Neurobehavioral Effects in Adult Rats after Maternal Exposure to Coplanar and Ortho-Chlorinated PCB Congeners

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Abstract

Introduction

Polychlorinated biphenyls (PCBs) are reported to induce alterations in several behavioral tests and it has been shown that the nervous system is particularly sensitive to PCB exposure during early development (1,2). PCBs are known to affect the neurotransmitter status in the brain as well as intracellular signaling mechanisms (3,4). In addition, it has been suggested that some of the effects on the developing nervous system are mediated by alterations in thyroid hormone levels (5,6). Most of the PCB-induced effects on nervous tissue *in vitro* have been ascribed to *ortho*-chlorinated congeners (3,4), whereas coplanar congeners are reported to have a higher general toxicity (7). Therefore, the present experiments were conducted to compare the effects of different PCB congeners on behavior and electrophysiological measures after maternal exposure in rats. Different behavioral tests were used which are sensitive to changes in different neuronal subsystems in order to establish a profile of effects. Moreover, long-term potentiation (LTP), which is suggested to be a model of functional neuronal plasticity and an electrophysiological correlate of learning and memory processes (8), was studied in slices from different brain areas of maternally exposed rats and controls.

Methods

Details of the methods are given elsewhere (9). Briefly, time-mated Wistar albino rats were exposed to the ortho-chlorinated 2,2',4,4`-tetraCB (PCB-47; 1 mg/kg sc) or the coplanar 3,3',4,4'-tetraCB (PCB-77; 1 mg/kg sc) or to the vehicle (olive oil) from day 7 to 18 of gestation. The pups were weaned on postnatal day (PND) 21.

Naive male rats from the offspring were used for each behavioral task. Rats were tested for spatial learning and memory in an automated eight-arm radial maze starting on PND-95. The training methods followed a previously described procedure (10). Briefly, the rats were food deprived to 80% of their normal food intake. Prior to each trial, a food pellet was placed at the end of each arm and the rat was required to find all 8 pellets. The trial was stopped when all 8 pellets were taken or 10 min had elapsed, whichever occurred first. Each rat was given one daily trial on 14 consecutive days. A correct choice was recorded when the rat entered an arm and took the pellet, and an error when the rat entered an arm previously chosen.

The methods for the examination of catalepsy and passive avoidance are fully described in (9). Haloperidol-induced catalepsy was examined on about PND-180. In this tests the time was measured that the rat needed to return to a normal position from an unusual body posture 30 and 60 min after the injection of haloperidol (0.3 mg/kg ip). Three different positions were chosen: placing one fore-paw on a block (3 cm high), both fore-paws on a bar (9 cm high), and putting the rat on a vertical grid. If the rat failed to move each trial was terminated after 180 s.

Passive avoidance behavior was tested in a step-down apparatus on PND-220. Rats were placed on a platform which was centrally located 4.5 cm above the grid floor of a quadratic box. When the rat stepped down and all four paws were on the the grid floor it received a foot-shock of 1 mA for 1 s. Thereafter, the rat was taken out and replaced on the platform 5 min, 4 and 24 h after the shock

trial. Latency to leave the platform was recorded on these test trials without application of any further shocks.
From PND-180 to PND-220 measurement of LTP was conducted *ex vivo* in brain slices of rats maternally treated with PCB-77 and controls. Details of the methods are given in (11,12). Slices of the hippocampus and the occipital cortex were cut and incubated in artificial cerebrospinal fluid for at least 1 h. In hippocampus, the Schaffer collaterals/commissurial fibers were electrically stimulated and the population spike recorded in the pyramidal cell body layer. Following baseline recordings with single stimuli, LTP was induced by 10 high-frequency bursts. Testing with single stimuli was continued for 1 h after tetanic stimulation. To achieve favorable conditions for the expression of LTP, procedures were different in the cortex. Bicuculline (2 μM) was added to the medium in cortex measurements, since LTP induction in the visual cortex of adult animals requires a reduction of inhibition. In occipital cortex, the border of layer VI/white matter was stimulated and extracellular field potentials recorded in layers II/III. After a period of baseline recordings 20 high-frequency pulses were used to induce LTP followed by testing with single stimuli for 2 h.

Results and Discusssion

The exposure conditions chosen did not result in significant body weight reductions or in other impairments of physical development.
Maternal treatment with the coplanar PCB-77 caused a significant elevation of descent latencies from the bar (median test, $p<.05$), while changes by the ortho-substituted PCB-47 were not significant (fig. 1).

