Effects of Acute and Repeated Exposures to Aroclor 1254 in Adult Rats: Motor Activity and Flavor Aversion Conditioning

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While considerable research has focused on the neurotoxicity of developmental exposures to polychlorinated biphenyls, including Aroclor 1254, relatively little is known about exposures in adult animals. This study investigated the behavioral effects of acute and repeated Aroclor 1254 exposures to adult rats on motor activity and flavor aversion conditioning. Male Long-Evans rats (60 days old) were tested for motor activity in a photocell device after acute (0, 100, 300, or 1000 mg/kg, po) or repeated (0, 1, 3, 10, 30 or 100 mg/kg/day, po, 5 days/week for 4 to 6 weeks) exposure to Aroclor 1254. Motor activity was decreased dose-dependently at doses of 300 mg/kg or more after acute exposure. Severe body weight loss and deaths occurred at 1000 mg/kg. Recovery of activity occurred over 9 weeks but was incomplete. After repeated exposure, motor activity was decreased dose-dependently at doses of 30 mg/kg or more, and severe weight loss and deaths occurred at 100 mg/kg. In contrast to acute exposure, complete recovery of activity occurred 3 weeks after exposure. Additional rats were water deprived (30 min/day) and received acute po administration of Aroclor 1254 (0, 10, 15, 25, 30, 100, or 300 mg/kg) shortly after consuming a saccharin solution. Three days later they were given the choice between consuming saccharin or water, and saccharin preferences were recorded. Saccharin preference was decreased at doses of 25 mg/kg or more. Additional experiments determined the effect of repeated saccharin–Aroclor 1254 pairings (0, 3.75, 7.5, or 15 mg/kg/day, 14 days) followed by a choice test 1 day after the last dose. Repeated exposure to 15 mg/kg produced robust flavor aversion conditioning. Repeated exposure to 7.5 mg/kg produced flavor aversion conditioning in four of 12 rats. These results demonstrate that Aroclor 1254 causes hypoactivity and flavor aversions in adult rats; the no observable effect level (NOEL) for motor activity was 100 mg/kg for acute exposure and 10 mg/kg for repeated exposure for a period of up to 6 weeks. The acute NOEL for flavor aversion conditioning was 15 mg/kg while the repeated NOEL was 7.5 mg/kg.

Key Words: polychlorinated biphenyl; Aroclor 1254; motor activity; flavor-aversion conditioning; rats.

Polychlorinated biphenyls (PCBs) have been identified as widespread environmental contaminants due to their extensive industrial use and persistence in the environment (Erickson, 1986). PCBs were commercially synthesized as mixtures by the chlorination of biphenyls, with the resulting products designated by their chlorine content (Hutzinger et al., 1974). For example, Aroclor 1254 contains 54% chlorine by weight. PCB mixtures may contain up to 209 possible congeners and Aroclor 1254 has been reported to contain up to 81 of them (Albro et al., 1981).

Most neurobehavioral studies have focused on the developmental neurotoxicity of PCBs. For example, it has been reported that exposure of mice, rats, and monkeys to PCBs during early development can adversely affect later behavioral and cognitive function (Shiota, 1976; Tilson et al., 1979; Bowman and Heironimus, 1981; Storm et al., 1981; Schantz et al., 1989). It has been suggested that PCB-induced developmental neurotoxicity may be caused by a thyroid hormone deficiency during a critical developmental period (Porterfield, 1994).

Compared to the effects of developmental PCB exposure, relatively little is known about the neurobehavioral effects of exposure to PCBs during adulthood, although some neurotoxic signs such as numbness and weakness in the limbs were reported in human poisoning episodes (Kuratsune et al., 1974). A recent review of several epidemiological studies involving occupational exposure in adults indicated that the results were inconclusive (Swanson et al., 1995). Acute exposure to the PCB mixture Aroclor 1254 has been reported to decrease motor activity in mice, although it did not affect motor coordination or pentylentetrazol-induced convul-
sions (Rosin and Martin, 1981). Repeated exposure (14 days) to Aroclor 1254 had no motor activity effects in mice (Rosin and Martin, 1981). Seegal et al. (1986, 1991) reported that dopamine concentrations and/or metabolism in the striatum and lateral olfactory tract decreased in adult rats and in monkeys after both acute and subchronic exposure to Aroclor 1254. Alterations in neurochemical function following PCB exposure during adulthood suggest the possibility of neuro-behavioral changes as well.

