DRUG FACILITATION OF LEARNING AND MEMORY[1,2] 6563

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There is considerable evidence that drugs can impair and enhance the acquisition and retention of learned responses. This review focuses on recent studies of drug facilitation of learning and memory in infrahuman subjects. Earlier research concerning drug influences on learning and memory is summarized in a number of more comprehensive (1–7) as well as specialized (8–11) reviews.

THE PROBLEM OF ASSESSING DRUG INFLUENCES ON LEARNING AND MEMORY

There are no universally accepted definitions of learning and memory. The terms are used here to refer to the acquisition and retention of changes (presumably in the central nervous system) produced by experience. All studies of learning and memory are faced with the obvious but troublesome fact that learning and memory cannot be studied directly. We can only observe animals' behavior and make inferences about learning and memory on the basis of the observations. This problem is complicated by the fact that drugs influence behavior in many ways. Drugs affect sensory processes, states of mood, motivation and arousal, and they alter motor activity. In research studying the effect of drugs on learning and memory the major conceptual task is that of distinguishing the behavioral effects of drugs that are due to influences on learning and memory from other effects that influence behavior. The problem is complicated further by evidence that the processes underlying very recent or short term memory may be different from those underlying long term memory (6). Thus, drugs may well have different effects on short and long term memory processes. The studies reviewed here are concerned primarily with the effects of drugs on long term memory.

Many types of tasks and training procedures are used in studies of learning and memory. There is no standardized behavioral assay. The various tasks require different types of appetitive (e.g., food, water) and aversive (e.g., footshock,

[1] Abbreviations used in this review are: PTZ (pentylenetetrazol), AMPT (amphetamine), ECS (electroconvulsive shock), α-MT (α-methyl-p-tyrosine), DOPA (3,4-dihydroxyphenylalanine), 5HTP (5-hydroxy-tryptophan), PCPA (p-chlorophenylalanine). Drugs were administered I.P. unless otherwise indicated.

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water immersion) motivation and different types of responses. Mazes, discrimination tasks, and active and inhibitory (passive) avoidance tasks are those most commonly used. Most studies of drug influences on learning and memory typically employ only one task. However, if it is to be concluded that a drug affects learning processes rather than simply performance of some particular task, it is important to examine the effect with a variety of tasks and procedures. This is an important consideration since most, if not all, of the studies on this problem have as a general aim the application of the findings to an understanding of the neurobiology of memory, including human memory.

As summarized in Table 1, there are several types of studies of drug effects on learning and memory. Drugs can be given at different times either before or after training in order to study the drugs' effects on acquisition, memory storage, and retention. Although each type of procedure is useful, each is subject to methodological problems which make interpretations difficult. In some studies, drugs are given repeatedly for long periods of time before training. The findings of such studies are difficult to interpret because the effects of the drugs on processes other than learning (designated "nonspecific effects") are difficult to rule out. The most frequently used procedure is that of administering drugs just before training. In order to discover if enhanced acquisition is due to lasting effects on learning, the animals can be given a retention test days or weeks later. However, a drug might enhance retention because it influenced the animals' sensitivity to shock or degree of arousal during the original training, rather than by directly modifying memory storage processes. Further, if enhanced acquisition is not followed by enhanced retention this lack of effect could be due to "state dependency": The difference in "brain states" during acquisition and retention might make retrieval of the learned response difficult (12).

To avoid these problems, many studies have used the procedure of administering drugs *after* rather than *before* the training session. With this procedure the animals can be trained and tested while they are not under the direct influence of the drugs. The assumption underlying this procedure is that the memory processes initiated by a training experience require time for fixation or consolidation into long term memory and, consequently, the processes remain susceptible to modifying influences for a period of time following training (6). Experiments using this procedure must examine the effect of varying the time between the training and the drug administration. Further, such experiments must consider the possible rewarding and punishing effects of posttraining injections.

Another type of procedure is that of repeatedly administering a drug for a number of days between training and retention testing. Obviously, any nonspecific effects of the drug administration are difficult to assess. Finally, in some experiments drugs are administered only prior to the retention test. Such experiments must provide controls for nonspecific performance effects, as well as possible effects of state dependency. In view of these conceptual and methodological problems, interpretations of the findings of experiments concerning drug facilitation of learning and memory must be made cautiously. A more extensive review of these issues is available (13).

