inforcement. The procedure may be designated control of extinction (the condition in which reinforcement is not obtainable) by the organism.

Four subjects have given similar results, indicating that the time spent under conditions of extinction is a function of the number of responses required to produce the food reinforcement. Figure 1 shows this relationship for one subject for which the number of responses required per reinforcement was increased from 65 to 200, in daily sessions of 60 minutes each. At low ratios, only a few seconds were spent in time-out. As the ratio was raised, the subject extended the time-out condition for longer periods. At a ratio requirement of 200 responses, the subject spent about 50 percent of the experimental period in time-out. Each point in Fig. 2 is an average for 5 days, but performance was often allowed to stabilize for several weeks.

Figure 2 presents a typical segment of a cumulative response record for one subject. The pattern of responding seen here is characteristic of fixed-ratio food reinforcement: a high rate prevails prior to reinforcement (top of each segment), and a long pause follows before another rapid run begins. The self-imposed periods of time-out are shown as a downward deflection of the recording pen (dotted areas). These occur typically during the long pause preceding the run. Occasionally there is a trickle of responses (as at *A*) before the subject initiates time-out. Once responding is well under way, however, time-out is not produced again until after reinforcement. Time-out is not initiated during the pause immediately following delivery of the food. Thus, time-out is not exclusively associated with lack of responding. Rather, the subject appears to initiate time-out just before making the number of responses required by the schedule.

Why should the pigeon impose a period of extinction upon itself? Accidental contingencies can be ruled out, since responses on the time-out key could not be indirectly reinforced by food, a standard period of several seconds having been interposed between any time-out response and food reinforcement. The change in stimuli was not itself reinforcing, since the pigeon imposed extinction periods regardless of whether an increase or a decrease in illumination was associated with time-out. A plausible explanation is that performance under a schedule of positive reinforcement may at certain stages be aversive in spite of the apparent absence of aversive stimuli (*2*).

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2. This investigation was supported by a grant from the Psychiatric Training and Research Fund of the Illinois Department of Public Welfare. Invaluable assistance and advice were provided by W. C. Holz.

20 October 1960

Effect of Psychotropic Drugs on the Uptake of H^3-Norepinephrine by Tissues

Abstract. Reserpine, amphetamine, imipramine, and chlorpromazine markedly reduced the uptake of circulating H^3-norepinephrine by several tissues and elevated the plasma concentration of the H^3-catecholamine.

Many drugs affect the physiological actions of catecholamines, but little is known about their mode of action at a biochemical level. Previous work has shown that the psychotropic drugs reserpine, amphetamine, imipramine, and chlorpromazine increase the rate of disappearance of administered epinephrine and norepinephrine in the body (*1*). These observations prompted a study on the effect of these drugs on the uptake and metabolism of circulating catecholamine hormones in tissues.

Adult male cats, prepared as described previously (*2*), were given 25 μg of H^3-norepinephrine per kilogram (3.44 mc/mg) intravenously. Blood samples were taken periodically and the animals were decapitated 1 hour after the end of the injection. The heart, spleen, adrenal glands, liver, and abdominal wall muscle were immediately removed and assayed for H^3-norepinephrine and its major metabolic product H^3-normetanephrine (*2*). Drugs were given before the administration of H^3-norepinephrine as follows: Reserpine, 3 mg/kg intraperitoneally, 24 and 2 hours; amphetamine, 10 mg/kg, intravenously, 10 minutes; imipramine, 20 mg/kg, intraperitoneally, 3 hours and 1 hour; chlorpromazine, 20 mg/kg, intraperitoneally, 24 hours and 1 hour, and 5 mg/kg, intravenously, 20 minutes. Each drug was given to three cats; seven untreated cats served as controls.

The effect of psychotropic drugs on the tissue concentrations of H^3-norepinephrine is shown in Fig. 1. In those organs where the concentration of administered norepinephrine has been shown to be greatest (heart, spleen, and adrenal gland), treatment with reserpine, amphetamine, imipramine and chlorpromazine caused a profound reduction in the tissue levels of the administered hormone. The concentration of H^3-norepinephrine was reduced in the liver to a lesser extent while the catecholamine levels in the skeletal muscle were unaffected. H^3-normetanephrine concentrations were reduced by one half in heart and spleen after treatment with reserpine, amphetamine, imipramine, and chlorpromazine, but these drugs had little or no effect on the level of the metabolite in other tissues.

