monoamino oxidase (MAO) inhibition. Chlordimeform is a formamidine pesticide which is a very weak inhibitor of MAO although it has been also described to produce neurodevelopmental toxicity. According to all above, we hypothesized that chlordimeform induced permanent alteration of noradrenergic system through a mechanism which is regardless of MAO inhibition.

METHODS

In order to confirm that formamidines induce permanent alterations of monoaminergic neurotransmitter systems regardless of MAO inhibition, the effects of maternal exposure to chlordimeform (5 mg/kg bw,orally on days 6–21 of pregnancy and 1–10 of lactation) on brain region serotonin levels of male and female offspring rats at 60 days of age were evaluatedin brain regions by HPLC.

RESULTS

In male and female offspring, chlordimeform induced a significant decrease in the striatum and prefrontal cortex 5-HT and its metabolite 5-HIAA levels. This effect was with statistical distinction of sex in the prefrontal cortex. In contrast, chlordimeform caused an increase in 5-HT and 5-HIAA content in the hippocampus in male and female offspring with sex interaction. Chlordimeform evoked increases in 5-HT turnover in the prefrontal cortex and hippocampus from females and males respectively but evoked a decrease in these regions from males and females respectively.

CONCLUSIONS

The present findings indicated that maternal exposure to chlordimeform altered serotonergic neurochemistry in their offspring in prefrontal cortex, striatum and hippocampus, and those variations show that other mechanisms different from MAO inhibition are implicated.

Table 1. Tissue 5-HT and 5-HIAA concentrations in male and female rat pups observed at 60 days of age after the exposure of dams to chlordimeform (5 mg/kg bw orally on days 6 to 21 of pregnancy and 1 to 10 of lactation).

Tissue	5-HT (ng/g)		5-HIAA (ng/g)		5-HIAA/5-HT	
	Control group	Treated group (pups from treated dams)	Control group	Treated group (pups from treated dams)	Control group	Treated group (pups from treated dams)
HT	2211,69 ± 39,58	2246,49 ± 43,96	1175,98 ± 39,15	1210,17± 43,53	0,53 ± 0,02	0,54 ± 0,03
MB	2605,67 ± 23,42	2619,96 ± 22,86	1721,96 ± 11,30	1725,23 ±13,72	0,66 ± 0,01	0,66 ± 0,01
CB	131,96 ± 7,43	136,73 ± 7,52	116,42 ± 4,06	120,80 ± 5,12	0,90 ± 0,06	0,90 ± 0,08
MO	1204,19 ± 28,25	1206,92 ± 43,62	838,13 ± 17,51	845,56 ± 17,22	0,70 ± 0,02	0,71 ± 0,03
BS	858,80 ± 14,96	869,82 ± 19,58	452,34 ± 9,25	456,68 ± 15,93	0,53 ± 0,01	0,53 ± 0,03
PFC	1172,90 ± 26,90	[b]890,30 ± 30,44	644,05 ± 15,48	[b]471,59 ± 6,84	0,55 ± 0,02	[b]0,53 ± 0,02
ST	848,38 ± 4,72	714,77 ± 5,54***. [a](-15,75)	726,27 ± 8,55	574,37 ± 26,03***. [a](-20,92)	0,86 ± 0,01	0,80 ± 0,04
HC	534,01 ± 4,45	[b]669,83 ± 16,23	474,60 ± 6,82	[b]594,50 ± 20,10	0,89 ± 0,01	[b]0,89 ± 0,02

HT: hypothalamus; MB: midbrain; CB: cerebellum; MO: medulla oblongata; BS: brainstem; PFC: prefrontal cortex; ST: striatum; HC: hippocampus.
Data represent means ± S.E.M. with values for males and females combined (n=12: 6 males + 6 females).
Statistical significance is reported for the *P<0.05, **P<0.01 and ***P<0.001 levels compared with the control group.
[a]Percentage change from control values.
[b]Significant treatment × sex interaction.

Table 2. Statistical analysis for tissue values with significant treatment × sex interaction.

Tissue		5-HT (ng/g)		5-HIAA (ng/g)		5-HIAA/5-HT	
		Control group	Treated group (pups from treated dams)	Control group	Control group	Treated group (pups from treated dams)	Control group
CF	Males	1157,41 ± 38,51	960,77 ± 2,78***. [a](-16,99%)	679,37 ± 4,49	464,96± 8,78***. [a](-31,56%)	0,59 ± 0,021	0,4 8± 0,010**. [a](-18,02%)
	Females	1188,40 ± 8,72	819,82 ± 6,68***. [a](-31,01%)	608,73 ± 6,96	478,23 ± 2,84***. [a](-21,44%)	0,51 ± 0,01	0,58 ± 0,007***. [a](13,92%)
HC	Males	536,10 ± 4,09	702,58 ± 5,21***. [a](31,05%)	466,56 ± 3,45	641,25 ± 3,01***. [a](37,44%)	0,87 ± 0,008	0,91 ± 0,010**. [a](4,89%)
	Females	531,91 ± 5,00	637,09 ± 11,10***. [a](19,77%)	482,64 ± 8,04	547,74 ± 2,39***. [a](13,49%)	0,91 ± 0,011	0,86 ± 0,017***. [a](-5,08%)

PFC: prefrontal cortex. Other tissue values were not evaluated because of the lack of treatment × sex interactions.
Values are mean ± S.E.M.; control animals (n= 6 males, n= 6 females); treated group (n= 6 males, n= 6 females).
Statistical significance is reported for the **P<0.01 and ***P<0.001 levels compared with the control group within each sex as determined by one-way ANOVA, followed by the Student's t test.
[a]Percentage change from control values.