EFFECT OF SINGLE EXPOSURE TO TOLUENE ON SIDMAN AVOIDANCE RESPONSE IN RATS

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Abstract—Effects of single exposure to toluene on Sidman avoidance response in rats were studied. The animals, in which the behavioral base line had been established, were exposed 0, 1,000 and 3,000 ppm of toluene vapor for 4 hours and the effects on the behavioral pattern were investigated using Sidman avoidance test for one hour after the termination of toluene exposure.

1) Exposure to 0 or 1,000 ppm of toluene did not produce marked change on the operant behavior. After the exposure to 3,000 ppm, the animals produced increased responses with shortening of the inter-response-time (IRT) and no changes in shock counts from the beginning to the 50 min. zone of the Sidman avoidance test when compared with those before exposure. The behavioral change indicated here appears to be caused by a temporary breakdown of the established timing of lever pressing.

2) The effect of toluene on the operant behavior was strongest immediately after the termination of the exposure and the behavior recovered in about an hour. This result suggested that toluene is rapidly transferred to and removed from the brain.

Key Words: Operant Behavior, Toluene, Toluene and Sidman Avoidance Response, Organic Solvent

Toluene, which is widely used in industry, is known as one of the organic solvents that affects the central nervous system. Recently, a behavioral technique has been applied to evaluate the effects of central nervous toxicants. Several studies have reported behavioral disorders in animals exposed to toluene (Battig and Grandjean 1964, Maeda 1970, Tadokoro and Ogawa 1969). However, all of these studies,
except for that of Tainaka et al. (1974), were concerned with chronic effects from repeated exposure. In the work reported here, the authors present the effect of a single exposure to toluene on Sidman avoidance response for 1 hour immediately after the termination of toluene exposure in rats.

**MATERIALS AND METHODS**

Animals: Wistar male rats 70 days of age (CLEA Japan) were in the experiment. Each rat was individually housed in the animal room and maintained at a temperature of $23\pm3^\circ C$ and a relative humidity of $55\pm10\%$. The animals were fed CE-2, a standard laboratory diet (CLEA Japan), and given tap water ad libitum during the experiment except at the time of behavioral training and toluene exposure.

Behavioral Study: Sidman avoidance procedure was used for the behavioral study. The animals were trained 1 hour every day with a reinforcement schedule of 5 sec. of shock to shock interval and 25 sec. of response to shock interval. The apparatus for the behavioral test was similar to that described in Kuribara’s report.

![Diagram](image_url)

1. Air flowmeter  
2. Toluene in glass bottle  
3. Vaporizing chamber  
4. Compressor  
5. Gas flowmeter  
6. High-concentration mixing chamber  
6'. Low-concentration mixing chamber  
7. Exposure chamber (control)  
8. Exposure chamber (high-concentration)  
8'. Exposure chamber (low-concentration)

*Fig. 1. Apparatus for generation and administration of vapor*
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(1975). The behavioral base line of the animals was established after 10 to 15 sessions of training.

Exposure System and Technique: As shown in Fig. 1, the exposure system consisted of a vaporizing chamber, two mixing chambers and three inhalation chambers. Toluene vapor was generated by spraying toluene with compressed hot air. High (3,000 ppm) and low (1,000 ppm) concentrations were obtained by changing the toluene vapor/air ratio. Air flows were adjusted so that the actual vapor concentrations determined with a Hitachi Type 163 gas chromatograph were maintained within 5% of the nominal concentrations during the exposure. All control animals were subjected to identical chamber conditions except that no vapor was generated. Toluene used in the experiments was tested beforehand by gas chromatography and no impurities were detected.

Procedure: Eighteen animals, selected after the establishment of the behavioral base line, were randomized and divided into three groups. They were placed in the respective exposure chambers of 3,000, 1,000 and 0 ppm for 4 hours. Immediately following the termination of 4 hour exposure, the rats were placed in the test cages, and the effects on the behavioral pattern were investigated using Sidman avoidance procedure. The experiments were performed at a temperature of 22±3°C and relative humidity of 55±10%.

The behavioral pattern was considered to be measured on the day of exposure when animals could successfully press the lever to avoid shock every 10 minutes within 60 minutes following the termination of toluene vapor inhalation.

