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Taste aversion by the intraperitoneal administration of toluene and benzene in rats

Aversión a Sabores por la Administración Intraperitoneal de Tolueno y Benceno en Ratas

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ABSTRACT

Water-deprived rats allowed access to 0.25% saccharin during 10 min followed by an intraperitoneal injection of either toluene (Exp. 1) or benzene (Exp. 2) acquired a dose-dependent conditioned aversion to the saccharin taste, whereas control groups receiving pairings of either saccharin and saline, saccharin and oil (solvent vehicle), or water and the solvent failed to develop the aversion to saccharin. It is concluded that solvents, through the intraperitoneal route, function as unconditioned stimuli in the conditioned taste aversion paradigm.

DESCRIPTORS: Conditioned aversion, Toluene, Benzene, Intraperitoneal route, Stimulus properties, Rats.

RESUMEN

Ratas privadas de agua a las que se les permitió el acceso a una solución de sacarina al 0.25% durante 10 min y después se les inyectó intraperitonealmente tolueno (Exp. 1) o benceno (Exp. 2) adquirieron una aversión condicionada, dependiente de la dosis, al sabor de la sacarina, mientras que grupos control que recibieron apareamientos de sacarina y salina, sacarina y aceite (vehículo del disolvente), o agua y el disolvente, no desarrollaron la aversión a la sacarina. Se concluye que los disolventes, a través de la ruta intraperitoneal, funcionan como estímulos incondicionados en el paradigma de la aversión condicionada a sabores.

DESCRIPTORES: Aversión condicionada, Tolueno, Benceno, Ruta Intraperitoneal, Propiedades de estímulo, Ratas.

Taste aversion learning refers to an animal's avoidance of a specific food flavor following the pairing of a toxicant with the food having a characteristic

taste (cf., Garcia & Koelling, 1966). This paradigm has attracted considerable research attention for several reasons. The long delay between stimuli challenges well established ideas regarding the necessary immediacy of stimuli in classical conditioning procedures (Garcia, Ervin & Koelling, 1966). It aroused interest in what has been known as the limitations to the laws of learning (Garcia, McGowan & Green, 1972). Furthermore, it appears to be a useful method for determining some stimulus functions of psychoactive substances (e.g., Cappell & LeBlanc, 1977). For instance, the taste aversion paradigm was recently employed to assess the unconditioned and the conditioned stimulus properties of industrial solvents, such as lacquer thinner (Miyagawa, Honma, Sato & Hasegawa, 1984; Vila & Colotla, 1981; Vila, Colotla, Miranda & Arzate, 1982), a solvent mixture employed as a drug of abuse by children and adolescents in Mexico City (e.g., Natera, 1977) and other parts of the world, e.g. in Sweden (Nylander, 1965). In one of those experiments (Vila & Colotla, 1981) exposure to lacquer thinner during a 15-or a 30-min period paired with the presentation of a saccharing solution did not produce in rats the conditioned aversion to the saccharin taste, and it was therefore concluded that solvents do not act as unconditioned stimuli with this experimental paradigm when the inhalation route is employed. However, exposure to the solvent during a 4-hr period did produce the conditioned taste aversion (Miyagawa et al., 1984). In addition, these Japanese investigators found conditioned aversions with both toluene intraperitoneal (i.p.) and intravenous (i.v.) administrations. The present experiments confirm the i.p. toluene findings and extend them to another toxic solvent, benzene.

METHOD

Subjects

Seventy-two rats were used, 36 in each experiment. They were male adult albino rats of the Wistar strain from the breeding colony of the National Autonomous University of Mexico. The animals were divided in 6 groups of 6 rats each and housed in individual cages with unlimited access to Purina Chow food, but access to water was restricted to a 10-min period each day, in their home cages.

Procedure

Experiment 1. Intraperitoneal administration of toluene.

