Cadmium-Induced Behavioral Changes in Growing Rats

Key words: Cd²⁺—Motor Activity—Conditioned Avoidance—Growing Rats—Behavior—Toxicity

Cadmium (Cd²⁺) has been recognized as an environmental hazard since the incidence of the 'Itai-Itai' disease in Japan.¹⁾ Exposure to Cd²⁺ in animals has been shown to cause neuropathological³⁾ and neurochemical changes.⁴⁾ But experimental studies assessing the behavioral effects of Cd²⁺ are scant and we undertook this preliminary investigation to assess the effects of Cd²⁺ on locomotor activity and learning performance in growing rats since young animals have been shown to be more susceptible to the neurotoxic effects of Cd.²⁺⁵⁾

Sixty growing male albino rats of the ITRC bred colony, weighing 150–160 g (2 months old), served as subjects. They were housed in stainless steel cages, in groups of ten and maintained on a 12:12 photoperiod (lights on 06.00–18.00 hr) in a temperature controlled ($22 \pm 2.0^\circ$) room. Hind Lever Laboratory chow and water were provided ad lib.

The animals were divided into two equal groups and the experimental group was administered 0.5 mg Cd²⁺/kg, i.p., as cadmium acetate (volume of injection 1 ml/kg) daily for 21 days. The vehicle (0.9% NaCl) injected rats served as controls. The animals were weighed weekly and the following behavioral and chemical parameters were measured at the end of the treatment period.

The rats were placed individually in a photoactometer (Techno, India) and after 5 min. acclimation period, the activity counts for 15 min. were recorded. Twelve rats (in batches of 6) from each group were used.

The conditioned avoidance behavior was assessed in a pole climbing chamber (Techno, India). Each animal, after a 5 min. habituation in the experimental chamber, was subjected to 50 trials. A trial consisted of the presentation of continuous 90 dB 1500 Hz tone conditioned stimulus (CS) for 10 sec. followed by the unconditioned stimulus (US), a 0.5 mA constant current scrambled foot shock for 10 sec. and a 40 sec. intertrial interval. The tone remained on when the shock was presented. The animals could avoid the shock by climbing the pole suspended from the middle of the roof and ending 5 cm from the grid floor. Responses were designated as follows: (a) conditioned avoidance response (CAR) when the animal climbed the pole in response to the CS, (b) Escape response (ER) when it climbed the pole during the foot shock, and (c) escape failure (EF) if it did not respond to the CS and US, when the shock was turned off and the next intertrial interval was started. The CAR, ER and EF responses as well as the intertrial responses, i.e., climbing the pole during the intertrial interval, were recorded. Twelve rats from each group (in batches of 6) were used

for the assessment of the learning performance. The behavioral tests were conducted in a quiet, air-conditioned room ($22 \pm 2^\circ\text{C}$) between 10.0 and 16.0 hr by observers unaware of the treatment schedules and both the time and day of testing were counterbalanced within groups.

The animals (6 rats/group) were killed by decapitation on day 22nd of treatment. Brain samples were wet ashed in nitric: perchloric acid (6:1) and cadmium residues were determined by Atomic absorption spectrophotometer (Perkin Elmer Model 5000).

Statistical evaluation of the data for the conditioned avoidance experiments, i.e., CAR, ER and EF, was done by a 3×2 Chi-square (X^2) test,⁶⁾ using the frequency of the different responses. The data for body weight, motor activity, brain Cd^{2+} levels and intertrial response was analysed by the student's 't' test. The accepted level of significance in either test was $p < 0.05$.

Fig. 1 shows the effect of Cd^{2+} exposure on the body weight growth pattern. The Cd^{2+} treated rats showed a significant growth retardation over the experimental period.

The SMA was significantly depressed in the Cd^{2+} treated rats compared to the controls and the 15 min. counts in the control and experimental groups were

Fig. 1. Body weight growth pattern of control and Cd^{2+} -exposed rats over the experimental period.

Each point represents the mean weight $\pm$ S.E. of 10 rats.

* $p < 0.05$

Fig. 2. Effect of Cd²⁺-exposure on the CAR, ER and EF responses as tested in the pole climbing chamber, at the end of the treatment period.

Each bar represents the mean percentage response ± S.E. of 12 rats.

588 ± 33 and 297 ± 21 (Mean ± S.E.; $p < 0.001$), respectively.

The effect of Cd²⁺ exposure on CAR, ER and EF is shown in Fig. 2. The X² test revealed that the results of the conditioned avoidance experiment were not independent of the treatment ($X^2_{(2)} = 6.87, p < 0.05$). As evident from Fig. 2, the considerably higher incidence of EF in the Cd²⁺ treated group seems to have contributed to the significant value of X². The intertrial response means did not differ significantly as tested by student's 't' test (Control = 16 ± 3, Cd²⁺-treated = 14 ± 4).

The brain Cd²⁺ level in the control group was 0.275 ± 0.25 whereas in the experimental group it was 0.386 ± 0.028 µg/g fresh weight ($p < 0.02$).

The results indicate that the Cd²⁺ exposure, in growing rats resulted in a significant growth retardation, decrease in SMA and a marked increase in the escape failure response. The brain Cd²⁺ level registered a low residue accumulation.

The reduction in body weight due to Cd²⁺ exposure is well documented.^{7,8)} The few reports on the effects of Cd²⁺ on the locomotor activity in rats, seem to be variable and direct comparison of these results is made difficult by the differences in the age, dose and route of administration. But on the whole, the picture emerges that at low dose levels, Cd²⁺ exposure results in hyperactivity⁹⁾ whereas at higher dose levels, decreases in locomotor activity,⁹⁾ open field ex-

ploratory activity and rearing response¹⁰⁾ have been observed. It is likely that the effect of Cd²⁺ on SMA varies with the age of the animals as well as the dose and route of administration.

The exact nature of the mechanism responsible for the increase in the EF response is not clear. Experimental studies indicate that Cd²⁺-exposure causes alterations in the sensory perception,^{3,11)} neuromuscular blockade,²⁾ deficit motor performance¹⁰⁾ and increased reactivity to physical stressors.³⁾ These alterations, which are incompatible with goal oriented responding, may be responsible for the increase in the escape failure response.

Thus, our results show that, in spite of the low accumulation of Cd²⁺ in the brain it does appear to cause certain behavioral dysfunctions in growing rats, even after a short term exposure.

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Metal Toxicity Project
Industrial Toxicology Research Centre
P.O. Box No. 80, Lucknow-226 001, India

Satya V. CHANDRA
Ramesh C. MURTHY
and Mohd. M. ALI

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