BEHAVIOURAL EFFECTS OF POSTNATAL EXPOSURE TO PCB CONGENERS 126 and 153 IN RATS

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Introduction

Polychlorinated biphenyls (PCBs) which theoretically exist of 209 different congeners are widely dispersed and persistent environmental pollutants (1-3). The main route of adult human intake of PCBs and related compounds is dietary. Thus, the embryo and foetus may be exposed to PCBs transplacentally as well as through mother's milk postnatally. The risk assessment of PCBs is complicated by the fact that the 209 congeners exert different toxicity to living organisms (4,5). The development of scientifically based regulations for the risk management of PCBs requires analytical and toxicological data on the individual PCB congeners present in environmental samples.

Besides inducing non-neurological effects, PCBs are reported to be developmental neurotoxins altering cognitive functions and motor activity both in humans (6-8) and animals (9-11). However, which class of the PCB congeners that plays the more active role in inducing the behavioural outcomes is not yet clarified and neither are the mechanisms underlying the PCB-induced developmental neurotoxicity. Depending on their chlorine substitution pattern the PCB congeners may be divided into three main structural classes (2,3): the coplanar PCBs, their mono-*ortho*-substituted analogues and the *ortho*-substituted PCBs.

In different studies we have investigated the behavioural effects of individual PCB congeners in offspring of dams exposed to low doses of these PCBs during pregnancy or lactation (12-14). Operant analysis of behaviour is a method that makes it possible to focus on one or a few aspects of behaviour. Further, a common nomenclature has been established and comparative research is possible since the behavioural laws seem to be similar in animals and human (15). The congeners selected (PCBs 126 and 153) may be regarded as model substances for the different structural classes of PCBs. In the present study, male and female offspring were tested by two different schedules of reinforcements: a multiple fixed interval (FI) extinction (EXT) schedule and a variable interval (VI) schedule of reinforcement. The FI-EXT schedule has proven sensitive in revealing increased motor activity in PCB-exposed rats (13, 14). The VI schedule was designed as a visual discrimination task and included in order to investigate visual attention in the animals.

This presentation reports the preliminary results of the behavioural testing on the VI schedule.

Materials and Methods

Pure powder of 3,3',4,4',5,-pentachlorobiphenyl (IUPAC no.126) and of 2,2',4,4',5,5'-hexachlorobiphenyl (IUPAC no.153) were bought from Promochem, Sweden. The PCBs were dissolved in corn oil and administred to the dams by gavage every second day from day 3 to 13

after delivery in the following doses: 5 mg/kg b.w. of PCB 153 or 2 μg/kg b.w. of PCB 126. The dams serving as controls were given 5 ml/kg b.w. of pure corn oil in the same manner.

Operant behaviour testing was conducted in six identical operant chambers for rodents (Model 4109, Campden Instrument, UK). The chambers had one 2.8-W house light and were equipped with two levers. Located in between the levers was one liquid dipper housed in a small cubicle with a 2.8-W cue light. A 7x5-cm transparent plastic lid separated this cubicle from the animal's working space. A light push by nose or paw was sufficient to open the lid, thereby activating a microswitch that was recorded by the computer. Control of experimental stimuli and data recording was performed automatically by a computer.

One male and one female representing eight dams per group were randomly picked to attend the behavioural test. Operant conditioning started when the rats were about 5 weeks old and was conducted 5 days a week for about six months. The animals were on a 22-h water deprivation schedule and they were gradually trained to press levers for water reinforcement. The following schedule-controlled behavioural tests were utilised:

The multiple 2-min fixed interval 5-min extinction schedule of reinforcement (mult 2-min FI 5-min EXT) Each session had a duration of about 40 min. The rats were first run for thirty sessions on this schedule and then for another six sessions after they had been on the VI-schedule.

The variable interval schedule of reinforcement (VI-schedule) was designed as a visual discrimination task. The rats were trained to press one of two alternative levers, the correct one being indicated by a cue lamp. Pressing the correct lever was reinforced by giving access to a drop of water. When the pressing of the correct lever is reinforced according to a VI schedule, the variable interval specifies the probability with which a response will be reinforced. In contrast to the FI schedule, it was not possible to predict the precise time interval before the next reinforcer was set up in this VI schedule, but to pay attention to the cue lamp. The variable interval was gradually altered from 0.1s to 120s. Thus, on the 0.1s-VI virtually every lever press was reinforced, while on the 120s-VI a reinforcement was set up on average every second minute. The rats were run several sessions on low VI constants in order to aquire the task. The duration of each session varied from 5 to 30 min depending on the VI constant. The rats were 114 days old when starting and were run for a total of sixty sessions on this schedule until the age of 209 days. The total number of lever presses, the per cent correct lever presses (presses on the lever above which the cue lamp was lit), the number of reinforcers delivered and the number of tray visits when no reinforcer were present and no lamp was lit in the water cubicle, were calculated.

