Water maze test

Figure 3 shows the results of the water maze test on the fifth trial day. Swimming speed calculated from time and distance data was obtained in this test. A1254 (18 mg/kg body weight) exposure resulted in a significantly longer time for the mice to reach the platform. PCB exposure did not affect the swimming speed. These results indicate that swimming speed is not directly related to the time required to reach the platform.

Spontaneous locomotion activity

Spontaneous locomotion activity was measured over a period of 24 h. The total number of movements was not affected by PCB exposure. In either time domain, which was obtained by dividing 24 h by 6 h, the number of movements was not affected by the treatment.

Discussion

In the present study, we observed the developmental and neurobehavioral effects of perinatal PCB exposure to mice. We used A1254: lot 124–191, because it contains a high proportion of ortho-substituted (>99%) and highly chlorinated biphenyls. Both these characteristics have been associated with developmental neurotoxicity (Frame 1999; Kodavanti et al. 2001), although the toxic equivalent quantity (TEQ) of these congeners is low due to their low activity in Ah-receptor-mediated responses (Van den Berg et al. 1998; Kodavanti et al. 2001). The PCB dose range was chosen by taking into consideration a previous report indicating clear neurobehavioral alterations after perinatal exposure to A1254 (LOAEL = 11 ppm in diet; Storm et al. 1981). In that report, mice were exposed to A1254 at 11 ppm in chow from 3 days before mating to postnatal day (PND) 21, and they showed an increase in the number of squares traversed at PND27. Since a mouse requires chow about 18% of its body weight per day (Jones and Balster 1997), the lowest dose (6 mg/kg body weight/3 days) in our study is considered to provide almost the same body burden as LOAEL.

The developmental effects of exposure to PCBs during gestation and lactation were assessed before weaning. Although PCB exposure did not alter the body weight of offspring, poor adult-like responses in the negative geotaxis were observed in all exposed groups at only PND7. Because a difference in response was not observed among treatments at any other time point, it was considered that the developmental delay is transient. In one previous study, perinatal exposure to PCBs was found to affect the negative geotaxis of mice (Overmann et al. 1987). However, such a effect was not reported in another study of prenatal exposure to PCBs (Pantaleoni et al. 1988). This difference in the findings of both studies might be due to the difference in the strain or selected time points. In the former study, the delay of negative geotaxis was observed on PNDs7 and 8, whereas the delay was not observed in the latter study on PNDs10 and 15. The delay might have been caught up by PND10. Because we performed the assessment in more time points than in the previous studies, we might have been able to observe both the transient delay and catch-up.

The neurobehavioral effects of exposure to PCBs were observed in the 8 and 9-week old mice. The spontaneous locomotion activities of the PCB-exposed mice were monitored in two different environments: an unfamiliar one (open field) and a familiar one (home cage). In the open field, we observed that PCB exposure decreased the walking speed. Because this was the first time the mice experienced the white and brightly illuminated open field, this environment caused an emo-

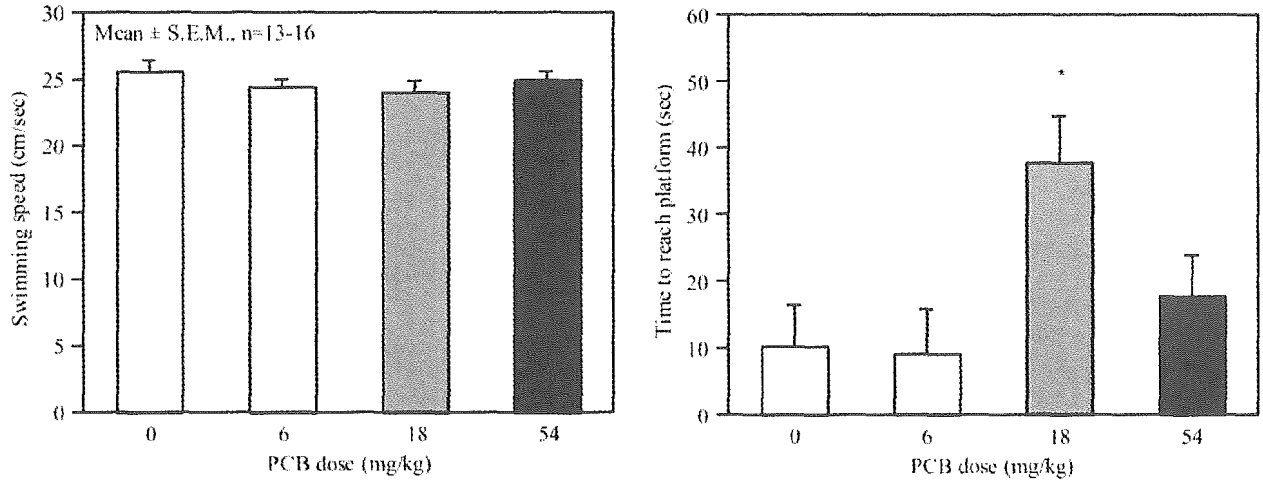

Fig. 3 Time to reach the platform and swimming speed in water maze test in the 8-week old. *Asterisk* indicates a significant difference from control

tional stress. In addition, there was no significant difference in the spontaneous locomotion activity evaluated in the home cage among groups. Therefore, we consider that the result in the open-field test is independent of spontaneous activity, and is caused by emotional stress.

Spatial learning ability was examined in the water maze test. PCBs prolonged the time to reach the platform as shown in Fig. 3. Many factors can affect the time in this test, and swimming ability is one possible factor. However, because swimming speed has not been influenced, it is considered that a disturbance of spatial memory is a cause of the delay.

Behavioral deviations in the open-field test and water maze test were observed in the that A1254-treated group with 18 mg/kg body weightexposure. However, there was no significant difference in the 54 mg/kg body weight A1254-treated group. In a previous report concerning perinatal PCB exposure, the dose-dependent behavioral deviations were not observed although there is a significant difference between the control and exposed groups in the open-field test (Storm et al. 1981). Moreover, there is a report that mice perinatally exposed to A1245 (12.5 ppm in diet) showed a long time to reach the platform in the Morris water maze test (Provost et al. 1999). However, there are other reports that mice exposed to higher doses (6 and 8 mg/kg body weight/day) did not show this delay (Gilbert et al. 2000; Zahalka et al. 2001). A possible explanation for these dose-independent results is that exposure to high PCB dose during perinatal periods could trigger a compensation phenomenon, as in the case of other compounds. For example, the reversal of inhibitory effect of lead (Pb) on glutamate release at higher Pb exposure level was reported in the dentate gyrus of rats (Gilbert et al. 1999). Such a kind of mechanism may contribute to our results. Another explanation is that the inverted dose-response relationship may be due to a prepartum selection. Because the most vulnerable individuals died during gestation in the high-PCB-exposed group, the surviving individuals were more resistant and showed only subtle behavioral alterations in the open-field test and water maze test. However, this hypothesis could not be supported by our litter viability data. Moreover, we often observed dose-independent results in these behavioral tests.

In conclusion, we performed the follow-up observation in mice up to 9-week old and showed that perinatal PCB exposure influenced the neurobehavior of mice. The neurobehavioral effects such as a decreased walking speed in the open-field test and prolonged time to reach the platform in the water maze test remained until adulthood after their seeming recovery from the transient delay of development before weaning. This may have relevance for predicting the effects of perinatal exposure to PCBs on human health.

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