alterations in amino acid transport. However, measurement of tyrosine blood levels (*10*) in two patients following tyrosine administration showed that α-methyl-dopa did not affect the absorption of tyrosine from the intestine; in all cases the values rose to more than 5 times control levels. In other studies, it was shown that α-methyl-dopa did not influence the uptake of tyrosine by brain and muscle (*11*).

The effect of α-methyl-dopa was also reflected in a lowered excretion of 5-hydroxyindoleacetic acid and indoleacetic acid after the 5-hydroxytryptophan and tryptophan loads. The inhibitor did not influence the renal clearance of these acids. To ascertain further the effect of α-methyl-dopa on 5-hyroxytryptophan decarboxylation, the inhibitor was administered to two patients with metastatic carcinoid. A greater than fivefold increase in urinary 5-hydroxytryptophan and a decrease in urinary 5-hydroxyindoleacetic acid were observed in both cases (*12*).

Since the initial studies were carried out on hypertensive patients whose blood pressures were regularly measured, it became immediately apparent that α-methyl-dopa was a hypotensive agent. Accordingly, the blood pressure effects of α-methyl-dopa were investigated in ten hospitalized patients with primary hypertension. The lying and standing blood pressures were recorded four times daily. Placebo medication was given in pre- or posttreatment control periods, or both. α-Methyl-dopa was administered orally for periods of 7 to 28 days, initially as a single daily dose but later in divided doses at 8-hour intervals.

A summary of the blood pressure alterations produced by α-methyl-dopa is presented in Table 2. Appreciable reduction of the standing blood pressure occurred in all cases. In addition, a lowering of recumbent pressures was observed in five of the patients. In two patients (F. J. and F. N.), the postural hypotension was of such a magnitude as to necessitate reduction of dosage. For a period of 24 to 72 hours after initiating α-methyl-dopa, or after increasing its dosage, all patients had a temporary change in mental status, apparent to observers and manifested as sedation, tranquility, or fatigue. These obvious central effects seemed limited to the first 72 hours but further evaluation is required to determine whether more subtle effects may persist beyond that period.

These studies demonstrate unequivocally that aromatic amino acid decarboxylation can be inhibited in man by α-methyl-dopa, and indicate once more a relationship between amine metabolism and blood pressure regulation. The sedative effects of the drug are also in line with current thoughts concerning the role of amines in brain function. The effect of α-methyl-dopa on blood pressure has been of a sufficient magnitude to warrant extensive therapeutic evaluation of this compound and related aromatic amino acid decarboxylase inhibitors in hypertension. In fact, therapeutic trials in all disorders characterized by a relative or absolute excess of aromatic amines are indicated (*13*).

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11. We are greatly indebted to Dr. Gordon Guroff for carrying out these experiments.
12. A description of details of the latter studies is in preparation.
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Behavior in the Cold after Acclimatization

Abstract. Experimentally naive albino rats begin to press a lever for short bursts of radiant heat earlier in a 16-hour session at 2°C than rats that have been living at this temperature for about a month. This difference reflects the different rates at which body temperature in the cold falls in acclimatized and nonacclimatized animals.

If a rat's fur is clipped, and the rat is then put into a cold environment (2°C), it will almost always die within 24 hours. If, however, it has lived in the cold for at least a month before being clipped, it will probably survive (*1*). Adaptation of this kind is called acclimatization. The present experiment examines the way this physiological acclimatization is accompanied by changes in thermoregulatory behavior (*2*).

Sixteen male albino rats from Sprague-Dawley stock, about 100 days old, were each given one 16-hour trial in a heat reinforcement chamber (*3*) located in a room maintained at 2° ± 1°C. While in this chamber, the rat, by pressing a plastic lever, could get 2-second bursts of radiant heat from a 250-watt infrared lamp (red bulb) located 10 inches above the floor of the chamber. Each press of the lever gave it one such burst; presses made while the lamp was on had no effect. The animals had received no previous experimental experience.

Eight of the 16 rats (randomly chosen) lived at 2°C for from 30 to 41 days before their experimental sessions. The other eight lived at 25°C. All were housed two or three to a cage and had free access to food (Purina Lab Chow) and water. Eight hours before an animal from the acclimatized group started an experimental session it was removed from the cold room to a cage near the control animals. This was done to make conditions immediately prior to the session comparable for the two groups (*4*). The rats were clipped completely with an electric clipper about 30 minutes before a session began.

During the first half-hour in the chamber the rats obtained between 4 and 25 reinforcements; the means for the control and acclimatized groups (13.0 and 16.8, respectively) did not differ significantly ($p > .30$). Almost all of these reinforcements occurred in the first few minutes. From then on most rats responded only occasionally until they made an abrupt transition to a steady rate. These data on early responding make it unlikely that differences in the time required to achieve a steady rate were due to differences in activity.

Acclimatized rats generally waited longer than control rats before starting to work at a steady rate for heat. The individual curves in Fig. 1 are ranked in terms of these latencies. The difference in latency is significant at the .01 level by a Wilcoxon unpaired replicates test (*5*).

All eight of the normal rats, but only five of the acclimatized rats, had been responding steadily for at least an hour by the end of the 16-hour session. The mean rates for these two groups were 5.6 reinforcements per minute (S.E. = .24) for the acclimatized rats, and 6.3 reinforcements per minute (S.E. = .52) for the control rats. This difference is not significant ($p > .20$).