TABLE 1. Times at which drugs are administered in studies of drug facilitation of learning and memory

Time of Drug Administration	Drug Effects Examined	Some Problems of Interpretation	Representative Experiments
Before Training			
Weeks	Development of Learning	Nonspecific effects	23
	Longlasting influences on learning	Nonspecific effects	34, 35
Hours to minutes	Acquisition	Nonspecific effects State dependency	40, 41
After Training			
Seconds to hours	Memory consolidation or storage	Nonspecific effects Rewarding and punishing effects	29, 51
Days	Maintenance of memory	Nonspecific effects	22
Before Retention			
Minutes to hours	Retrieval or retention	Nonspecific effects State dependency	83, 84

STUDIES OF DRUG FACILITATION OF LEARNING AND MEMORY

Strychnine.—Recent research findings provide additional evidence (10, 14) that learning is enhanced by strychnine. However, different interpretations of the basis (or bases) of the effects have been offered. Whishaw & Cooper (15) reported results suggesting that when injected before training, strychnine sulphate (1.0 mg/kg) facilitated maze learning performance by suppressing the rat's tendencies to explore. Strychnine administered before training (0.125 mg/kg) appears to enhance the rate at which mice habituate to a sound stimulus (16), suggesting that the drug acts by attenuating responsiveness. Such an interpretation, while consistent with other results obtained with animals tested while drugged, cannot account for findings of numerous experiments that retention is enhanced by injections of subconvulsive doses of strychnine and other stimulants, if the drug is administered within an hour or so following training on a variety of tasks, including mazes, discrimination tasks, and active and inhibitory avoidance tasks (10). Recent studies indicate that posttraining injections of strychnine enhance the learning of an association between two stimuli. Humphrey (17) found that posttraining strychnine sulphate (1.0 mg/kg) facilitated sensory preconditioning. Rats were first given paired presentations of a sound and light followed by saline or strychnine. Then the sound was associated with a footshock. Subsequent tests indicated that the strychnine treated animals showed greater emotional responsiveness to the light stimulus presented alone. Oliverio (18) trained mice in an active avoidance task using a buzzer CS. The mice then received 25 trials with a light and buzzer CS either preceded or followed by saline or strychnine (0.3 mg/kg). In a subsequent test with light CS alone the light was more effective as a CS for the animals that had received pre- or posttraining strychnine. No enhancement was produced by strychnine given 1 hour after the 25 trial light plus buzzer training session.

Under some conditions strychnine impairs learning. Administered to rabbits (0.5 mg/kg) after daily training sessions, it retarded the acquisition of a classically conditioned nictitating membrane response (19). The effect was found only if the CS-US interval was less than optimal or if the animals were returned to their home cages following training. These results emphasize the importance of the training used in such studies and confirm earlier evidence (1) that the posttraining conditions influence the effects of strychnine on learning.

The facilitating effects of strychnine, as well as other stimulants, on learning have been interpreted as indicating that the drug enhances storage processes (6). This hypothesis is supported by evidence that strychnine attenuates retrograde amnesia produced by electroconvulsive shock (ECS) if the drug is administered either before training or within a few hours after the ECS treatment (10). Recent evidence concerning this effect is conflicting. Miller & Springer (20) failed to replicate the effect. However, confirming evidence was obtained by Duncan & Hunt (21). The reasons for the conflicting findings are not apparent.

Alpern & Crabbe (22) have reported that, in mice, retention of a learned discrimination response is enhanced by administering strychnine sulphate

(0.2 mg/kg) daily for 10 days following training. The original learning was not affected by a series of daily injections given before training. They interpret the results as suggesting that the drug may retard forgetting or enhance the accessability to information in the long term memory store.

Other studies (23–25) have shown that, in rats, learning can be enhanced by a series of injections of strychnine given before training. Injections (1.0 mg/kg) given daily from age 21–52 days or 51–70 days enhance maze learning when tested several weeks later. The effect was found only in rats reared in an "enriched" laboratory environment. Strychnine appears to impair learning if given to animals reared under relatively restricted stimulus conditions or if administered to very young rats (ages 1–25 days) reared in a standard colony (23–25). The bases of these effects have not been determined.