The present series of experiments investigated the effects of acute and repeated Aroclor 1254 exposures in adult rats. Two behavioral preparations were used: motor activity and flavor aversion conditioning. Motor activity refers to a broad class of naturally occurring behavior that has been used to evaluate the effects of a wide variety of chemical exposures, including metals, solvents, pesticides, and drugs, as well as direct damage to the central nervous system (e.g., Crofton et al., 1991; MacPhail et al., 1989). Flavor aversion conditioning refers to the learned alteration of flavored fluid preferences by pairing intake of the fluid with subsequent chemical treatment; altered fluid preference is thought to reflect the aversive ornoxious properties of chemical administration. Flavor aversion conditioning has also been used to evaluate the effects of many metals, solvents, pesticides, and drugs, as well as direct damage to the nervous system (e.g., Riley and Tuck, 1985; Peele et al., 1987). The two behavioral preparations have the advantage of simplicity and ease of testing, since each utilizes behaviors that have a high probability of occurrence in laboratory rats. Additionally, results of the two behavioral test methods may provide insights into the biological basis for chemical-induced alterations in motor activity (see MacPhail et al., 1989).

MATERIALS AND METHODS

Effects of Acute and Repeated Aroclor 1254 Exposure on Motor Activity

Subjects. Three groups of 36 male Long-Evans rats (Charles River Laboratories, Inc., Raleigh, NC) were obtained at 60 days of age and acclimated to the animal quarters for 1 week prior to study. The colony room was maintained at 21.0 ± 2.0°C with 55% relative humidity and had a 12-hr:12-hr light:dark cycle with lights on at 0600 hr. Animals were housed in groups of two in standard plastic cages lined with wood shavings. They were allowed unlimited access to food (Purina Lab Chow) and water in their home cages.

Chemical. Aroclor 1254 (Lot 602A; AccuStandard, New Haven, CT) was dissolved in warm corn oil. Solutions were prepared the day before dosing in the acute exposure study, and once each week or two in the repeated exposure studies.

Apparatus. Six automated motor activity devices (Motron Motility Meter, Stockholm, Sweden) were used. Each device was composed of a 20.5 × 32-cm platform housing a 5 × 8 matrix of photodetectors, with illumination provided by a single overhead 30-Watt incandescent lamp. Movements that occluded these detectors were recorded as horizontal activity. In addition, an array of 6 photoemitters and detectors was placed 16 cm above the platform and was used to record vertical activity. Animals were individually placed in a Plexiglas chamber (22 × 33.5 × 29 cm) positioned on each platform. Each device was housed in a larger ventilated sound- and light-attenuating enclosure. Programming and data recording equipment were located in an adjacent room.

Acute exposure. Thirty-six rats were divided into four groups (N = 9) and administered Aroclor 1254 by oral gavage at doses of 0 (i.e., corn oil vehicle), 100, 300, or 1000 mg/kg in a volume of 2 ml/kg. The dosing was conducted between 1115 and 1410 hr. Motor activity was measured during a 30-min session beginning 45 min after dosing (day 0). Motor activity was also measured before dosing (day −7), and 1, 7, 14, 21, 28, and 62 days after dosing. Body weights were recorded once every 2 or 3 days throughout the experiment.

Repeated exposure. Two experiments were conducted to assess the effects of repeated exposure to Aroclor 1254 on motor activity. In the first experiment, 36 rats were divided into four groups (N = 9) and were administered Aroclor 1254 at doses of 0 (i.e., vehicle), 10, 30, or 100 mg/kg in a volume of 2 ml/kg by oral gavage once daily, 5 days a week. The dosing period was 4 weeks, except for 100 mg/kg which was terminated after 2 weeks because of significant body weight loss and mortality. Aroclor 1254 was given 45 min before motor activity measurement on the test day and between 0800 and 1000 hr on the other days. Motor activity during a 30-min session was measured before dosing, 45 min after the first dose (day 0), and once weekly thereafter. To examine the reversibility of motor activity changes produced by Aroclor 1254, testing was continued weekly for 5 weeks after the final dose. Body weights were recorded every 2 or 3 days throughout the experiment.

