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A State-Dependent Learning Effect Produced by Amylobarbitone Sodium

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Introduction

Learning is said to be state-dependent when a response which is learned in a given internal state shows disproportionate decrement in retention when the internal state of the learner is changed. Research on this phenomenon has a long history. It was first noted by investigators who were concerned with the problem of whether overt responses were necessary for the formation of classically conditioned responses. Curare was used to eliminate the overt response, and it was found that:

(1) conditioned responses formed under curare did not transfer to the non-curarized state; and

(2) conditioned responses formed in the non-curarized state did not transfer to the curarized state.

These effects were found for skeletal and autonomic responses by investigators using curare or, later, erythroidine (Girden and Culler, 1937; Culler *et al.*, 1939; Girden, 1940; Girden, 1942a, 1942b). All of these experiments were conducted with animals.

More recently, research with d-tubocurarine has failed to produce state-dependent effects, and it has been suggested that the original findings were due to the central depressant effects of the drugs used in the earlier experiments (Black *et al.*, 1962; Solomon and Turner, 1962; Black and Lang, 1964; Smith, 1964).

If the central effects of the early drugs were the important factor in producing the state-dependent effect it might be expected that other drugs with central action could produce state-dependent phenomena. Overton (1964) investigated this possibility and found a strong state-dependent effect produced by sodium pentobarbital in a T-maze learning situation. Other findings which could be interpreted as state-dependent effects have been reported (Hunt, 1956; Miller, 1961; Barry *et al.*, 1962; Barry *et al.*, 1965; Krieckhaus, 1965; Krieckhaus *et al.*, 1965 and Crow, 1966). These experiments were carried out with animals and the drugs used have included alcohol, amphetamine, barbiturates and chlorpromazine.

There is also some evidence that state-dependent effects can be demonstrated in human subjects. Bustamante *et al.* (1967) reported on a group experiment in which subjects rote-learned nonsense syllables, under placebo, amylobarbitone or amphetamine, and were tested for recall immediately after the learning period and on two later occasions. On the second occasion the drug state was different from the learning state, and on the third occasion it was the same as the learning state. It was found that changing the state led to decrement in retention.

An experiment by Storm and Caird (1968) demonstrated a state-dependent effect in a serial learning task with chronic alcoholic subjects. Subjects learned a list of twelve two-syllable common nouns under alcohol or no alcohol. Forty-eight hours later subjects were tested by having them relearn the list. Retention was less in the groups whose relearning state differed from their learning state.

Finally, Goodwin *et al.* (1969) have reported an experiment on the state-dependent effects of alcohol in human subjects. Four tasks were used: avoidance learning; word association recall; rote learning; and picture recognition. It was found that recall showed decrement on three of the four tasks if the subject's state was different on learning and recall occasions.

In view of these findings, we have in the present study investigated further the existence

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of state-dependent effects associated with sodium amytal in human subjects, with learning tasks chosen to cover motor learning and verbal learning at varying levels of complexity.

Method

Subjects

The subjects used were 16 volunteers, all senior nursing or hospital administrative staff undergoing a management course. They comprised 14 women and 2 men, age range 29–51 years ($\bar{X}$ = 39 years; SD = 3·9 years). All were over 7 stone in weight and were not receiving any medication.

Procedure

Each subject completed the tasks on two occasions separated by a 48-hour interval. A double-blind procedure was used, subjects being randomly assigned to one of four groups (Drug-Drug, Placebo-Placebo, Drug-Placebo, or Placebo-Drug) by a psychologist not involved in the experimentation. The drug used was amylobarbitone sodium and the dose was 200 mg. The subjects had not taken food or drink for 2½ hours before receiving the drug. The drug was in tablet form, identical in size and appearance to the placebo. After administration of the tablets subjects waited 30 minutes before commencing the tasks.

The five tasks used were as follows:

(a) Serial Learning Test.
(b) Paired Associate Learning Test.
(c) Neologisms Learning Test.
(d) Pursuit Rotor Learning.
(e) Visual Reaction Time.

All subjects carried out the tasks in the same order on both occasions, but the subjects' starting point was varied so that some subjects did the tasks in order (a)–(e) on both occasions, some (b)–(a), and so on, thus balancing for the effects of fatigue or change in drug effects over the period of testing. The total period for completion of the tasks was approximately 90 minutes including waiting between tests where necessary.

Tests

(a) *Serial learning test*

The material for this test consisted of nine C.V.C. trigrams (all having 100 per cent Association Value). These were presented visually on a memory drum, allowing 1½ seconds exposure to each with a 3 second gap between successive trigrams. In both test sessions, before the first trial, the subject was instructed to try to remember the syllables for anticipatory recall on later trials. On these later trials the subject attempted to anticipate each syllable in the 3 second period before it became visible. The first eight subjects received ten learning trials in each session. Because this was found to take an inordinate length of time, the remaining subjects received only five learning trials in each session. By chance this resulted in two subjects from each group receiving five trials, and two receiving ten. Subjects' scores were the mean number of correct anticipations per trial for each session.

(b) *Paired associate learning test*

This is a verbal learning test in which a subject learns to associate pairs of nonsense-syllables, so that when presented with the first syllable of a pair (stimulus term) he can recall the second syllable (response term). Nine pairs of C.V.C. trigrams (all with 100 per cent Association Value) were written on separate cards, with the stimulus member of a pair also printed on the reverse side of the card.

Subjects were given ten learning and ten test trials in alternate order on both occasions. On each learning trial the cards were shuffled, and the subject given 2 seconds exposure to a pair of trigrams which he was asked to pronounce. After all nine pairs had been presented, the cards were reshuffled and reversed. The test trial was then completed by requiring the subject to supply the correct response term for each stimulus trigram presented, all stimuli being presented for 4 seconds each. The number of correct responses on every test trial was recorded.