Other convulsants: Picrotoxin, Bemegride, and Pentylenetetrazol.—Recent studies have confirmed earlier findings (7) that maze learning is enhanced by posttraining administration of low doses of picrotoxin. Although the effect has not been studied in a wide range of tasks, facilitation has been found with active avoidance tasks, as well as with mazes (26). As yet, there have been no reports of studies in which the time of posttraining administration has been varied. Posttraining injections of bemegride (β-ethyl-β-methyl glutarimide) (10 and 20 mg/kg) enhance learning of rats and mice in tasks using shock motivation (27, 28). The generality of the effects of bemegride on learning has not yet been studied.

Recent studies have also confirmed earlier findings (10) that learning is facilitated by either pre- or posttraining injections of pentylenetetrazol (PTZ). Krivanek & McGaugh (29) found that in mice, the degree of facilitation of discrimination learning (in an appetitively motivated task) produced by posttraining injections increased directly with the dose up to a dose of 20 mg/kg. With a dose of 15 mg/kg the facilitation was found only if the drug was administered within 15 minutes before or after the training session. However, in a study using rats, Hunt & Bauer (30) found that the degree of facilitation of discrimination learning varied in a somewhat more complex way. With a dose of 7.5 mg/kg greatest facilitation was obtained with immediate injections. With a slightly higher dose (10 mg/kg) greater facilitation was found with injections given 10 or 15 minutes following training. The reason for these conflicting "gradients of facilitation" is not apparent. Krivanek (31) studied the effect of posttraining administration of PTZ (2.5–25 mg/kg) on the learning, by mice, of an active avoidance (wheel turn) task. Motivational levels were varied by depriving one half of the animals of food and by using two levels of footshock. Facilitation of learning was found with each condition of motivation, but the optimal dose varied with the motivational conditions. Under some conditions, the higher drug doses impaired learning. No facilitation was found with injections given 1 hour following training. Ott & Matthies (32) found that a single injection of PTZ (20.0 mg/kg) administered to rats prior to a discrimination training task using footshock motivation facilitated learning and retarded extinction. Elliott &

Schneiderman (33) reported that, in rabbits, PTZ (25 mg/kg s.c.) enhanced the acquisition of conditioned nictitating membrane and respiration responses but did not affect heart rate conditioning. Preliminary results of studies by Bowman & Harlow (personal communication) indicate that posttraining injections of pentylenetetrazol (5, 10, or 20 mg/kg, I.M.) facilitate discrimination learning in rhesus monkeys. Learning facilitation was obtained with injections administered up to 30 minutes after training. These highly interesting results provide the first evidence of drug facilitation of learning in monkeys.

In many of the studies discussed above, drug injections were given each day shortly before or after a session of several training trials. In these studies drugs given daily did not affect learning unless the injections were administered within a few minutes or hours after the training session. Recently, however, Bauer (34) reported that, in rats, avoidance learning and discrimination learning can be enhanced by injections of PTZ (10, 20, or 30 mg/kg) given daily for 20 days prior to training. Comparable effects have been obtained with amphetamine (35). From a methodological point of view, these findings emphasize the need for varying the time of drug administration in studies of the effects of posttraining drug administration on learning. It is worth noting that the effects are similar to those obtained with strychnine sulphate in studies of the effects of repeated injections on learning (23–25) discussed above. However, other studies have indicated that discrimination learning is not enhanced by 4 daily injections of PTZ (32) or 10 daily injections of strychnine (22) administered prior to training. The basis of the effect of repeated drug administration on learning has not been studied.

In studies of learning facilitation using convulsant drugs the doses used are always subconvulsive. Most (but not all) of these drugs, as well as other convulsant drugs, produce impairment of memory (retrograde amnesia) when administered in convulsive doses (11, 36).

It is generally assumed that CNS stimulants affect learning by influencing brain activity. Several earlier studies (6) indicated that learning is enhanced by administration of strychnine and PTZ directly into the brain either before or after training. More studies of this kind are needed in order to determine whether the effects can be localized.

Amphetamine.—Numerous recent studies have confirmed earlier findings (7) that, in rodents, learning is enhanced by amphetamine (AMPT). Doses of 0.5–2.0 mg/kg facilitate learning in a variety of active avoidance tasks (37–39). Since AMPT enhances motor activity, it is important to consider whether the enhanced acquisition might be due to a direct effect of the drug on activity. Most findings indicate that AMPT administered prior to training enhances both acquisition and retention performance (40, 42). However, under some conditions performance is not enhanced on retention tests given without the drug (43–45). When given with amylobarbitone sodium (15 mg/kg) AMPT (0.75 mg/kg) enhances acquisition but not retention of an appetitively motivated discrimination task (46) suggesting that the learning under the drug mixture may either be