Based on results obtained in the first repeated-dosing experiment indicating a significant decrease in motor activity at one time point after 10 mg/kg, the second study sought to determine more precisely PCB-induced effects on motor activity. Thirty-six rats were divided into four groups (N = 9) and administered Aroclor 1254 at doses of 0 (i.e., vehicle), 1, 3, or 10 mg/kg in a volume of 2 ml/kg by oral gavage once daily, 5 days per week. Aroclor 1254 was given 45 min before motor activity measurement on the test day and between 0800 and 1000 hr on the other days. The dosing period in this experiment was extended to 6 weeks. Motor activity during a 30-min session was measured before dosing, on the day dosing commenced, and once weekly thereafter. Body weights were recorded every 2 or 3 days throughout the experiment.

Data analysis. Motor activity data were converted to percentages of predose values and then analyzed. Motor activity and body weight data were analyzed using one-way analyses of variance (ANOVA) followed by Dunnett's t tests. The data from the 100-mg/kg rats in week 3 and thereafter were excluded from analysis in the first repeated dose study because only one animal survived. For all statistical analyses, p < 0.05 was considered significant.

Flavor Aversion Conditioning by Aroclor 1254

Subjects. Five groups of 18 male Long-Evans rats (Charles River Laboratories, Inc., Raleigh, NC) were obtained at 60 days of age. Rats were individually housed in metal ceiling-suspended cages and allowed unlimited access to food (Purina Lab Chow) and water in their home cages. Six automated motor activity devices (Motron Motility Meter, Stockholm, Sweden) were used. Each device was composed of a 20.5 × 32-cm platform housing a 5 × 8 matrix of photodetectors, with illumination provided by a single overhead 30-Watt incandescent lamp. Movements that occluded these detectors were recorded as horizontal activity. In addition, an array of 6 photoemitters and detectors was placed 16 cm above the platform and was used to record vertical activity. Animals were individually placed in a Plexiglas chamber (22 × 33.5 × 29 cm) positioned on each platform. Each device was housed in a larger ventilated sound- and light-attenuating enclosure. Programming and data recording equipment were located in an adjacent room.

Acute exposure. Thirty-six rats were divided into four groups (N = 9) and administered Aroclor 1254 by oral gavage at doses of 0 (i.e., corn oil vehicle), 100, 300, or 1000 mg/kg in a volume of 2 ml/kg. The dosing was conducted between 1115 and 1410 hr. Motor activity was measured during a 30-min session beginning 45 min after dosing (day 0). Motor activity was also measured before dosing (day −7), and 1, 7, 14, 21, 28, and 62 days after dosing. Body weights were recorded once every 2 or 3 days throughout the experiment.

Repeated exposure. Two experiments were conducted to assess the effects of repeated exposure to Aroclor 1254 on motor activity. In the first experiment, 36 rats were divided into four groups (N = 9) and were administered Aroclor 1254 at doses of 0 (i.e., vehicle), 10, 30, or 100 mg/kg in a volume of 2 ml/kg by oral gavage once daily, 5 days a week. The dosing period was 4 weeks, except for 100 mg/kg which was terminated after 2 weeks because of significant body weight loss and mortality. Aroclor 1254 was given 45 min before motor activity measurement on the test day and between 0800 and 1000 hr on the other days. Motor activity during a 30-min session was measured before dosing, 45 min after the first dose (day 0), and once weekly thereafter. To examine the reversibility of motor activity changes produced by Aroclor 1254, testing was continued weekly for 5 weeks after the final dose. Body weights were recorded every 2 or 3 days throughout the experiment.