Previous treatment with psycho-

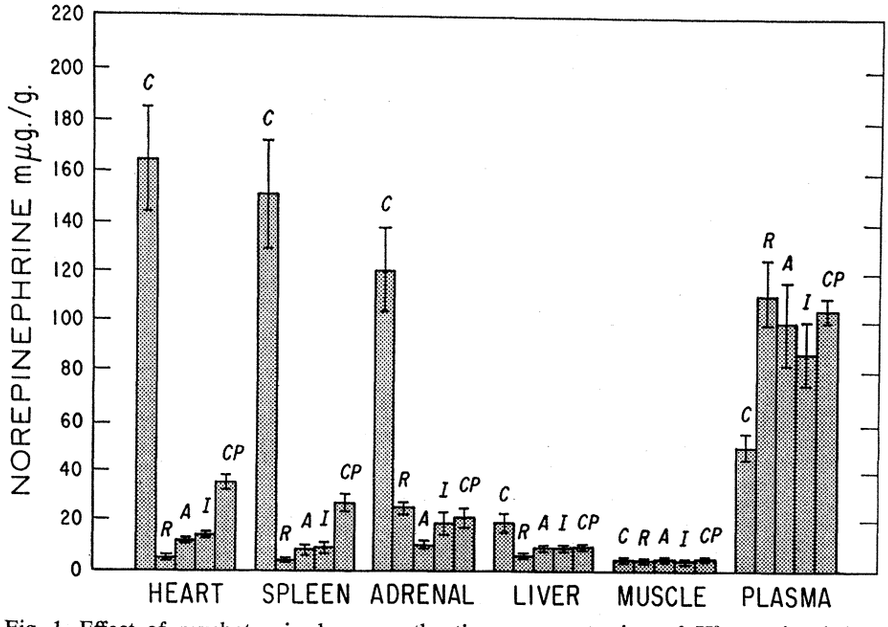

Fig. 1. Effect of psychotropic drugs on the tissue concentration of H^3-norepinephrine. The following drugs were used: reserpine (*R*), amphetamine (*A*), imipramine (*I*), chlorpromazine (*CP*), untreated animals (*C*). The vertical bracketed lines represent the standard error of the mean.

tropic drugs also resulted in a considerable elevation in the plasma levels of H^3-norepinephrine for the first 5 minutes after the injection of the hormone. Fig. 1 includes the plasma concentrations of the hormone after 2 minutes. No significant differences in the plasma concentration of the catecholamine in the control and drug-treated groups were found after 5 minutes.

Other psychotropic drugs such as sodium pentobarbital and J-B 516, a monoamine oxidase inhibitor, had no effect on the tissue and plasma concentration of norepinephrine. The monoamine oxidase inhibitor, however, raised the tissue and plasma levels of H^3-normetanephrine.

The psychotropic drugs might reduce the tissue levels of noradrenaline by speeding its passage across membranes to the site of intracellular transformation, by increasing the rate of enzymatic destruction, or by interfering with its binding. If the transfer of norepinephrine across cell membrane were to be enhanced, plasma as well as tissue concentrations of the hormone would be reduced. In connection with the second proposal, it is unlikely that these drugs act by increasing enzymatic destruction since we have found that they do not activate catechol-O-methyl transferase, the enzyme primarily concerned with the metabolism of circulating catecholamines (*3*). However, it is possible that these drugs are producing their effects of catecholamine metabolism by influencing the binding mechanism. Interference with binding would affect the uptake of circulating norepinephrine and consequently lower the tissue concentration and elevate the plasma levels of the catecholamine. We have recently shown that the uptake of circulating norepinephrine by tissues is dependent upon the intact sympathetic nerve endings (*4*). The present finding indicates that psychotropic drugs may exert their effect on the disposition of catecholamines by altering the binding sites at the nerve endings.

