Title: EXPOSURE TO ISOFLURANE AFFECTS LEARNING FUNCTION OF MURINE PROGENY

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Introduction. It has been shown that halothane and enflurane adversely affected the learning function of murine progeny [1]. This effort was conducted to assess if isoflurane had similar effects.

Methods. Thirty white Swiss Webster mice, randomly divided into 5 equal groups, were tested, after 24 hours of starvation, in a maze containing two 20 mg food pellets. The time taken to traverse 6 compartments bisected by a central partition and with fixed and reversible exits was measured. Three maze patterns were set: 1) all exits on the right; 2) all exits on the left; 3) alternately right and left exits. The dams of four groups had received 1.3% or 2.6% isoflurane in oxygen (5 l/min) for 30 minutes, either on days 6 and 11 or 14 and 17 of gestation. The dams of the fifth group (controls) had breathed oxygen at an FIO_2 of 1 for 30 minutes on days 6, 11, 14 and 17 of pregnancy. The oxygen or isoflurane in oxygen was introduced into a 5 liter transparent chamber containing the mice. The floor of the chamber was filled with barium hydroxide lime, U.S.P. (1 Kg), separated from a layer of wood shavings, by a perforated plate. Between the ages of 6 to 10 weeks, mice were tested 3 times a day on 10 separate days, and the time taken to cover the maze recorded. Arterial blood gases and pH were measured using abdominal aortic blood from an extra mouse anesthetized with 3% isoflurane in oxygen (5 l/min). Statistical significance was assessed by Student's t test. Values of $P < 0.05$ were considered significant.

Results. On the first day of training, only the pups of mice which had received 1.3% and 2.6% isoflurane on days 14 and 17 of gestation were significantly slower than controls in the right and alternate maze pattern settings respectively (table). By the third day of training, these same groups were significantly slower than controls (alternate pattern for 1.3% and all patterns for 2.6%). By the fifth day, all groups except pups exposed to 1.3% isoflurane on days 6 and 11 of gestation, were significantly slower than controls. On the seventh and tenth day of training, all groups were significantly slower than controls, in all maze settings. Controls and the groups which had received 2.6% isoflurane on days 6 and 11, and 1.3% isoflurane on days 14 and 17 of gestation, improved significantly by the third day of training, when compared to their first training day. All other groups had made significant progress by the fifth day of training. Blood gas analysis revealed a PaO_2 of 352 torr, a $PaCO_2$ of 43 torr and a pH of 7.38, during isoflurane inhalation.

Discussion. The group most affected, as in the case of halothane [1] was that exposed to the highest anesthetic concentration on days 14 and 17 of gestation. All groups performed poorly on day 1 of training. By day 3, there was a marked retardation in the progress of the group exposed to 2.6% isoflurane on days 14 and 17 of gestation. By day 7, all groups performed significantly slower than controls. Results correlate closely with halothane and enflurane studies [1].

Reference.

1. Chalon J, Tang C-K, Ramanathan S, Eisner M, Katz R, and Turndorf H: Exposure to halothane and enflurane affects learning function of murine progeny. Anesth Analg 60: 794-797, 1981

GROUP	MS	DAY 1	DAY 3	DAY 5	DAY 7	DAY 10
CONTROL	R	92±21.3	8±0.9	8±1.1	5±0.5	4±0.4
	L	112±21.6	26±4.6	12±1.6	5±0.3	5±0.4
	A	42±8.8	17±2.5	14±2.6	7±0.8	5±0.6
1.3% DAY 6 AND 11	R	63±17.6 NS	10±1.3 NS	7±0.8 NS	7±0.8 =	7±1.0 ‖
	L	80±13.3 NS	26±4.5 NS	9±1.1 NS	9±1.4 ‖	8±1.2 =
	A	26±3.5 NS	23±5.9 NS	12±1.0 NS	10±1.4 +	9±1.8 =
2.6% DAY 6 AND 11	R	140±25.3 NS	13±2.7 NS	13±1.1 ⊥	10±1.8 ×	6±0.6 ‖
	L	195±28.3 NS	17±2.4 NS	17±2.0 +	13±1.6 =	6±0.4 +
	A	98±20.0 NS	21±3.9 NS	22±2.4 =	18±2.4 =	9±0.5 =
1.3% DAY 14 AND 17	R	161±27.2 +	13±1.5 NS	15±2.4 ×	14±2.6 ⊥	10±1.4 =
	L	159±21.8 NS	21±3.8 NS	20±3.8 +	16±2.5 =	11±1.4 =
	A	65±10.7 NS	31±6.1 =	21±1.9 =	15±1.8 =	14±1.8 =
2.6% DAY 14 AND 17	R	80±13.7 NS	31±6.1 =	40±12 ‖	30±6.0 =	14±2.0 =
	L	112±16.1 NS	54±14.4 +	45±6.9 =	36±5.3 =	15±2.2 =
	A	83±8.7 ⊥	99±25.2 ⊥	36±4.5 =	36±4.8 =	21±1.8 =

Table. Performance of mice born to dams exposed to isoflurane. Values are means ± SEM. Abbreviations used are: MS, maze setting; R, right; L, left; A, alternate. N= 3 runs by 6 mice in each instance. Paired data (progress made by each group in relation to time): one vertical line $P < 0.05$, two vertical lines $P < 0.01$; three vertical lines $P < 0.025$. Comparison between the performance of all groups exposed to isoflurane and that of controls (unpaired data): NS, not significant; + $P < 0.05$; = $P < 0.025$; ≡ $P < 0.0125$; X $P < 0.01$; ‖ $P < 0.005$; ⊥ $P < 0.0025$; ≈ $P < 0.0005$.