Based on results obtained in the first repeated-dosing experiment indicating a significant decrease in motor activity at one time point after 10 mg/kg, the second study sought to determine more precisely PCB-induced effects on motor activity. Thirty-six rats were divided into four groups (N = 9) and administered Aroclor 1254 at doses of 0 (i.e., vehicle), 1, 3, or 10 mg/kg in a volume of 2 ml/kg by oral gavage once daily, 5 days per week. Aroclor 1254 was given 45 min before motor activity measurement on the test day and between 0800 and 1000 hr on the other days. The dosing period in this experiment was extended to 6 weeks. Motor activity during a 30-min session was measured before dosing, on the day dosing commenced, and once weekly thereafter. Body weights were recorded every 2 or 3 days throughout the experiment.

Data analysis. Motor activity data were converted to percentages of predose values and then analyzed. Motor activity and body weight data were analyzed using one-way analyses of variance (ANOVA) followed by Dunnett's t tests. The data from the 100-mg/kg rats in week 3 and thereafter were excluded from analysis in the first repeated dose study because only one animal survived. For all statistical analyses, p < 0.05 was considered significant.
Procedure. Five experiments were conducted on Aroclor-1254-induced flavor aversion conditioning. Eighteen rats were used in each experiment. The first three experiments involved acute exposures to Aroclor 1254. Four days after arrival at the laboratory, rats were placed on a restricted water schedule that allowed 30 min access each day beginning at 0900 hr. Total water intakes were calculated (to the nearest 0.1 g) from drinking tube and spout weights determined before and after the 30-min access period. The rats were maintained on the water restriction schedule until daily intakes stabilized (group mean intakes over 5 successive days showed coefficients of variation of 10% or less). In order to acclimate the rats to the gastric intubation procedure for Aroclor 1254 dosing, 2 ml/kg of corn oil was administered via 18-gauge feeding tubes 20 min after water consumption on days 12 and 15.

On day 16, a 0.1% (w/v) sodium saccharin solution was presented for 30 min instead of water during the daily access period. The rats were then divided into three groups (N = 6). About 20 min following saccharin availability, each group of rats was administered Aroclor 1254 by oral gavage at a dose of 0 (i.e., vehicle), 100 or 300 mg/kg (experiment 1) or 0, 10, or 30 mg/kg (experiment 2) or 0, 15 or 25 mg/kg (experiment 3) in a volume of 2 ml/kg. On days 17 and 18 rats were again exposed to the limited water schedule (30 min/day). On day 19, tap water and the saccharin solution were concurrently available for 30 min (choice test).

The fourth and fifth experiments involved repeated exposures to Aroclor 1254. In these experiments, once daily (30 min) water intakes had stabilized, saccharin solution was provided (30 min) daily and followed by treatment with either 0, 7.5, or 15 mg/kg (experiment 4) or 0, 3.75, or 7.5 mg/kg (experiment 5) of Aroclor 1254. Saccharin-Aroclor 1254 pairings were continued for 14 consecutive days. During this phase of the experiments, access to water (30 min) was provided approximately 4 hr after saccharin consumption in order to minimize any effect of Aroclor 1254 on total daily fluid intake. Saccharin preference was determined 1 day after the last dose using a two-bottle choice test as described above for the acute exposure flavor aversion conditioning experiments.

Data analysis. Total fluid intake (ml saccharin intake + ml water intake) and relative saccharin intake ([ml saccharin intake/total fluid intake] × 100) during the choice test comprised the major data. For the acute exposures, relative saccharin intake data from the three experiments were combined and analyzed because there were no significant differences between the saccharin preferences for the control groups from these experiments. Total fluid intake data were also combined and analyzed. An ANOVA was used to statistically evaluate treatment effects on total fluid intake and relative saccharin intake. Dunnett's t-test was used to compare the control mean and those of the treated groups. For the repeated Aroclor 1254 flavor aversion experiments, repeated measures ANOVAs were carried out for daily saccharin intake and daily post-saccharin water intake. Choice-testing data, collected 1 day after the last daily dose, were analyzed in the same manner as were the acute flavor-aversion data. For all statistical analyses, p < 0.05 was considered significant.