temporary or state dependent. Del Rio (47) found that avoidance learning as well as 1 week retention is enhanced by d-AMPT (0. 5, 1.0, or 2.0 mg/kg) given alone or with chlorpromazine (1.0 or 2.0 mg/kg) prior to training. Chlorpromazine given alone did not affect learning. Learning was impaired by mixtures of the highest doses of the two drugs. The optimal mixture for producing learning enhancement was 0.5 mg/kg AMPT and 1.0 mg/kg chlorpromazine. It is important to note that while degree of learning facilitation produced by this mixture was comparable to that produced by 1.0 mg/kg AMPT given alone, the mixture did not produce the increase in intertrial responses produced by AMPT. These findings are consistent with evidence that chlorpromazine inhibits the metabolism of AMPT and attenuates the stimulating effects of AMPT on locomotor activity (48).

Evidence from studies in which AMPT is administered shortly after training clearly indicates that learning facilitation cannot be due solely to effects on locomotor activity. Several studies have found that posttraining administration of AMPT facilitates discrimination learning in rats. The degree of facilitation varies with several conditions, including the dose, task, and age of the subjects (7, 49). Krivanek & McGaugh (50) found that, in mice, discrimination learning in an appetitively motivated task was facilitated by d-AMPT (0.5 or 2.0 mg/kg) administered either before or within 15 minutes after training. With posttraining injections the degree of facilitation increased with the dose, over the range from 0.5–2.0 mg/kg. A dose of 2.5 mg/kg was ineffective. Other studies (51, 52) indicate that, while posttraining injections of AMPT (1.0–5.0 mg/kg) facilitate maze learning during early trials, performance is subsequently impaired by repeated posttraining drug administration. The effect can be blocked by amylobarbitone. No impairing effect is produced by pretrial drug injections or by posttraining saline injections. These findings suggest that AMPT has aversive effects when repeatedly administered after training. Comparable aversive effects were obtained with PTZ but not with strychnine (52). Obviously, in studies using repeated posttraining drug administration it is important to control for possible aversive (or rewarding) effects of the drugs. As indicated above, studies using repeated drug injections must also control for possible general facilitating effects of the injections.

Other recent studies comparing the effects of pre- and posttraining administration of AMPT on avoidance learning (53, 54) indicated that a single pretraining administration of dl-amphetamine (2.0 mg/kg) facilitated acquisition but not retention tested 5 days later, whereas posttraining injections or pre- and posttraining injections of AMPT enhanced retention on tests 5 days later. Posttraining administration of AMPT has also been found to enhance learning of an inhibitory (passive) avoidance response. The retention of rats given methylamphetamine hydrochloride (5.0 mg/kg s.c.) immediately after a single training trial was enhanced on tests given from 1–7 days later (55).

In view of evidence (48) that the central actions of amphetamine require the synthesis of catecholamines, several experiments have studied the effects of AMPT on learning and retention in animals treated with drugs affecting catecholamine levels and biosynthesis. The findings of these studies are conflicting

and thus difficult to interpret. Roffman & Lal (42) found that α-methyl-p-tyrosine (α-MT) (50 mg/kg) did not block the facilitating effects of AMPT (2.0 mg/kg) on avoidance learning and retention in rats. However, Orsingher & Fulginiti (56) reported that AMPT (dl 2.0 mg/kg) impaired avoidance learning in animals treated with α-MT (30 mg/kg) and that the impairing effect was blocked by dl-DOPA (200 mg/kg). It is interesting to note, in view of evidence that training and performance affect norepinephrine metabolism (57, 58), that α-MT did not affect learning when given alone (56). However, avoidance learning is apparently impaired by diethyldithiocarbamate (DDC), a dopamine-β-hydroxylase inhibitor, at doses that decrease norepinephrine biosynthesis (59, 60). Further, l-DOPA appears to enhance learning and retention in goldfish (61). Thus, it is not clear why learning is facilitated by some beta adrenergic blocking agents, including propranolol and pronethalol (62), but impaired by dichloroisoproterenol (60). Retention is impaired by reserpine (1.5 mg/kg) administered immediately after training (60). The impairment is blocked by l-DOPA (100 mg/kg) but not by AMPT (2.0 mg/kg) or dl 5 HTP. Thus the reserpine effect is apparently not due to depletion of serotonin. Further, neither learning nor retention are impaired by p-chlorophenylalanine (PCPA) (316 mg/kg) administered 3 days before training (60, 63). Under some conditions, PCPA appears to facilitate learning (64).