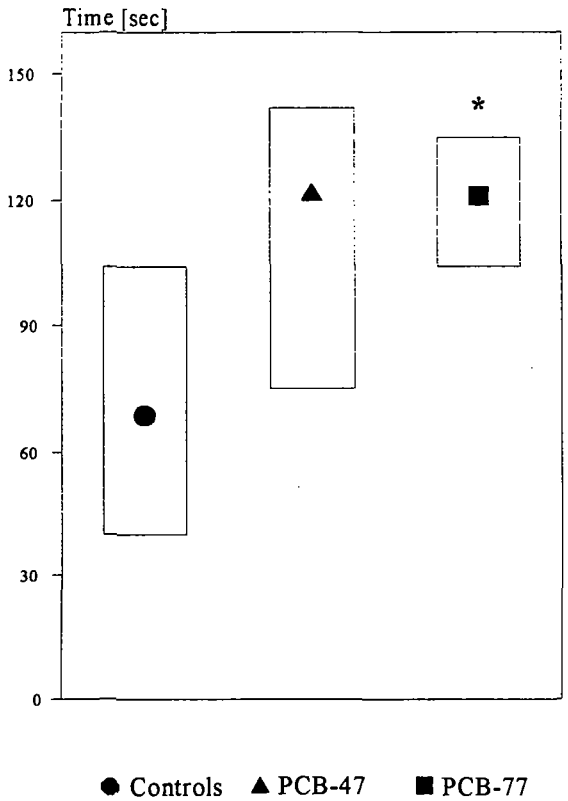

Fig. 1 Descent latencies from the bar 60 min after the injection of haloperidol (median, 25%,75% quartiles). There was a significant increase in PCB-77 rats. Effects by PCB-47 did not reach statistical significance [* $p<.05$; n=10; modified after (9)].

The PCB-77 group exhibited also alterations on the passive avoidance task (Kruskal-Wallis; $p<.05$), whereas the PCB-47 rats were not statistically different from controls (fig. 2).
In contrast, testing of spatial learning in the radial arm maze failed to detect any differences between groups in time to complete the task, trials to achieve the learning criterion, correct choices, total errors, or correct choices before the first error (fig. 3). A similar result was obtained for another spatial task, the Morris water maze, in one of the following experiments comparing the effects of the coplanar PCB-77 with perinatal exposure to the thyreostatic

compound propylthiouracil (PTU). Spatial learning, expressed as time to find the hidden platform, was not altered by either treatment (13).

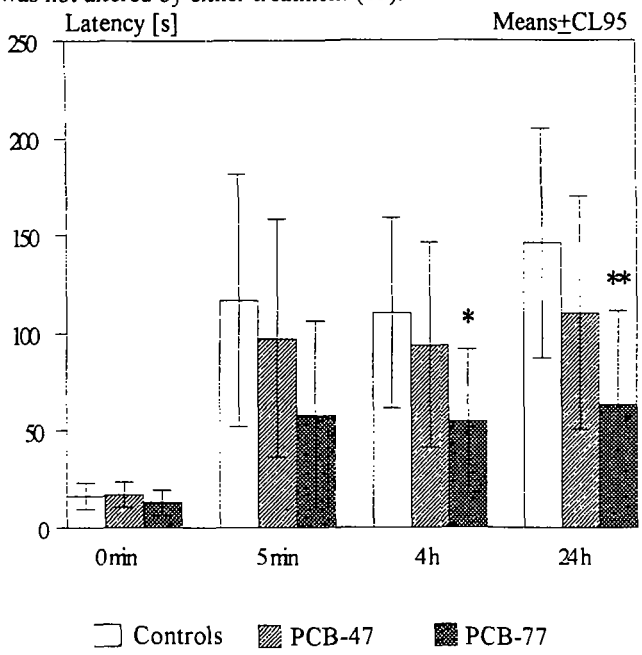

Fig. 2 Passive avoidance latencies. Differences were observed between controls and rats after maternal exposure to PCB-77 [* $p<.05$ ** $p<.01$; n=15; modified after (9)].

