Effects of Nicotine and Its Withdrawal on the Performance of Rats on Signalled and Unsignalled Avoidance Schedules

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Abstract. Rats were trained while under the influence of nicotine on a Sidman avoidance schedule. When saline was substituted for nicotine the animals which had been trained on an unsignalled schedule showed poor avoidance and took significantly more shocks than their saline-trained partners. When the schedule included either a warning signal preceding each shock or a feedback signal following each response this dependence did not develop. It is suggested that dependence on nicotine is related to the stressfulness of the situation and that the behavioural disruption found in its absence is due to an accentuation of the normal warmup process and not to dissociation of learning.

Key words: Nicotine Dependence — Sidman Avoidance — Stress — Warmup — Dissociation — Rats.

Introduction

Previous attempts to demonstrate dependence on nicotine in animals have been unsuccessful, although some species, for example the rhesus monkey (Deneau and Inoki, 1967), have been shown to self-administer nicotine. The experiments now reported were designed to investigate the possibility that dependence on nicotine might be demonstrable in rats following prolonged administration of the drug, provided that a suitable test situation could be found. A shock-avoidance schedule (Sidman, 1953) was chosen, because any disruption of behaviour resulting from the withdrawal of nicotine would be readily detectable as an increase in the number of shocks received. In preliminary studies it was found that rats could become dependent on nicotine for successful avoidance performance, the degree to which this occurred apparently being related to the stressfulness of the schedule (Hall and Morrison, 1973). These studies have now been extended to compare the effects of nicotine and its withdrawal on the performance of rats on one unsignalled and two signalled avoidance schedules.

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Twenty-five pairs of rats, 9 male and 6 female Sprague-Dawley and 7 male and 3 female cross-bred (F1 of a Sprague-Dawley, Lister black-hooded cross) were used for this experiment, each rat being paired with another of the same age, sex and strain. At the start of the experiment their ages ranged from 85–214 days.

**Training.** The rats were trained in Grason Stadler 2-lever rat chambers on a Sidman avoidance schedule (Sidman, 1953). During training, electric shocks of 0.5 sec duration were delivered through the grid floor every 3 sec. Each lever-pressing response postponed the next shock for 30 sec (RS 30", SS 30".). Some rats were trained by shaping directly on the avoidance schedule. The remainder were trained initially to press on a continuous reinforcement (crf) schedule for water. After a few sessions, during which crf and avoidance were programmed simultaneously, the water reinforcements were discontinued. During avoidance training by both methods shock settings were gradually increased from 0.1–0.4 mA. It was not possible to standardise the training period as the rats varied greatly in the number of sessions (10–23) required to reach the final schedule. However, animals in each pair received the same number of training sessions. When the rats had learned to avoid most of the shocks they were placed on the final schedule in which 0.5 sec 0.4 mA shocks were programmed every 30 sec, each response postponing the next shock for 30 sec (RS 30", SS 30".). The first day of this final schedule was considered as day 1 of the experiment.

**Procedure.** Each rat was run singly for 60 min at the same time each day for 5 days a week throughout the training period and the experiment. Animals of a pair were run in the same chamber during consecutive 60 min sessions.

One rat of each pair received 0.4 mg nicotine/kg subcutaneously immediately before each training session (nicotine-trained, N) the other receiving saline (saline-trained, S). Nicotine (n) and saline (s) injections continued throughout the experiment except that saline was substituted for nicotine on day 4 (20 pairs) or day 12 (5 pairs) of the experiment and this substitution was repeated at intervals of 1 week on 3 further occasions (Table 1). The nicotine injections were made by dissolving nicotine hydrogen tartrate in 0.9% saline to give an injection volume of 0.1 ml/100 g body weight. The dose is expressed as base.

**Experiment 2, Signalled Avoidance (Warning Signal)**

Nine pairs of male rats, 6 Sprague-Dawley and 3 cross-bred were used. Training methods, pairing of rats and experimental procedure were the same as in Experiment 1 with the exceptions specified below. The schedule was identical except that a 10 sec white-noise warning signal preceded the presentation of each shock. A response during the signal ended the sound and restarted the 30 sec. During training, the sound continued until the rat pressed the lever. In the final schedule the signal stopped immediately before the single shock. Saline was substituted for nicotine on day 4 of the final schedule and also 1 week later. After 3 further sessions with the warning signal (Experiment 2a) the sound was discontinued (Experiment 2b). Two further saline substitutions were then carried out, the first being delayed until the 5th session without the stimulus. One pair of rats did not receive the last substitution test.

**Experiment 3, Signalled Avoidance (Feedback Signal)**

Eight pairs of male rats, 3 Sprague-Dawley and 5 cross-bred were used. Training and procedure were the same as in Experiment 1. In Experiment 3a the schedule