RESULTS

Effects of Acute and Repeated Exposure to Aroclor 1254 on Motor Activity

Effects of acute exposure to Aroclor 1254. ANOVA showed that Aroclor 1254 had a significant effect on body weights. Severe weight loss was seen in the 1000-mg/kg group (Fig. 1), and four of nine rats died between 14 and 28 days after dosing (Fig. 1). The 300-mg/kg group showed either a slight decrease in weight or no growth through day 10 and then increased at a rate similar to the control group. Body weights of animals receiving 100 mg/kg were not affected. Aroclor 1254 treatment also produced a significant effect on horizontal activity. Subsequent comparisons showed that the horizontal activity of rats receiving 1000 mg/kg was significantly less than that of the control group at 45 min and 7 days after dosing (Fig. 2A). There were no other significant effects on horizontal motor activity in this study. The effect of Aroclor 1254 on vertical activity was also significant. Subsequent comparisons showed that the vertical activity of rats receiving 300 mg/kg or more was significantly less than that of the control group 45 min after dosing (Fig. 2B). The animals receiving 100 mg/kg were not significantly affected. Therefore, the lowest NOEL in this study was 100 mg/kg for decreases in body weight and vertical activity and the corresponding LOEL was 300 mg/kg (Table 1).

Effects of repeated exposure to Aroclor 1254. Repeated exposure to Aroclor 1254 significantly affected body weights. Severe weight loss was seen in the 100-mg/kg group (Fig. 3), and eight of nine rats died between days 14 and 21. The 30-mg/kg group showed either slight weight loss or no growth through day 28, followed by a steady body weight gain thereafter. Animals receiving 10 mg/kg were not affected. Repeated exposure to Aroclor 1254 also significantly affected horizontal activity. No effects were seen on horizontal or vertical activity 45 min after the first dosing (day 0; Fig. 4). Statistically significant changes in horizontal activity were seen on day 22 at 10 mg/kg, on day 14 through day 42 at 30 mg/kg, and on days 7 and 14 at 100 mg/kg (Fig. 4A). Complete recovery was seen on day 49 (3 weeks after exposure had ceased) at both 10 and 30 mg/kg. Statistically significant changes in vertical activity were seen on day 22 through day 42 at 30 mg/kg and on days 7 and 14 at 100 mg/kg. Complete recovery was seen on day 49 (3 weeks after exposure) at 30 mg/kg. There were
no significant effects on vertical activity in animals receiving 10 mg/kg. In order to verify the NOEL for effects of Aroclor 1254 on horizontal activity, an additional study examined the effects of 0, 1, 3 and 10 mg/kg given repeatedly for 6 weeks. In this study, Aroclor 1254 had no significant effect on horizontal or vertical activity (data not shown). Therefore, for repeated dosing, the NOEL in this study was 10 mg/kg for decreases in body weight and motor activity, and the LOEL was 30 mg/kg.

**Flavor Aversions Induced by Aroclor 1254**

**Effects of acute exposure to Aroclor 1254.** The effects of acute Aroclor 1254 on relative saccharin intake in the choice test is shown in Fig. 5. When given the choice between water and saccharin, rats treated with vehicle had a mean relative saccharin intake of 63 ± 6% (mean ± SEM). Acute Aroclor 1254 treatment produced a significant effect on relative saccharin intake. Subsequent comparisons showed that the relative saccharin intake of rats receiving Aroclor 1254 at doses of 25 mg/kg or more was significantly decreased when compared to vehicle-control rats. The effect of Aroclor 1254 on relative saccharin intake was independent of its effect on total fluid intake. As shown in Fig. 5, a significant decrease in total fluid intake occurred in rats receiving 15 mg/kg, but not at higher or lower doses. There were no significant effects of Aroclor 1254 on body weight during 6 or 7 days following treatment. The NOEL for conditioned flavor aversion following acute exposure to Aroclor 1254 was 15 mg/kg, and the LOEL was 25 mg/kg.