Once the animals were habituated to the water deprivation regime, they were randomly assigned to one of the following groups:

GROUP	PAIRING
A	Saccharin – 2.00 ml/kg saline
B	Water – 0.94 ml/kg toluene
C	Saccharin – 2.00 ml/kg oil (vehicle)
D	Saccharin – 0.47 ml/kg toluene
E	Saccharin – 0.94 ml/kg toluene
F	Saccharin – 1.175 ml/kg toluene

The last three groups evaluated different doses of toluene administered through the i.p. route in a corn oil solution (50%) when paired with the presentation of a saccharin solution (0.25%). The first three sets of animals were control groups for assessing the injection per se (Group A), the association of toluene administration with a neutral stimulus (water, Group B), and the administration of the oil vehicle (Group C).

The design involved repeated pairings of saccharin and toluene, with a single test trial for assessing saccharin preference after the last pairing trial. Five trials were conducted with each pairing, consisting of the presentation of either water or saccharin during a 10-min period, followed 5 min later by the i.p. injection of either toluene, saline or oil. There was only one trial each day. On the following day after the fifth pairing trial, the animals received a test trial in which two drinking bottles were offered during 10 min, one with water and the other with saccharin. The position of the bottles was reversed half-way in each trial for all animals to obviate side preferences.

Experiment 2. Intraperitoneal administration of benzene.

The procedure for the evaluation of benzene was essentially the same as in the previous experiment, except that the following groups received the treatments indicated below:

GROUP	PAIRING
A	Saccharin – 2.00 ml/kg saline
B	Water – 0.75 ml/kg benzene
C	Saccharin – 2.00 ml/kg oil
D	Saccharin – 0.50 ml/kg benzene
E	Saccharin – 0.75 ml/kg benzene
F	Saccharin – 1.00 ml/kg benzene

RESULTS

Experiment 1. Intraperitoneal administration of toluene.

The upper portion (A) of Fig. 1 shows the average consumption of fluid

for each group of animals when toluene was administered i.p. Groups A, B, and C did not display an aversion to the saccharin solution, drinking it more than water in the test trial in the case of Groups A and C and about the same amount in Group B: average consumption of saccharin for these groups was 9.6 (A), 5.8 (B), and 10 (C) ml. In contrast, Groups D, E and F showed a reduced preference for the saccharin fluid, with a mean intake of 4.6, 1.5 and 0.5 ml, respectively, indicating an acquired aversion to the saccharin flavor ($F = 2.57$, $df = 5$, $p<05$, for the Treatment factor; and $F = 7.69$, $df = 5$, $p<.01$, for the Interaction). Fig. 2A shows the saccharin preference ratio for all groups employed. Note the dose-related reduction in saccharin drinking with increasing solvent doses during the experimental treatment. On the other hand, the fluid intake of the control groups further confirms the indication that saccharin-toluene pairings are responsible for the reduced fluid drinking in the three experimental groups.