On the basis of a series of recent studies, Knoll (65) has suggested that AMPT affects learning by altering levels of both norepinephrine and serotonin. Rats were injected with drugs before training on an active avoidance task. Learning was enhanced by low (1.0 or 2.0 mg/kg) doses of AMPT and impaired by higher doses (3.0–10.0 mg/kg). The impairing effect of the higher dose was blocked either by α-MT (60 mg/kg) or PCPA (100 mg/kg administered daily for 3 days prior to training). The facilitating effect of the lower doses of AMPT was blocked by α-MT. Knoll also investigated the effects of two newly synthesized amphetamines, V-111 (para-bromo-methamphetamine) and I-1703 (N_1-O-carboxyphenyl-N_2-p-/2-methyl-aminopropyl-l-/-phenylacetamidine). I-1703 enhanced learning at doses at 2.0–50 mg/kg. The effects of α-MT plus I-1703 on learning were not reported. V-111 reduced serotonin levels and enhanced learning when administered daily (15 mg/kg s.c.) for 72 days prior to training. These findings suggest that learning may be enhanced either by an elevation of catecholamine levels or a decrease in serotonin. However, in view of the conflicting evidence concerning the involvement of catecholamine levels and synthesis in the effects of AMPT on learning an evaluation of this hypothesis must await further research.

It has been reported that reserpine (1.0 mg/kg) and PCPA (200 mg/kg) attenuate the amnesic effects of ECS (66, and Boggan & Schlesinger, personal communication). However, the evidence concerning this effect is conflicting (63).

A large number of studies have found that learning is impaired by drugs such as puromycin and cycloheximide, which inhibit protein synthesis (8, 67). It has been generally assumed that the amnesia, whether permanent or temporary, (68, 69) is due to the impairment of protein synthesis. However, recent findings indicate that the amnesic effects of these drugs can be blocked by injections of

AMPT or metaraminol administered within a few hours after training (70, 71). Whether such effects are specific to drugs affecting catecholamine activity is not yet known. Thus it is premature to conclude that protein synthesis inhibitors affect memory by interfering with adrenergic mechanisms involved in memory.

Nicotine.—Most recent studies of the effect of nicotine on learning have confirmed earlier findings (72) that, in rats, nicotine facilitates acquisition in a variety of tasks. There have, however, been several failures to find facilitation of learning with nicotine (0.25–1.0 mg/kg) administered either before or after training (73, 74) on aversively motivated tasks. In view of the numerous studies reporting positive effects the reasons for these negative findings are not apparent. Battig (75) obtained facilitation of maze learning with either pre- or posttraining injections of nicotine (0.15 mg/kg). Garg & Holland found facilitation of maze learning with posttrial administration of nicotine (0.8 mg/kg) in several studies using different strains of rats (76). In a study cited above, Oliverio (18) reported that nicotine (0.5 mg/kg) as well as strychnine given either before or immediately after 25 trials in which a light was paired with a buzzer CS enhanced the effectiveness of the light when the light was subsequently used alone as the CS. Erickson (77) found that nicotine (0.1 mg/kg) enhanced avoidance conditioning when injected either before or after training. The enhancement was not state dependent; the facilitating effects were observed on tests without drug administration. Learning was not affected by the quaternary compound nicotine bismethiode. This suggests that the effects of nicotine on learning are probably due to central rather than peripheral effects of the drug. However, other evidence (54) indicates that both nicotine (0.2 mg/kg) and the quaternary compound hexamethonium (5.0 mg/kg) enhance learning when given either before or after training on an active avoidance task. Additional research is needed to clarify this issue. Orsingher & Fulginiti (56) reported that the facilitating effect of nicotine (0.2 mg/kg) on active avoidance learning is blocked by pretreatment with the α-adrenergic blocking drug dibenamine (10 mg/kg) or by α-MT (30 mg/kg), but is not blocked by the β-adrenergic blocking drug pronethalol (5.0–10.0 mg/kg).

These findings suggest that the facilitating effects of nicotine on learning may be based on adrenergic mechanisms. However, this view would seem to have difficulty handling the findings that active avoidance is not impaired by α-MT, or adrenergic blocking agents.

