One interpretation of these results would be that neurotransmission slowed more rapidly than did transmitter biosynthesis in the mice that became hypothermic, but that biosynthesis, nevertheless, was slower in their brains than in the brains of mice which had not become hypothermic.

Hypothermia is not a necessary concomitant of cold-stress when one is working with homeothermic animals; it is a complicating factor. The purpose of this report is to direct attention to this complication and to emphasize that valid inferences cannot be drawn concerning the effect of cold-stress upon neurochemistry unless complications introduced by differences in body temperature are recognized and taken into account.

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Urinary catecholamine excretion after mescaline in man*

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ONE MIGHT expect that increased sympathetic nervous activity associated with administration of psychotomimetic drugs to man would be accompanied by an increased urinary excretion of catecholamines. In a previous study, however, we found that these were little changed after LSD.[1] In view of the general similarities between LSD and mescaline, it was anticipated that the latter drug might also, have little effect on urinary catecholamine excretion. Two experiments were conducted in the present study: one comparing the effects of mescaline against a trial with placebo, the other comparing the effects of mescaline against a nontreatment trial.

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Four measurements of urinary catecholamine excretion were made. Epinephrine and norepinephrine were determined by the basic technique of Anton and Sayre.[2] Determination of 3-methoxy-4-hydroxymandelic acid (vanilmandelic acid, VMA) was made by a combination of several published procedures.[3-5] The procedure of Pisano was used for isolation of the methoxy derivatives of epinephrine and norepinephrine and their subsequent conversion to vanillin.[6] Recovery of materials added to urine varied between 76 and 86 per cent for the above techniques.

The first experiment was conducted in 12 volunteer psychiatric patients awaiting discharge from a rehabilitation ward. These men were physically active and not on any psychotropic drugs. They were kept resting and fasted during the experimental procedure. Three successive 2-hr urine collections were made, the first before drug administration and the latter two over the first 4 hr after drug, as well as a subsequent 20-hr urine to complete a 24-hr urine collection. Order of treatments was alternated, with mescaline sulfate, 6 mg/kg orally, being given on one occasion and placebo on the other; the two trials were 1 week apart.

The second experiment involved 12 nonhospitalized normal volunteers. All were healthy young men in the third or fourth decade of life, who were subjected to 2 successive days of testing, both in the resting and fasted state. During the test period on both days, they were kept under a 1000-ml water load as part of a study of antidiuretic effects of the drugs. On the first day, the control periods the experimental procedure was carried out without administration of the drug. On the second day, the procedure was exactly the same except that a dose of 5–6 mg/kg of mescaline sulfate was administered orally. Urine was collected for the first 8 hr after drug administration and pooled in one sample, and for the next 16 hr and pooled in another sample.

Results of the first experiment are summarized in Table 1. During the placebo trial, epinephrine excretion tended to increase early and decrease later. Norepinephrine excretion showed a reciprocal

TABLE 1. URINARY EXCRETION OF CATECHOLAMINES AFTER A PLACEBO TRIAL OR MESCALINE (6 mg/kg) IN 12 SUBJECTS

Treatment	Epinephrine Mean (S.D.) (ng/min)	Norepinephrine Mean (S.D.) (ng/min)	VMA Mean (S.D.) (μg/min)
Placebo			
2 hr preceding	16·6(7·6)	20·5(16·5)	4·26(1·45)
0–2 hr trial	21·4(8·0)	14·1(11·8)	3·68(1·99)
2–4 hr trial	16·3(10·4)	15·7(9·6)	3·39(1·38)
24-hr total (μg)	12·4(2·1)	31·6(21·1)	4040(1630)
Mescaline			
2 hr preceding	18·2(9·2)	17·6(11·5)	4·88(1·80)
0–2 hr trial	15·5(7·6)	10·8(9·0)	3·45(1·28)*
2–4 hr trial	8·9(6·0)*	18·0(10·8)	3·82(1·01)
24-hr total (μg)	12·5(3·1) (ng/mg creatinine)	26·9(12·7) (ng/mg creatinine)	4400(2700) (μg/mg creatinine)
Placebo			
2 hr preceding	13·0(6·3)	14·7(9·2)	3·24(1·12)
0–2 hr trial	20·2(9·4)†	12·1(9·3)	3·08(1·24)
2–4 hr trial	13·6(4·4)	13·9(7·3)	3·17(1·08)
Next 8 hr	6·6(3·3)*	22·9(11·5)*	2·74(0·51)
Mescaline			
2 hr preceding	11·7(6·0)	10·9(5·9)	3·06(0·71)
0–2 hr trial	15·4(8·3)	10·0(7·9)	3·25(0·66)
2–4 hr trial	8·1(11·4)	14·6(8·4)	3·21(0·52)
Next 18 hr	7·7(3·2)	16·9(9·6)*	3·09(0·63)