Carlton and Marks reported that rats exposed to cold for 10 days turn on a heating device more frequently than rats living at room temperature (*6*). As they themselves have noted, this behavior was probably due to the fact that acclimatization was so incomplete at 10 days that rats were still losing weight at that time (*7*), and weight loss

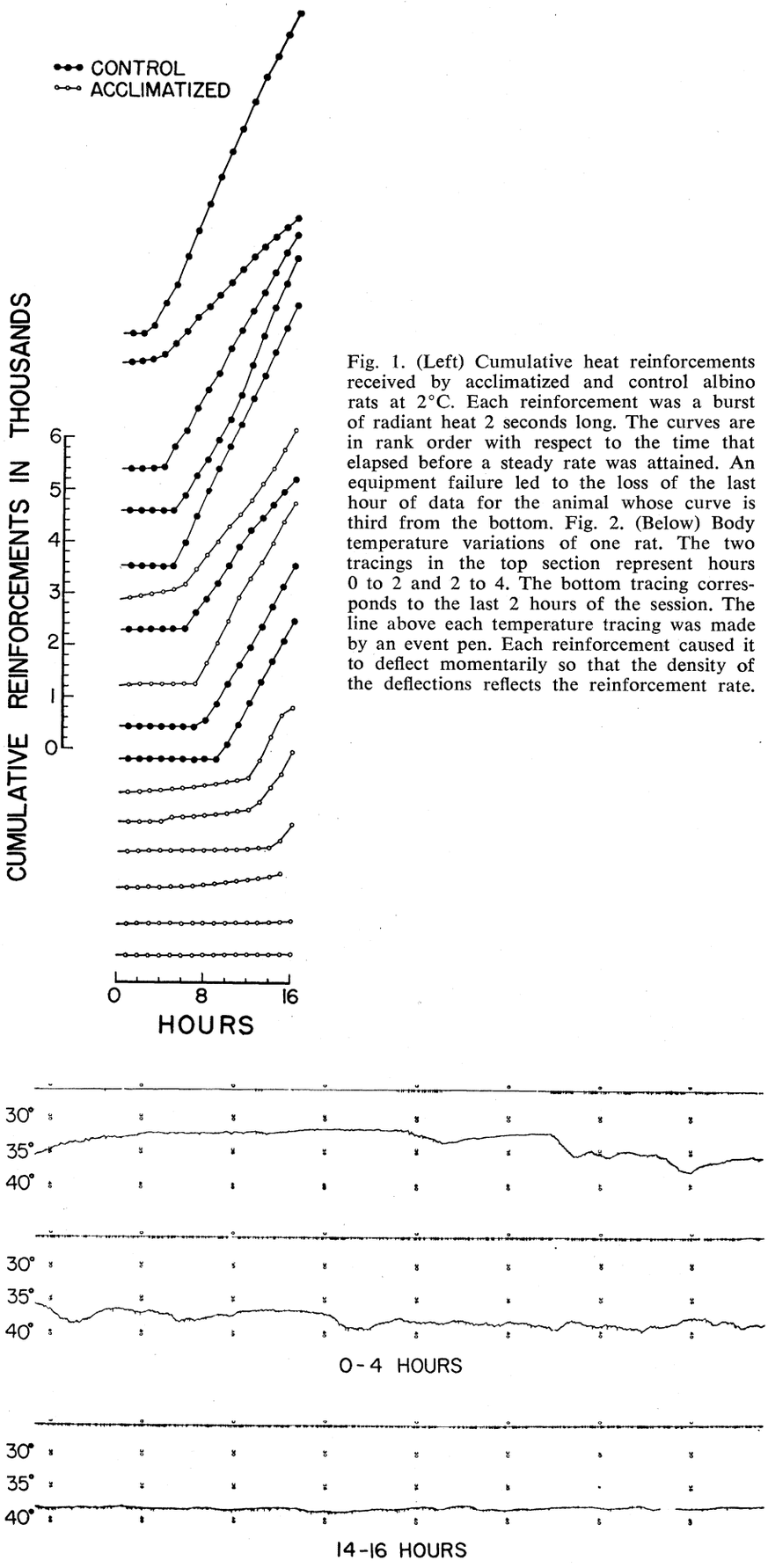

Fig. 1. (Left) Cumulative heat reinforcements received by acclimatized and control albino rats at 2°C. Each reinforcement was a burst of radiant heat 2 seconds long. The curves are in rank order with respect to the time that elapsed before a steady rate was attained. An equipment failure led to the loss of the last hour of data for the animal whose curve is third from the bottom. Fig. 2. (Below) Body temperature variations of one rat. The two tracings in the top section represent hours 0 to 2 and 2 to 4. The bottom tracing corresponds to the last 2 hours of the session. The line above each temperature tracing was made by an event pen. Each reinforcement caused it to deflect momentarily so that the density of the deflections reflects the reinforcement rate.

itself leads to higher rates of responding for heat (*8*). In the present experiment the acclimatized rats showed a significant increase in latency and an insignificant decrease in rate despite the fact that they averaged 35 grams less than the controls.

The most likely physiological basis for the difference in latency is a difference between the two groups in how quickly body temperature falls. Others have shown that during exposure to cold acclimatized rats maintain a constant body temperature much longer than nonacclimatized rats (*9*).

Evidence that body temperature and working for heat in the cold are related has been obtained by observing the subcutaneous temperature of eight other rats working for heat. Figure 2 shows the first four and last two hours from a typical record. A plastic tube was inserted under the skin of the back and tied to the supraspinous ligament. The wound was allowed several days to heal. The animal was then shaved and put into the heat reinforcement chamber for the first time, with a thermocouple inserted into the tube. There was little responding at first, only 34 reinforcements being obtained in the first 85 minutes. The rat's temperature declined from 36° to 32.5°C. It then started to respond regularly and got 5634 reinforcements during the rest of the 16-hour session, keeping its subcutaneous temperature between 35.0° and 39.5°C during this time. During the last 2 hours the temperature remained between 37.8° and 39.0°C. This is a direct demonstration of how rats adjust their behavior to maintain a fairly constant peripheral temperature.

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