Sleep as a conditioned response¹

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Abstract

A sleep response was conditioned in dogs using morphine or pentobarbital as the UCS. The effect of morphine on rat EEG and behavior was also studied. Data indicated that in dogs morphine was the more powerful UCS and that in rats morphine produced catatonia rather than sleep.

Problem

Pavlov (1927) reports the conditioning of a sleep response in dogs upon repeated injection of morphine. The UCR to morphine was nausea, secretion of saliva, and vomiting, followed by deep sleep. After five or six days the preliminaries of injection produced all these symptoms, including sleep.

Kleitman & Crisler (1927) and Crisler (1930), in a series of studies on conditioned salivation with morphine, report that about 20 minutes after injection the dogs became somnolent and salivation ceased. The authors discontinued observation without observing the sleep behavior further.

Clemente et al. (1962) successfully conditioned sleep in cats. These animals were presented with a conditioning sequence of tone followed by basal forebrain stimulation. A conditioned EEG synchronization accompanied by behavioral manifestations of sleep developed rapidly to the tone when stimulation in the basal forebrain was used as the UCS. Generalization and discrimination were also demonstrated.

Levitt & Webb (1964, in press) attempted unsuccessfully to condition sleep in rats. Forty-two injections of pentobarbital were administered every 48 hours to a group of four rats, producing sleep within ten minutes in all cases. A 43rd injection of sterile water did not produce sleep in any animal within a one-hour observation period.

The present experiments are concerned with the possibility of conditioning a sleep response in rats using morphine and in dogs using pentobarbital or morphine.

Method

Experiment I. Six adult male Long-Evans rats were injected subcutaneously with doses of morphine sulfate ranging from 8 to 240 mg/kgm body weight to determine the feasibility of conditioning sleep in this species. Behavioral and EEG observations were made.

Experiments II and III. Adult dogs were injected daily with either a drug or an equal volume of sterile water. The S was removed from its living quarters to an isolated room where it received injections. E remained in the room until S slept. Ss were observed for 1 hour after each injection. If sleep had not occurred within the hour, the trial was considered not to have produced sleep. Behavioral observation was used to determine whether Ss

were asleep. The Ss were to receive a series of daily intramuscular injections. Trials 1 to 10, 12 to 17, and 19 to 25 were drug trials. Trials 11 and 18 were test trials during which sterile water was administered. Extinction began on the 26th trial (injection of sterile water). Extinction was considered to have occurred when two consecutive trials did not produce sleep within 1 hour.

Experiment II. In an exploratory study one adult female dog received daily injections of morphine sulfate in doses ranging from 5 to 10 mg/kgm. This animal died on the 12th day of the experiment. A post mortem indicated death due to pneumonia and intestinal ulceration, probably not directly associated with the experiment. Two adult male dogs were started on the conditioning series. One of these Ss was accidentally sacrificed after the 16th trial and a third dog received the full schedule of injections. The dose of morphine sulfate used was 5 mg/kgm unless otherwise indicated.

Experiment III. Two adult male dogs received the schedule of daily injections of pentobarbital sodium. The initial dose used was 20 mg/kgm. Latencies increased from time to time during the experiment probably due to tolerance and doses were aperiodically increased up to a maximum of 35 mg/kgm.

Results

Experiment I. All doses produced catatonia. The Ss exhibited muscular rigidity and maintained any position in which they were placed. When stimulated by touch or sound they would run a short distance and freeze. The Ss kept their heads erect and eyes open and did not assume a sleeping posture. The catatonia lasted from 3 hours for the low doses up to 24 hours with the higher doses (200-300 mg/kgm). The EEG showed persistent sleep waves even when the Ss were moving following stimulation.

Experiment II. The sleep latencies on only three of the four dogs are summarized in Table 1. Subject 4 did not sleep on either of the test trials or during extinction. This S developed a severe mouth ulcer during the first few days of the experiment and it is felt that this interfered with the conditioning process. Subjects 1, 2, and 3 slept on all test trials. Sleep latencies during drug trials seem to have shortened for dogs 1 and 2. This may be a potentiation of the morphine effect by conditioning. The only S extinguished (S-3) slept for 2 trials before extinction occurred.

Salivation, vomiting and defecation were among the UCR's to morphine observed, with salivation occurring on every trial and the other responses only on occasion. The unconditioned salivation had an initial latency of 5 to 8 minutes. After about 5 trials, salivation occurred

Table 1. Mean Sleep Latencies for Morphine and Pentobarbital Injected Dogs (1)

	Morphine			Pentobarbital	
	1	2	3	4	5
Trials 1 - 5	20	25	23	15	17
6 - 10	13	24	28	12	21
Test Trial	10	25	28	19	NS
12 - 17	(2)	11 ⁽³⁾	18	13	37
Test Trial			50	21	39
19 - 25			33	22	17
Extinction 1			45	31	50
2			45	NS	NS
3			NS ⁽⁴⁾	NS	NS
4			NS		

(1) mean sleep latency in minutes.

(2) died.

(3) trials 11 - 16 only, accidentally sacrificed.

(4) no sleep within one hour after injection.

immediately after injection and later to the appearance of the E. The initial unconditioned salivation was moderate. After conditioning the quantity of saliva increased and was profuse. The sleep latency for S-3 increased on trials 19 and 20, and fearing tolerance, the dose of morphine was increased to 7.5 mg/kgm.

Experiment III. The data are summarized in Table 1. Both Ss slept on every drug trial. S-5 did not sleep on the 1st test trial but did sleep on the 2nd one. Both Ss slept on 1 trial before extinguishing. The data on latency is confounded by the necessity of changing dosage levels.

Discussion

The response of rats to morphine is not sleep but a catatonic stupor. Because this response is qualitatively different from the sleep response, sleep conditioning procedures were not continued in this group. It is of interest to note that the animals continued to exhibit EEG synchronization even when moving about the cage.

It appears that sleep can be conditioned in dogs with either morphine or pentobarbital. The pentobarbital conditioning was weak. There was no decreased latency on drug trials and one of the dogs did not exhibit conditioning until the 2nd test trial.

All three morphine-injected dogs slept on the 1st test trial. The one dog who had a 2nd test trial slept during that trial and also on 2 of the extinction trials. There was also evidence that conditioning was potentiating the morphine effect in producing reduced latencies for S-1 on trials 6 through 10 and S-2 on trials 12 through 16. It was noted that the morphine injected dogs assumed the sleeping position immediately after the injection when conditioning had been established, while the pentobarbital injected dogs did not do this.

The apparently more effective conditioning resulting from the morphine injections may well be attributable to the sequence mediating rg - sg's of salivation and nausea when compared with the less effective conditioning of the pentobarbital procedure.

References

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Note

1. The author wishes to express his thanks to Wilse B. Webb for his comments and criticism and William Walker for assistance in data collection. The investigation was supported in part by an NIH grant (NIH-MH-03881-03) to W. B. Webb, and by a NASA Predoctoral Fellowship (NASA-BSG(T)-13) to Robert A. Levitt.