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21 September 1960

Evaporative Water Loss of Small Vertebrates, as Measured with an Infrared Analyzer

Abstract. Evaporation is linearly and inversely related to absolute humidity at 26° to 27°C. The relative rate of loss in desert reptiles, rodents, and anurans is about 1:10:40. The maximum rate of water loss is about 2.5 and 5 times the basal rate, respectively, in pocket mice and sand lizards. The ratio of loss from lung to loss from skin is about 84:16 in kangaroo rats and 70:30 in rattlesnakes.

Although evaporative water loss is an important item in the water balance of vertebrates, it has been difficult to measure directly under biologically meaningful conditions. Direct measurements made to date on small mammals (*1, 2*) and lizards (*3*) are of limited value because they involve exposure of the animals to dry air, an unusual biological condition. Almost all measurements on larger mammals (*4*) have been made indirectly.

The modern infrared gas analyzer provides a means of easily making accurate measurements of evaporative water loss over a complete range of ambient humidities. Prototype analyzers were used to study insensible water loss in human beings (*5*). The recent work of Decker (*6*), who used an infrared analyzer to study plant transpiration, was the stimulus for the work reported here (*7*).

In the method discussed here, animals that had been without food 12 to 24 hours were individually placed within a cylindrical glass chamber of 400-ml volume, and air of controlled humidity was drawn through the chamber and then through a Beckman 15A infrared analyzer. Air could also be drawn directly through the analyzer via a by-pass. It was thus possible to change quickly from monitoring the water content of the air leaving the chamber to monitoring the content of the air entering it.

Constant, known humidities were obtained by passing room air through drying tubes of Anhydrone, or by bubbling it through saturated potassium acetate solution, saturated sodium acetate, or distilled water, kept at 20.0° ± 0.1°C. The humidities thus obtained, for animal-chamber temperatures of 26° to 27°C, were 0.0, 3.3, 10.0, and 12.3 mg of water, respectively, per liter of air (15.6 mg/lit. = saturation).

When recording over the humidity range of 0.0 to 15.0 mg/lit., with an air flow of 423 ml/min, it was possible to measure water-vapor loss to ± 0.04 mg/min. For animals that had a rate of loss near this value, measurements were made by sealing the animal in the chamber without air flow for 15 to 30 minutes and then flushing out and recording the amount of water vapor accumulated. The responsiveness of the instrument is such that the water expired with individual breaths of slow-breathing vertebrates, such as rattlesnakes, can be recorded. Recording was continued at a particular humidity until a minimum rate of loss was maintained for 15 to 30 minutes while the animal was sleeping (mammals) or remaining quiet (others).

Some measurements were made with animals that had been deliberately excited. Other measurements were made

Table 1. Evaporative water loss of a series of small vertebrates, measured at 26° to 27°C and at four different absolute humidities (in milligrams of water per liter of air).

Species	Measurements (No.)	Wt. (g)	Av. water loss from evaporation (mg/g hr)			
			Absolute humidity			
			0.0 mg/lit.	3.3 mg/lit.	10.0 mg/lit.	12.3 mg/lit.
Mus musculus (white mouse)	6	9.0–23.9	3.92 ± 0.90*	3.61 ± 0.70	2.30 ± 0.69	1.36 ± 0.64
Dipodomys merriami (kangaroo rat)	6	30.1–37.4	1.46 ± 0.27	1.14 ± 0.21	0.94 ± 0.22	0.51 ± 0.14
Perognathus baileyi and *P. intermedius* (pocket mice)	8†	12.2–29.2	2.47 ± 1.02	2.18 ± 0.89	1.34 ± 0.43	0.95 ± 0.43
Uma notata (sand lizard)	3	15.5–16.0	0.361	0.327	0.120	
Dipsosaurus dorsalis (desert iguana)	1	32.0	0.197	0.159	0.0363	0.0329
Phrynosoma solare (horned lizard)	1	35.1	0.218			
Crotalus atrox (western diamond-back)	1	123	0.175			
Crotalus scutellatus (Mojave rattlesnake)	1	278	0.177	0.126		
Scaphiopus couchi (spadefoot toad)	1	24.4		6.07	3.40	

* One standard deviation. † Two measurements were made on *P. baileyi*, six on *P. intermedius*.