PSYCHOLOGY

Memory Enhancement by Anticholinesterase as a Function of Initial Learning

WHEN a well learned habit is clearly remembered its recall is blocked by an intracerebral injection of the anticholinesterase di-isopropyl fluorophosphate (DFP)[1]. When, however, the same habit is almost forgotten its memory is enhanced by treatment with the same drug[2]. Here we show that when a habit is only partially learned its recall is enhanced by injection of the anticholinesterase DFP, and further that the better the original learning of the habit the worse the recall of the habit after treatment with the drug.

Seventy-two male albino rats (Sprague Dawley, Holtzman strain, 400 g) were trained in a Y-maze to escape a shock by running to the lit arm of the maze as previously described[1,2]. The light in the correct arm was dim to make the task difficult. The rats were randomly assigned to one of six groups before initial training. The first two groups were given thirty trials of learning. The second two were given seventy trials, and the third two 110 trials. The first group of each pair was injected with the drug in the same manner and quantity as already described[1,2], 5 days after initial learning. The second group of each pair was simply injected with the vehicle peanut oil, 5 days after training, again as previously described[1,2]. All groups were tested for recall of the habit 24 h after the injection. The difference between the number of correct choices during the last ten trials in original training and the number of correct choices during first ten trials of the post-injection test were used as an index of recall.

The three groups injected with peanut oil and trained to three different levels forgot approximately the same amount in terms of an increase in errors during the first trials of retraining (Table 1). On the other hand, the rats trained for only thirty trials and then injected with DFP showed a large and significant enhancement of recall when compared with their own performance in the last ten trials of initial training and the performance of the thirty trial control group in recall.

Table 1

Treatment (DFP or peanut oil)	No. of trials in initial learning	Learning score Mean	Learning score S.D.	Retention score Mean	Retention score S.D.	Difference score Retention mean	Difference score Learning S.D.
DFP	30	6·75	1·76	8·75	1·05	2·00	2·24
PO	30	8·00	2·08	6·75	1·48	−1·25	1·42
DFP	70	8·50	1·37	8·58	1·56	0·08	2·32
PO	70	8·25	1·48	7·92	1·16	−0·33	1·61
DFP	110	9·75	0·63	7·50	1·35	−2·25	0·90
PO	110	8·92	1·49	8·00	1·25	−0·92	2·02

Duncan's new multiple range test on difference scores

	30 DFP	70 DFP	110 DFP	30 C	70 C	110 C
30 DFP	—	*	**	**	**	**
70 DFP	*	—	ns	ns	ns	ns
110 DFP	**	*	—	ns	*	ns
30 C	**	ns	ns	—		
70 C	**	ns	ns	ns	—	ns
110 C	**	ns	ns	ns	ns	—

DFP, Di-isopropyl fluorophosphate; PO, peanut oil; C, control.

This enhancement of recall did not occur in the groups which had seventy or 110 trials when they were treated with DFP. Table 1 shows that the greater the number of initial trials of learning the greater the degree of forgetting after treatment with DFP and the smaller the amount of enhancement of recall with this drug. This trend is linear and statistically significant at the 0·01 level (analysis of variance). The difference in amount of forgetting displayed by the 110 trial DFP and control groups just misses significance.

An alternative test of the hypothesis in this investigation should show that there is more facilitation by DFP in animals which had learned less, and more impairment in those who had learned more within each group. Correlations between learning and retention were computed within each group and the correlations were compared (Table 2). The difference in the thirty trial groups is significant and in the correct direction. In the seventy trial groups it is in the right direction. It is to be expected on purely mathematical grounds that the correlation between initial performance and retention should fall off as the initial performance approaches a perfect score for all the members of a group, because any difference in amount of initial learning cannot be mirrored by a difference in score. The present results show the same effect of facilitation as a pilot study using an easier discrimination task with 14-day-old memories.

Table 2. COMPARISON OF INTRAGROUP CORRELATIONS BETWEEN LEARNING AND RETENTION

	DFP	Control	Standard error	Z	P
30	−0·18	+0·70	0·47	2·23	<0·03
70	−0·23	+0·28	0·47	1·10	ns
110	+0·17	−0·05	0·47	0·50	ns

DFP as an anticholinesterase delays the destruction of acetylcholine. At low effective levels of acetylcholine synaptic transmission is facilitated, a fact used in the treatment of myasthenia gravis. With increasing quantities of acetylcholine facilitation turns into progressive synaptic block. The findings reported here are therefore interpreted[3] to show that during learning a set of synapses is stimulated to increase their capacity to emit transmitter, and that with increased learning of the same habit the capacity of these synapses is boosted further. Consequently, facilitation is seen with poorly learned habits, while progressive blocking of recall is observed with well learned habits, keeping dose of drugs and learning task constant.

This work was supported by grants from the U.S. Public Health Service and the U.S. National Science Foundation.

J. A. DEUTSCH

Department of Psychology,
University of California, San Diego.

H. LUTZKY

Department of Psychology,
New York University.

[1] Deutsch, J. A., Hamburg, M. D., and Dahl, H., *Science*, **151**, 221 (1966).
[2] Deutsch, J. A., and Leibowitz, S. F., *Science*, **153**, 1017 (1966).
[3] Deutsch, J. A., *Diseases of Nervous System*, **27**, 7 (1966).

Effects of Neonatal Amygdalectomy in the Maternally Reared and Maternally Deprived Macaque

IN the monkey, bilateral amygdalectomy results in a number of behavioural changes which have been well documented[1–4]. These changes consist of (1) reduction in aggressiveness and relative tameness toward man; (2) increased orality, coprophagia and the mouthing of inedible objects; (3) hypermetamorphosis; and (4) hypersexuality. While these changes may be enhanced by extending the lesion to include the temporal neocortex and hippocampus, it has been established that these behavioural alterations can be produced by ablation of the amygdaloid nuclei alone[2].

This lesion produces a profound alteration in adult behaviour and so it would be of interest to examine the development of animals subjected to similar ablations at various ages. In the kitten[5,6], one of us (A. J. K.) found that lesions of the amygdaloid nuclei from 2–50 days of age did not result in the behavioural changes seen after similar ablations in the adult. Growth for the first year of life was unaffected as was the time of appearance of play and aggressive behaviour. This report will deal with the effects of amygdala lesions in the monkey produced during the first week of life (Fig. 1).