RESULTS

Response rates (lever pressing counts) during Sidman avoidance test before and after exposure to toluene are shown in Fig. 2. Responses before exposure showed low levels at the beginning of the test, then increased gradually and remained stable up to 30 min. in each group. In responses after toluene inhalation, there were no different response patterns from those before exposure in the 0 and 1,000 ppm exposure groups. Responses of the rats exposed to 3,000 ppm, however, increased remarkably immediately after the beginning of the test and maintained high levels for 50 minutes. The responses in the 10, 20, 40 and 50 minute zones after exposure to 3,000 ppm showed significant differences in Student’s t-test (P< 0.01 or 0.05) compared with those before exposure.

Differences of the average inter-response-time (IRT), which are the time intervals of lever pressing, were compared in each group before and after exposure. The results are shown in Fig. 3. IRT of the animals after exposure to 0 ppm of toluene did not differ from those before exposure throughout the tests. In the 1,000 ppm toluene exposure group, IRT were shorter but there was no significant differences in the 10 min. zone of the test. The IRT of the 3,000 ppm toluene exposed
Fig. 2. Responses per 10 min during Sidman avoidance test before and after toluene exposure

group were markedly shortened after exposure compared with those before exposure in the 10—50 min. zone of the test, and still showed significant shortening until the 50 min. zone of the test.

Shock counts of the animals before inhalation (Fig. 4) were at a high level in the first half period of the test in all groups. They then decreased gradually, and maintained stable levels in the latter half of the test. Shock counts of animals
Fig. 3. Mean inter-response-time during Sidman avoidance test after toluene exposure

exposed to 0 and 1,000 ppm showed similar patterns to those before exposure. Shock counts of the rats exposed to 3,000 ppm decreased from the beginning of the test, but there were no significant differences compared with those before exposure.

**DISCUSSION**

Ogata and Tomokuni (1973) indicated that toluene could pass the blood–brain barrier of rats easily. Carlson and Lindqvist (1977) also showed that toluene accu-
mulated in the brain of rats by inhalation decreased to one fifth in an hour after the termination of the inhalation. These findings suggest that the observation of the behavioral changes to investigate the effect of toluene to central nervous system by the behavioral test must be started immediately after the termination of toluene exposure.

Taking the above into consideration, we investigated the effect of toluene single exposure to the central nervous system of the animals using Sidman avoidance schedule immediately after the termination of exposure. Exposure to 0 and 1,000 ppm of toluene for 4 hours did not affect the conditioned avoidance responses in rats. Exposure to 3,000 ppm of toluene for 4 hours produced increased responses, shortening of the IRT and no change in shock counts from the beginning to 50 min.
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zone of the test when compared with those before exposure. Tadokoro and Ogawa (1969) also reported that a marked increase in lever pressing without change of the shock counts was seen when rats were exposed to 3,000 ppm of toluene. From the results of our experiment, it can be said that the behavioral changes caused by exposure to 3,000 ppm of toluene for 4 hours were brought about by a temporary breakdown of the established timing of lever pressing. Tainaka et al (1974) noted that decreases in responses and increases in shock counts were seen in rats exposed to 530 ppm of toluene for 20 min. Although these findings differ from our results, the cause of the difference between these results at the same level was the different methods of the behavioral test and crude exposure apparatus. The behavioral changes were strongest immediately after the termination of exposure and those recovered in about an hour. This indicates that toluene is rapidly transferred to and removed from the brain.

SUMMARY

The effects of a single exposure to toluene on conditioned behavior in rats were studied in this experiment.

1) Exposure to 0 and 1,000 ppm of toluene for 4 hours did not affect the established operant behavior of rats. Exposure to 3,000 ppm for 4 hours produced increased responses, shortening of the IRT and no change in shock counts from the beginning to the 50 min. zone of Sidman avoidance test when compared with those before exposure. The behavioral change indicated here appears to be caused by a temporary breakdown of the established timing of lever pressing.

2) The effect of toluene on the operant behavior was strongest immediately after the termination of the exposure and the behavior recovered in about an hour. This result suggests that toluene is rapidly transferred to and removed from the brain.

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