As the data analyses are in progress, the results are presented as descriptive SPSS plots (16).

Results and Discussion

The exposure did not affect the body weight of the dams or the physical development of the pups. Female offspring exposed to PCB 126 started to show decreased body weight gain from PND 60 on but the weight reduction was only 6.8% compared to the controls at the end of the experimental period. The reduction was below 20% and is not considered as a toxic response.

It is assumed that the behavioural sex difference in the control rats represents the normal sex differences under the current test conditions; a VI schedule of water reinforcement. The male controls (C-m) had with slight deviations to both sides, approximately equal activity level to the females (C-f) as measured as lever presses and reinforcements delivered (Figs. 1 and 2). Postnatal exposure to PCB 126 produced higher activity in male (126-m) than in female (126-f) rats, and the 126-m were the most active of all groups; in particular when the VI-constant was low (e.g. 0.1s or 15s). PCB 153-exposed females (153-f) had higher activity than 153-exposed males (153-m). The

opposedly sex-differences in the PCB-exposed groups persisted throughout testing. No impairment in visual attention following PCB exposure appeared as measured as per cent correct lever presses; which was on average higher in the exposed groups than that of the controls. However, on low VI-constants a high rate of lever presses produced a high density of reinforcers, which further enhanced an increased activity level and thus positive feed-back on the attention to the visual cue light indicating which lever to press in order to obtain a reinforcer. Thus, differences in the learning phase of the task may have occurred and may account for the lower per cent correct lever presses performed by the controls. An exception was the 153-m, which had activity that levelled the C-m, but still the per cent correct lever presses was higher. The implications of the animals previous testing history have to be considered in the final interpretation of the results. The neurotoxic potential of PCB have during the later years been related to the *ortho*-substituted congeners (17). It has been reported facilitated acqusition of a working memory task on the radial arm maze after perinatal exposure to TCDD or coplanar PCBs (18). Additionally, no effects of perinatal exposure to PCB 126 were found in rats on spatial delayed alternation (19), fixed interval-fixed ratio or DRL performances in rats (20).

In the present study, postnatal exposure to either of PCB congeners 126 and 153 produced altered activity in rat offspring: males seem to be more sensitive to PCB 126 and females seem to be more sensitive to PCB 153. Although the basic cellular mechanisms behind the behavioural effects of PCBs 126 and 153 may be similar in male and female rats, the functional expression can be different.

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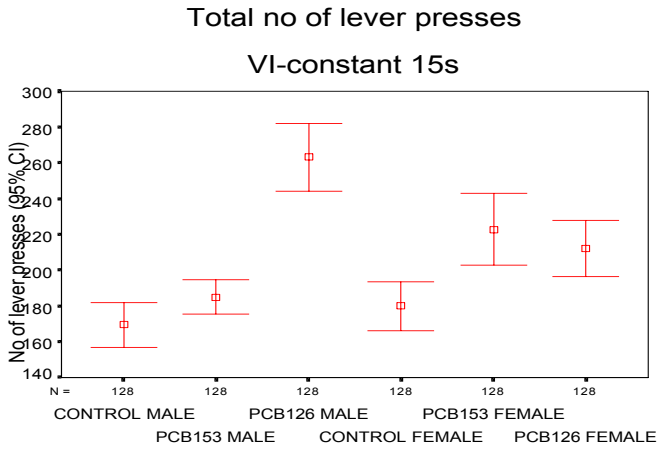

Figure 1. Mean number of lever presses per sex and group on a 15s variable schedule of water reinforcement (8 rats/sex). (N: 8 rats à 16 sessions gives 128 measures.)

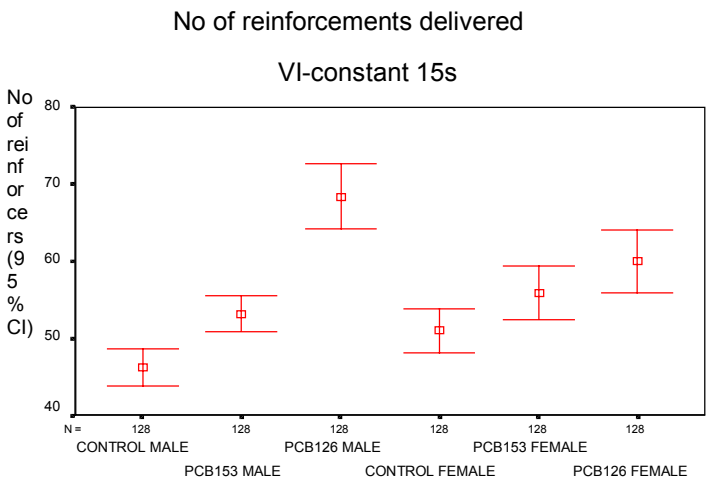

Figure 2. Mean number of reinforcements per sex and group on a 15s variable schedule of water reinforcement (8 rats/sex). (N: 8 rats à 16 sessions gives 128 measures.)

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