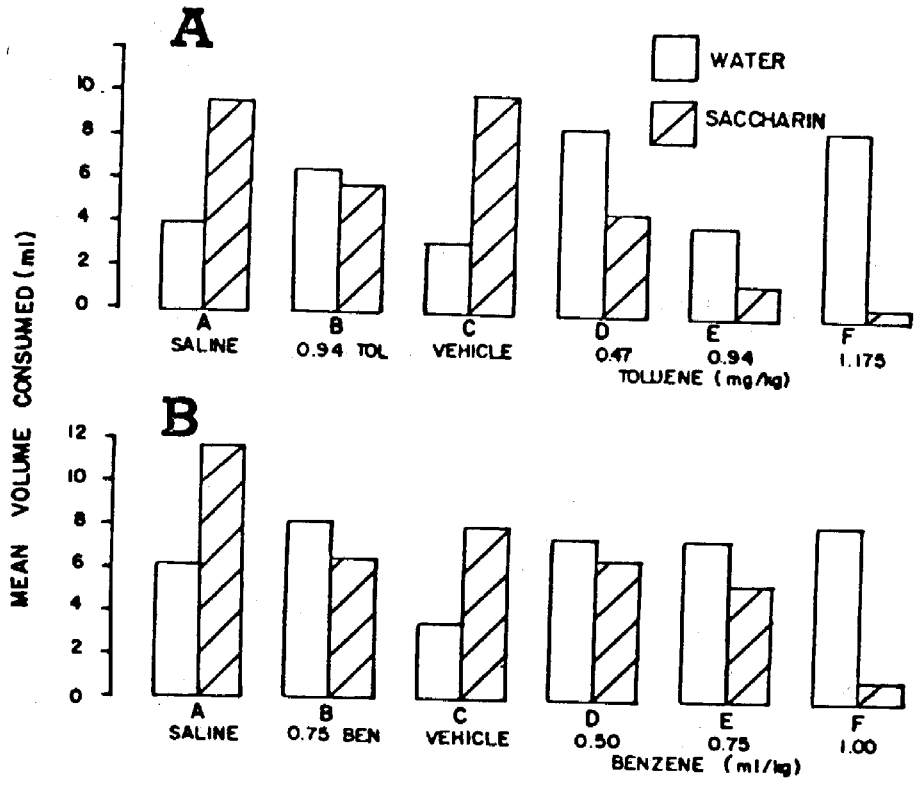

Fig. 1. Mean volume consumed (ml) of either water or a saccharin solution for the toluene (A) and benzene (B) experiments. See text for details.

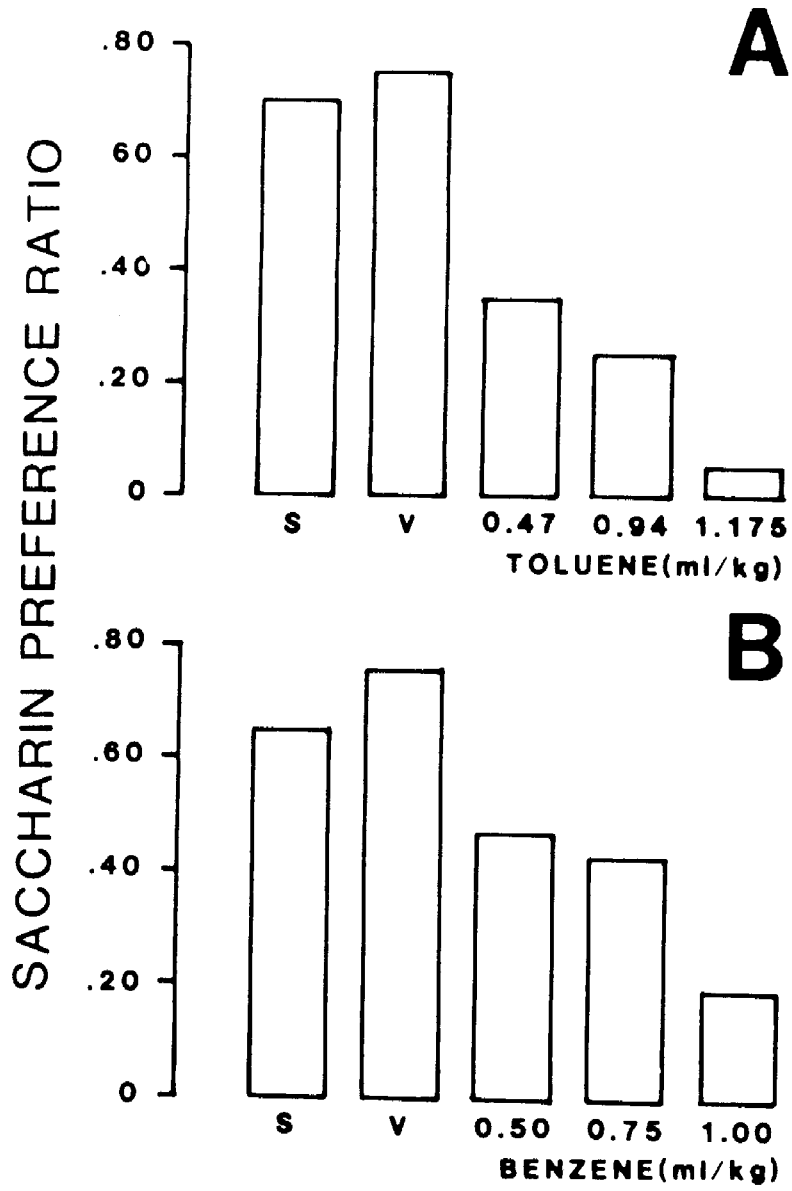

Fig. 2. Saccharin preference ratio for the toluene (A) and benzene (B) experiments. See text for details.