**Effects of repeated exposure to Aroclor 1254.** The results of the first repeated flavor aversion conditioning experiment are shown in Fig. 6. Overall, Aroclor 1254 produced a significant effect on daily saccharin intake. Repeated pairing of saccharin and 15 mg/kg Aroclor 1254 produced a gradual reduction in saccharin intake. Repeated pairing of saccharin and 7.5 mg/kg Aroclor 1254 produced no effect on saccharin intake when saccharin was the only fluid available to drink. Repeated dosing with Aroclor 1254 had no significant effect on daily post-saccharin water intake (data not shown). Choice testing was carried out 1 day after the 14 repeated saccharin–Aroclor 1254 pairings. Figure 7 shows that 15 mg/kg of Aroclor 1254 decreased the saccharin preference seen in vehicle-treated control rats. Saccharin preference was decreased approximately 50% after 7.5 mg/kg; however, the effect was not statistically different from control. The intermediate effect of 7.5 mg/kg appeared to be due to 3 rats that had a saccharin preference similar to control rats, while the other three rats displayed a saccharin aversion similar to those dosed with 15 mg/kg. As a result of the high variability, the effect of 7.5 mg/kg was not significant. Figure 7 also shows that repeated exposure to 15 mg/kg Aroclor 1254 reduced total fluid intake on the choice test.

Because of the equivocal results of 7.5 mg/kg in the preceding experiment, the next experiment examined the effects of 3.75 and 7.5 mg/kg given repeatedly. Repeated (14-days) exposure to Aroclor 1254 produced no statistically reliable effect on saccharin intake, either during repeated pairing or on the choice test occurring 1 day after the 14th pairing (data not shown). Therefore, the NOEL for the conditioned flavor aversion following repeated exposure to Aroclor 1254 was 7.5 mg/kg and the LOEL was 15 mg/kg.

**DISCUSSION**

The results of the present study indicate that Aroclor 1254 decreased motor activity in adult rats during acute and repeated exposures. Acute exposure at doses of 100 mg/kg or
TABLE 1
Summary of Aroclor 1254 Effects in Adult Rats

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Dosing duration</th>
<th>NOEL</th>
<th>LOEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Body weight</td>
<td>Acute</td>
<td>100*</td>
<td>300</td>
</tr>
<tr>
<td>2. Body weight</td>
<td>20 days (4 weeks)</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>3. Motor activity</td>
<td>Acute</td>
<td>300</td>
<td>1000</td>
</tr>
<tr>
<td>4. Motor activity</td>
<td>20 days (4 weeks)</td>
<td>100</td>
<td>300</td>
</tr>
<tr>
<td>5. Flavor aversion</td>
<td>Acute</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>6. Flavor aversion</td>
<td>14 days</td>
<td>15</td>
<td>25</td>
</tr>
</tbody>
</table>

Note. Abbreviations used: NOEL, no observable effect level; LOEL, lowest-observable effect level; HA, horizontal activity; VA, vertical activity.

° Values are given in mg/kg or in mg/kg/day.

less and 4- to 6-week repeated exposure to 10 mg/kg or less had no significant effects on motor activity, and, therefore, the no observable effect level (NOEL) of Aroclor 1254 was 100 mg/kg for acute exposures and 10 mg/kg for repeated exposures (Table 1). These results show the cumulative nature of the effect of Aroclor 1254. PCBs including Aroclor 1254 are quite stable and, because they are fat soluble, are accumulated in adipose and other lipid-rich tissues. Cumulative doses of Aroclor 1254 that rats had received were about 1000 mg/kg in the 100-mg/kg group after a 2-week treatment and about 200 and 600 mg/kg in the 10- and 30-mg/kg groups after the 4-week treatments. These cumulative doses were two to six times the NOEL for acute exposure (100 mg/kg). It is hypothesized that the body burden of Aroclor 1254 may exceed a threshold level that causes changes in motor activity during repeated exposure. Toxicokinetic studies are warranted to clarify this issue.