(c) *Neologisms learning test*

The Neologism Learning Test (Hetherington, 1967) is a measure of concept learning in which the subject is taught meanings for ten specially prepared neologisms. Standard materials and procedure were used, except that every individual was given the first five trials on the first occasion and the second five trials on the second occasion, regardless of reaching the normal criterion for stopping the test. The total number of correct definitions on each occasion was recorded.

(d) *Pursuit rotor learning*

In this task the subject learned to maintain contact between the tip of a stylus and the middle of an off-centre target area marked on a revolving turntable. On both occasions the turntable was set revolving at 0·5 r.p.s., and each subject was given five 1 minute learning trials, with 30 second rest periods between each trial. The apparatus was a turntable which had a target area marked off in three concentric circles. The score on each trial was time in contact with the innermost part of the target area.

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TABLE I

Results of analyses of covariance of the five measures

Source	df	Serial learning	Paired associates	NLT	Pursuit rotor	Reaction time
A. Change of state from first to second occasion	1	9·88***	0·00	7·62**	2·02	7·11**
B. Starting state (drug *v.* placebo) ..	1	0·32	0·74	0·09	5·92*	0·61
A × B interaction	1	4·52	0·53	0·01	2·50	0·12

***p ·01; **p ·025; *p ·05;

(e) *Visual reaction time*

Each subject was given ten trials on both occasions to learn the same fixed sequence of nine lights in a choice reaction-time situation. The manipulanda were ten buttons arranged in a semicircle around a central button. All buttons were mounted horizontally. The action of depressing and releasing the central button illuminated one of the buttons in the semicircle. Pressing this button cancelled the light, and the central button needed to be operated again to illuminate the second button in the sequence. This procedure was continued until the end of the sequence which marked the end of a trial. Time to complete each trial was recorded on an electrical timer.

RESULTS

The difference between total scores for a given task on the first and second occasions for each subject were treated by analysis of covariance. The covariate was the mean score on the last two trials of the first session. Analysis of covariance was used because of the possibility that the magnitude of difference scores might be affected by the degree of terminal learning on the first occasion. The two main factors were drug versus placebo on the first occasion; and change in state versus no change in state on the second occasion. The interaction term would, therefore, indicate whether state-dependent effects varied with starting condition. Table I shows the F ratios resulting from the analyses for the five measures.

For three of the five tasks the F ratio for the change in state factor reaches an acceptable level of significance. The values of the adjusted means are shown in Table II.

TABLE II

Adjusted mean improvement for the five tasks for subjects whose internal state was (1) the same or (2) different on the two occasions

	Internal state		
	(1) Same	(2) Different	
	Adjusted mean	Adjusted mean	P
Rote learning ..	3·51	1·98	·01
Paired associates ..	35·69	35·43	ns
Neologism learning test	13·89	8·11	·025
Pursuit rotor ..	37·03	24·84	ns
Reaction time ..	106·52	62·36	·025

DISCUSSION

The results obtained showed a state-dependent effect for three out of five tasks used. The tasks which failed to show state-dependence have no obvious similarities, and the reason for the failure is obscure. Goodwin *et al.* (1969) also failed to find a state-dependent effect with their pursuit rotor task, but say that the reason for this was that their task was too easy. In the present investigation the subjects showed improvement from first to second occasion, those on drugs on the first occasion improving more than the others, so the explanation cannot be that learning was asymptotic by the end of the first session.

Three main theories have been advanced to explain state-dependent effects. The earliest of these arose from the work on curare, and stated

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that conditioning in the normal state was mediated by cortical structures, while in the curarized state sub-cortical mechanisms were involved. Support for this came from studies in which the auditory cortex of the animal was destroyed before a response to an auditory stimulus was conditioned. Without the auditory cortex any conditioned responses formed would have to be dependent on subcortical structures. Thus it would be expected that conditioning would transfer from normal to curarized state in these animals, and this was found to be the case (Girden, 1940).

While it is possible that this theory can cope with Overton's (1964) results involving T-maze learning in rats, it would be difficult to apply such an explanation to the previous and present findings on humans. Overton himself proposes a hypothesis involving differential changes in synaptic thresholds in drugged and undrugged state, and thus different pathways involved in learning. This theory is as yet untested.

The third possibility is to subsume the state-dependent phenomenon under the general heading of stimulus generalization decrement. Changes in the stimulus situation from learning occasion to test occasion would be expected to result in reduced response strength. The internal state of the learning organism is an important feature of the total stimulus situation, and thus changes in it would lend to generalization decrement. While this is more an example of categorizing than theorizing, the generalization decrement hypothesis can account for all of the findings available.

The existence of state-dependent effects in humans has implications for many areas of clinical psychology and psychiatry. The effects of therapy under drugs would not be expected to transfer fully to the non-drugged state. Instructions given to patients before they are put on a course of drugs would be liable to be forgotten. This might be one of the factors involved in the frequent failure of patients to take drugs as prescribed (Ley and Spelman, 1967; Hare and Willcox, 1967). Some of the theoretical possibilities of state-dependency have been discussed by Storm and Smart (1965), who use the concept to explain some of the features of alcoholism. More research is urgently needed to discover what drugs show state-dependent effects in humans, what functions are particularly affected, what the magnitude of these effects is, and methods for overcoming them. It is also important to know the effects of long-term as opposed to single dose administration of drugs.

Summary

A state-dependent effect in human subjects is described. Learning under placebo showed less transfer to drugged state than a placebo state, and learning under a drugged state showed less transfer to a placebo state than a drugged state. The implications of these findings are discussed.

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