Methylmercury Chloride Induces Learning Deficits in Prenatally Treated Rats

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Abstract. Methylmercury chloride (MMC) was given to pregnant rats on the 6th, 7th, 8th, and 9th day after conception in doses of 0.05 and 2.0 mg/kg/day. The female offspring of these animals were tested 90 days after birth for learning ability using operant conditioning procedures. The rats were kept at 90% of their normal body weight and trained in a lever-box to press a bar in order to obtain a food pellet.

Significant differences in the acquisition speed became apparent when the ratio of bar presses to reward was increased in a classical contingency of differential reinforcement of high rates even at MMC-doses of 4 x 0.05 mg/kg. These differences were not found in the general motility level nor in motor coordination.

Key words: Rats - Methylmercury chloride - Prenatal treatment - Operant behaviour - Learning.


Signifikante Unterschiede traten bereits nach 4 x 0.05 mg/kg MMC auf, wenn die Tiere in dem klassischen Konditionierungsprogramm "Differential Reinforcement of High Rates" den Hebel innerhalb einer vorbestimmten, kurzen Zeitspanne zunehmend häufig drücken mussten, um Futter zu erhalten. Die allgemeine Motilität und die motorische Koordination waren unverändert.

Introduction

Changes of learning ability are generally described as a sensitive indicator of the impairment of CNS-functions provoked by ionizing radiation (Graham et al., 1959; Haley, 1962; Kimeldorf and Hunt, 1965; Walker and Furchtgott, 1970).
The work described in this paper was based on the hypothesis that — similar to results of radiation experiments — doses of environmental chemicals may induce analogous behavioural alterations before any histological or biochemical damages become apparent.

Application of the test substance during critical ontogenetic periods further increased the probability of demonstrating learning deficits as a consequence of low level treatment. Based on experience in experimental psychology (Kimble, 1961; Angermeier, 1972) and following the suggestions forwarded at the Symposium on Current Status of Behavioral Pharmacology (1974), a study was started to assess changes in behavioural performance due to methylmercury chloride by means of classical contingencies of reinforcement, described by Ferster and Skinner (1957).

MMC was chosen as the test substance because it complies with basic conditions required for the experiment: in a detailed review of mercury studies Koronowski (1973) pointed to the environmental risk of MMC due to its use in agriculture, forestry and industry, its high acute and chronic toxicity, its morphological and functional effects upon the central nervous system and its unlimited transfer through the placental barrier. The risk of methyl mercury for man was drastically demonstrated by the Minamata tragedy (Murakami, 1971).

Materials and Methods

Nulli-parous pregnant rats (inbred Wistar/Neuherberg) were treated with MMC. The substance, dissolved in distilled water was given by stomach tube in doses of 0.05 and 2.0 mg/kg/day on the 6th, 7th, 8th, and 9th day after conception (day after the mating night = gestational day 0). The control rats received analogous quantities of distilled water. The female offspring of these animals were subjected to learning tests when 3 months of age. All animals were kept without food for 24 h prior to the preliminary training and subsequently held at 90% of their normal body weight through a restriction of food access during test periods. Shaping occurred automatically in a lever-box with continuous reinforcement for a 10-h period for one night (9.00 pm—7.00 am). This preliminary training provided the rats with the opportunity to become acquainted with the test equipment and to associate between bar pressing and food reward.

To assess learning ability the operant conditioning schedule “Differential Reinforcement of High Rates” (DRH) was used. This program requires the rat to press the bar a predetermined number of times within a predetermined time interval to obtain one food pellet. If the time interval ends before the animal has performed the required number of bar presses, it gets no reward. The first bar press after the end of an interval indicates the start of a new interval. Hence, DRH 4/2 in the experiment signified that the rat had to press the bar 4 times within 2 s to get one food pellet.

After having made the connection between bar pressing and food reward, all animals were confronted with a stepwise increase in the learning demand from DRH 2/1 to DRH 4/2, finally to DRH 8/4. Each rat was tested only once. Every test session in the lever-box lasted ½ h per single DRH-program, each being followed by an intersession period of 7—10 days. The test performance was expressed by the ratio of total number of bar presses to the number of successful ones. (Example: If 200 reinforcements resulted from 800 bar presses the rate of success would be 100% at DRH 4/2, whereas it would be only 50% at DRH 2/1.)

Each lever-box was equipped with individual custom built electronic circuitry which controlled the different DRH-programs automatically. Thus, interactions between experimentator and subjects could be minimized during the test periods. All rats were tested in a sound-attenuated room and kept at constant temperature, air humidity and light-dark-rhythm.