Cholinergic drugs.—Most, but not all (78) recent experiments have confirmed earlier evidence (7) that learning is enhanced by posttraining administration of low doses (0.25–1.5 mg/kg) of physostigmine (79, 80). Since the facilitation can be obtained with posttraining injections, the findings suggest that physostigmine potentiates cholinergic mechanisms involved in memory storage. Facilitation of inhibitory avoidance with pretraining injections of physostigmine (0.25 and 0.5 mg/kg s.c.) is attributed to an enhancement of response suppression, since these doses impair active avoidance (81). The interpretation of the facilitating effect of posttraining physostigmine is complicated by the finding (53) that

posttraining administration of atropine (2.0 or 10.0 mg/kg) also facilitates learning. This latter effect is difficult to reconcile with evidence that retention is impaired with posttraining injections of scopolamine (10.0 mg/kg) (82).

In a series of experiments, Deutsch (83) has reported that retention performance is enhanced by physostigmine or DFP if the responses are recently acquired or are almost forgotten. In general, the effects of scopolamine on retention mirror those of the anticholinesterase drugs: Scopolamine impairs retention of recently acquired responses. Deutsch interprets these findings as suggesting that learning and forgetting are based on time-dependent changes in cholinergic synapses, possibly at the postsynaptic membrane. His findings are generally consistent with their interpretation. Somewhat comparable results have been obtained in research with mice (84). However, in mice, the effects of physostigmine on retention were antagonized by methscopolamine, suggesting that the physostigmine effects may be based, in part, on peripheral actions. It is not yet known whether comparable effects can be obtained with drugs affecting adrenergic mechanisms.

Other drugs reported to facilitate learning.—Findings of recent studies of the effects of pemoline on learning and memory (85) indicate that the effects of pemoline are, in general, similar to those of amphetamine. Although there are conflicting findings (1), facilitation has been obtained in a variety of tasks and with both pre- and posttraining administration (86). Pemoline has also been found to attenuate ECS-induced amnesia (85, 87). As yet there have been no systematic investigations of the pharmacological bases of these effects.

Recent studies (88, 89) of ribaminol have failed to confirm earlier evidence (90) of learning facilitation. Recent studies of the effects of TCAP (tricyanoaminopropine) (91–93) have not confirmed earlier reports (3) of learning facilitation and attenuation of ECS-induced amnesia. Giurgea & Mouravieff-Lesuisse (94) have reported that learning is enhanced by UCB 6215 (2-pyrrolidone acetamide). The findings of Wolthius (95) suggest that this drug, which is not a central nervous system stimulant, affects learning by acting on sensory processes rather than by influencing memory storage. However, more research is needed before any firm conclusions concerning the effect of UCB 6215 can be drawn.

RNA and RNA precursors.—In a series of experiments Cook & Davidson (96) have found that avoidance learning is facilitated and extinction is retarded by chronic administration of yeast RNA. Comparable effects are not produced by a single injection of liver RNA (97). In an extensive and carefully conducted series of studies, Matthies and his coworkers (98) have reported that, in rats, repeated administration of orotic acid prior to training impairs the extinction of a learned discrimination response. Comparable effects are obtained by a single intraventricular injection of uridine-5′-monophosphate (UMP) administered shortly before or after the training session. This latter effect can be blocked by cycloheximide. Pretreatment with UMP was also found to attenuate ECS-induced retrograde amnesia. Matthies suggests that the effects are due to an enhancement

of memory storage processes, possibly by affecting protein synthesis. It should be noted, however, that similar effects are produced by pentylenetetrazol (32).

CONCLUSION

The findings of the studies reviewed in this paper indicate that in animals learning and memory can be facilitated by drugs that affect the central nervous system. The research using posttraining drug administration provides information concerning time-dependent aspects of memory storage processes. As yet, however, the research has provided little understanding of the neurobiological bases of the effects. There is evidence that drugs influence learning by affecting adrenergic mechanisms, cholinergic mechanisms, and the synthesis of RNA and protein. Unfortunately, none of these obvious possible mechanisms has as yet been ruled out. It might be that all of the stimulating effects of drugs on learning are due to nonspecific effects on brain systems involved in arousal. Or, it might be that learning and memory processes can be modulated by any changes in neuronal activity produced by centrally acting drugs. The critical pharmacological actions underlying the facilitating effects of drugs on learning are not known. More systematic and extensive use of drugs with somewhat specific mechanisms of action should provide this much-needed information.

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