* $P < 0.01$; *t*-test correlated means, two-tail.
† $P < 0.05$.

pattern, with a slight early decrease and late rise. VMA excretion remained relatively constant. The pattern with mescaline was somewhat different from that of placebo, with a more conspicious decrease in epinephrine excretion during the 2- to 4-hr period, the time of greatest clinical effects of the drug. Once again, a late rise in norepinephrine excretion was evident, and VMA excretion

remained relatively constant. The 24-hr total excretion of epinephrine, norepinephrine and VMA was essentially similar for either the placebo or drug trials, confirming that the shifts between epinephrine and norepinephrine excretion were reciprocal.

Results of the second experiment are summarized in Table 2. Reduced excretion of epinephrine was observed during the first 5-hr period after mescaline, but not during the succeeding time periods.

TABLE 2. URINARY EXCRETION OF CATECHOLAMINES AFTER NO-DRUG TRIAL OR MESCALINE (5–6 mg/kg) IN 12 SUBJECTS

	Time after drug			
	0–8 hr		9–22hr	
Drug	Control	Test	Control	Test
Epinephrine (ng/min)	37·3(9·2)	21·1(9·9)*	11·4(8·2)	10·7(5·6)
Norepinephrine (ng/min)	21·7(8·5)	21·9(15·5)	32·8(16·7)	32·2(17·7)
VMA (μg/min)	3·0(0·7)	2·8(0·8)	2·6(0·8)	3·0(1·0)
Total metanephrines (ng/min)	397(92)	428(154)	299(137)	371(144)
Epinephrine (ng/mg creatinine)	34·5(8·5)	18·8(8·2)*	9·9(6·1)	9·9(5·8)
Norepinephrine (ng/mg creatinine)	21·1(11·4)	21·5(17·6)	30·5(15·1)	27·8(18·0)
VMA (μg/mg creatinine)	2·8(0·9)	2·6(0·6)	2·3(0·4)	2·5(0·7)
Total metanephrines (ng/mg creatinine)	371(121)	403(127)	264(94)	311(108)

* $P < 0{\cdot}01$; *t*-test correlated means.

It should be noted that in comparison to the previous experiment, epinephrine excretion rates were quite high. Quite possibly, this difference reflected the stress of the water load under which these subjects were tested. Nonetheless, the effect of mescaline in producing an early decrease in epinephrine excretion was clearly confirmed. In this experiment as in the first, a marked elevation of plasma free fatty acid levels was found, indicating increased sympathetic activity. These data have been published elsewhere.[7]

Both experiments were consistent in showing a decline in excretion of epinephrine during the 2- to 8-hr period of the action of mescaline. This decline paralleled the time course of maximum clinical action of the drug. The slight rise in total metanephrine excretion noted from mescaline in the second experiment raised the possibility of an increased catabolism of epinephrine by *O*-methylation as the cause for the lower rate of excretion.

Mescaline differed from LSD in decreasing epinephrine excretion. LSD was also tested in two experiments and found to have no appreciable effect on the excretion pattern of epinephrine, norepinephrine, metanephrines or VMA.[1] Besides an increased catabolism of epinephrine, mescaline may also have a direct or indirect effect on adrenomendullary function which is not shared by LSD.

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