After acute exposure to Aroclor 1254 at doses of 300 mg/kg or more, horizontal and vertical motor activity decreased at 45 min and 7 days postexposure, but was not statistically different from controls beyond 7 days postexposure. Thus, the effects of acute exposure to a high dose of Aroclor 1254 on motor activity appear to be reversible. With repeated exposure, motor activity was decreased only at 30 mg/kg or higher and these effects were also reversible after withdrawal of PCB exposure. One interpretation of these results is that, since there were corresponding decreases in body weight, PCB-induced alterations in activity may be due to nonspecific toxicity. A pair-fed experiment, in which the body weights of rats receiving vehicle are matched to those of rats receiving Aroclor 1254, is needed to evaluate any nonspecific effects of the mixture on motor activity. Alternatively, Seegal et al. (1986, 1991) showed that dopamine concentration and/or metabolism in the striatum and lateral olfactory tract was decreased in adult rats after both acute and subchronic exposure to Aroclor 1254. These brain regions are innervated by dopaminergic neurons, the cell bodies of which are located in the ventral tegmental area, and are considered to be important in the initiation and control of movement. Therefore, PCBs may decrease motor activity in adult rats via altering dopaminergic function in these brain regions.

Rosin and Martin (1981) showed that acute exposure of adult mice to Aroclor 1254 at a dose of 500 mg/kg resulted in a decrease in motor activity, while repeated exposure at 100 mg/kg for up to 14 days had no effects. In the present study, both acute (300 mg/kg) and repeated (30 mg/kg) exposure to Aroclor 1254 decreased the motor activity of adult rats. Although some differences in methods exist from our study (such as motor activity device and duration of dosing period), species differences in sensitivity to repeated Aroclor 1254 exposure must also be considered.

FIG. 3. Effect of 4-week repeated exposure to Aroclor 1254 (Ar; dose levels: 0, 10, 30, and 100 mg/kg) on body weight. Each symbol represents the mean ± SEM of nine rats. Because of deaths, the number of animals in the 100-mg/kg group decreased to 8 and 5 on days 14 and 16, respectively. Data from this group on day 19 and thereafter were excluded because only one or two animals survived. Asterisks indicate a statistically significant difference from the control group (p < 0.05).
HYPOACTIVITY AND FLAVOR AVERSION BY PCBS

In the flavor aversion conditioning experiments with adult rats using oral doses of Aroclor 1254, a robust flavor aversion occurred. In the acute dosing experiment, the lowest effective dose was 25 mg/kg (Table 1). This dose was less than \( \frac{1}{4} \) the effective dose (300 mg/kg) for motor activity after acute exposure to Aroclor 1254. Flavor aversions are induced by a number of classes of chemicals including heavy metals (e.g., MacPhail, 1982; Peele et al., 1987), pesticides (e.g., MacPhail and Leander, 1980), and psychoactive drugs (e.g., Miller and Miller, 1983) and are interpreted as reflecting an aversive effect(s) of exposure to these chemicals. Therefore, Aroclor 1254 causes an adverse effect as measured by this test at a much lower dose than that causing motor activity changes. However, drugs (such as morphine and amphetamine) which are self-administered by animals, and are therefore presumed to possess positive reinforcing effects, also induce a conditioned flavor aversion (Hunt and Amit, 1987). Thus, further studies are needed to clarify if Aroclor 1254 causes other adverse effects at these dose levels.

Since PCBs are ubiquitous compounds and bioaccumulate due to slow degradation, humans can be exposed from all the available sources. The most important route of exposure...
is through consumption of contaminated food products (fish, meat, and dairy products), especially fish from polluted waters. The levels of PCBs in drinking water ranged from 100 to 450 ng/liter, whereas the levels in food products were as high as 235 mg/kg (WHO, 1993). Bush and Kadlec (1995) reported that zebra mussels from Niagara River have PCB levels on the order of mg/kg. The present results indicate that the LOELs for motor activity and flavor aversion conditioning are 30 and 15 mg/kg, respectively. The doses that affected neurobehavioral function or induce toxic effects were within approximately an order of magnitude of the levels found in the environment.

In conclusion, the results from this study demonstrate that Aroclor 1254 causes hypoactivity and flavor aversions in adult rats. The NOEL for motor activity was 100 mg/kg for acute exposure and 10 mg/kg for repeated exposure for a period up to 6 weeks. The NOEL for acute flavor aversion conditioning was 15 mg/kg, and 7.5 mg/kg for repeated flavor-aversion conditioning. Additional studies are needed to determine the specificity of these effects with regard to a target site(s) of Aroclor 1254 in the central nervous system.

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