Experiment 2. Intraperitoneal administration of benzene.

Fig. 1B shows essentially the same data pattern as the former experiment: the average amount of liquid ingested in the test trials by each group of animals when benzene was injected i.p. and by the respective controls.

Again, more water than saccharin was consumed by the animals receiving the solvent treatment in association with the sweet taste: mean saccharin consumption was 6.5, 5.5, and 2 ml for Groups D, E, and F, respectively. Furthermore, the animals in the control groups did not develop an aversion to saccharin: average intake of this solution was 11.7, 6.5, and 8 ml for Groups A, B, and C, respectively. However, Group B fluid intake was only slightly lower than that of water. An overall ANOVA yielded non-significant results for the Treatment factor ($F = 1.03$, $df = 5$, $p > .05$), but a statistically significant interaction ($F = 2.75$, $df =$, $p < .05$). Because the contrasting drinking patterns of the control groups (drinking more saccharin than water) and the experimental groups (drinking more water than saccharin) would cancel each other in the overall ANOVA, a second analysis was carried out to compare the test trial intake of water and saccharin in the three experimental groups. Solvent administration resulted in reduced saccharin consumption ($F = 4.69$, $df = 2$, $p < .05$). It should be noted, moreover, that the insiduous and unpredictable toxicity of benzene (c.f., Cornish, 1980) resulted in the death of several rats during the course of the experiment and the data for the test trials did not include six animals for each group. The deaths occurred in the following groups: B (2 rats), D (1 rat), E (2 rats) and F (2 rats).

Again, as with Exp. 1, Fig. 2B shows the same data transformed into a saccharin preference rario, showing the dose-related decrease in saccharin preference in the solvent-treated rats.

DISCUSSION

Toluene and benzene are organic solvents that have attracted considerable research attention in recent years because they are widely used in the manufacture of paints and other products, and because they have been used as substances of abuse. In Mexico City, for instance, they form part of the lacquer thinner frequently employed by some youths for purposes of deliberate intoxication. In the present experiments it was found that when used through the intraperitoneal route, both solvents act as unconditioned stimuli (US) in the learned taste aversion paradigm, because pairing its administration with a saccharin taste produces an aversion to that flavor in subsequent taste probes. Furthermore, it was found that the conditioned aversion is dose-dependent. These findings corroborate those by Miyagawa et al. (1984), who also found a dose-dependent taste aversion with the i.p. injection of toluene. Moreover, it should be noted that the present effects were about equal to those observed by Miyagawa et al., although they used only a single pairing and we used five. This would suggest that repeated pairings do not necessarily enhance toluene-induced flavor aversion conditioning.

As indicated before, Miyagawa et al. also demonstrated that i.v. injections and exposure to long (4 hr) inhalation intervals to toluene can also act as

an aversive US. Other studies have provided additional information on other stimulus properties of organic solvents. In one (Vila & Colotla, 1981) it was found that the odor of thinner presented during water ingestion can acquire a function as conditioned stimulus, whereas Wood (1979, 1982) and Yanagita, Takahashi, Ishida and Funamoto (1970) showed that toluene has reinforcing stimulus properties, since monkeys will self-administer the substance with an operant conditioning procedure.

The present results add to the growing number of studies using conditioned taste aversion as a measure of behavioral toxicity (e.g., Anderson, Tilson & Mitchell, 1982; Braun & Snyder, 1973; MacPhail, 1982; Miranda, Arzate & Vila, 1982) and further emphasize its usefulness in an array of procedures to test new toxic substances (Colotla & Vila, 1985; Riley & Tuck, 1985).

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