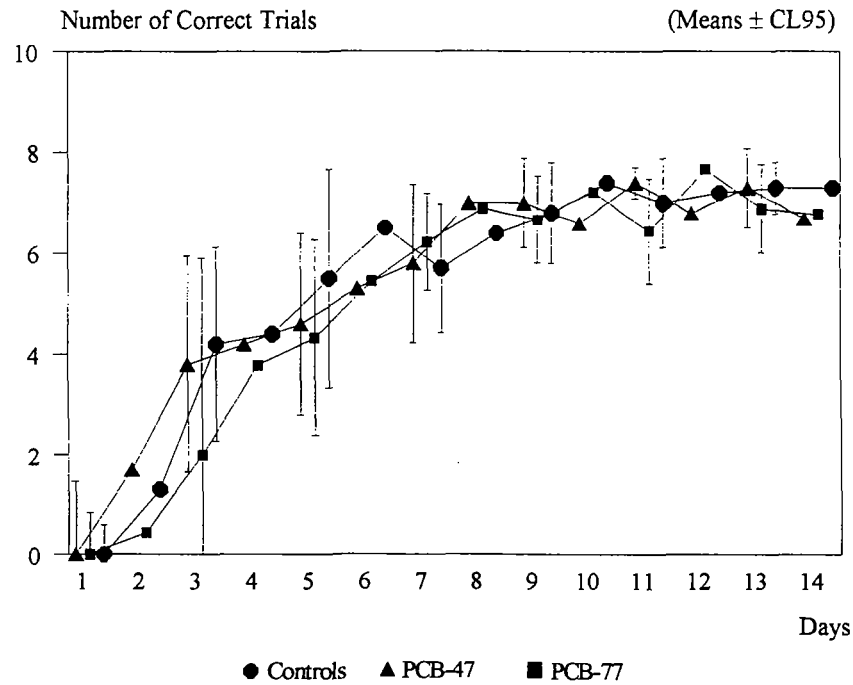

Fig. 3 Number of correct choices before the first error in the radial arm maze. There were no significant differences between groups on this spatial learning task (n=10).

In addition, maternal exposure to PCB-77 resulted in inhibited LTP in slices from the occipital cortex (Student's t-test, two-tailed, $p<.05$), but failed to induce significant changes in slices from the hippocampus (fig. 4). This outcome is supported by a recent experiment comparing the effects by the coplanar PCB-77 with the *ortho*-chlorinated PCB-47 in brain slices from rat pups (PND-11 to PND-19). The evaluation revealed long-term depression (LTD) due to PCB-77, while PCB-47 induced either a small LTP, LTD, or no change. Again, no effects were detected in slices from the hippocampus of these rat pups (14).

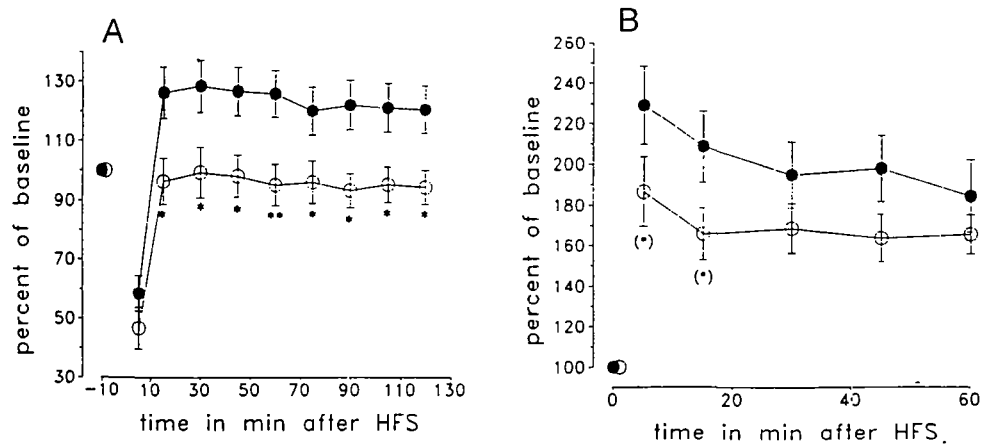

Fig. 4 (A) Summary of LTP data in slices from the occipital cortex (n=10) and (B) from the hippocampus [controls (filled circles): n=8; PCB-77 (open circles): n=7]. Shown are mean relative amplitude differences (±SEM) in relation to the baseline values at selected time points after high-frequency stimulation [modified after (12); (*) $p<.1$; * $p<.05$; ** $p<.01$].

These results indicate that maternal exposure to the coplanar PCB-77 exerts more pronounced effects on behavior than equal doses of the *ortho*-chlorinated PCB-47. No effects were detected on two behavioral tasks examining spatial learning and memory which are thought to be dependent on the hippocampus (15,16). Moreover, in contrast to the visual cortex, there were no significant alterations of LTP in hippocampal slices of adult rats and rat pups following maternal exposure to PCB-77. Recent results by Schantz et al. indicated no effects of *ortho*-chlorinated PCBs on working and reference memory in the radial-arm maze (17) and even slight decreases in errors of the coplanar congeners PCB-77 and PCB-126 (18). Taken together, these results suggest that the effects of developmental PCB exposure on hippocampal functioning are less pronounced and that other brain areas may be more sensitive to these environmental toxicants as indicated by significant PCB-77 related changes in haloperidol-induced catalepsy and passive avoidance behavior.

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