

## PHYSIOLOGICAL EFFECTS OF THE AMPHETAMINES DURING EXERCISE\*

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### SUMMARY

Oxygen consumption, heart rate, minute ventilation and blood lactate were measured on two champion cyclists at work rates from 45 to 362 W (2 000 - 16 000 ft-lb/min) on a bicycle ergometer after administration of a placebo and after 10 mg of methamphetamine, without their knowledge of which was given. No differences could be detected due to the ingestion of the amphetamine in submaximum or maximum oxygen consumption, heart rate, minute ventilation or blood lactic acid. However, after the amphetamine the men were able to continue to cycle at maximum effort for a longer period and in a run to exhaustion at 90-95% maximum effort one man increased the time 61% and the other 29% with marked increases in blood lactic acid. Thus the study shows that amphetamines do not increase the men's capacity for aerobic exercise. It does, however, allow them to continue to exercise at high levels of effort for a longer period and endure a higher level of anaerobic metabolism. In short-distance events this may not be dangerous but in events lasting for more than an hour the failure to be aware of 'danger signals' and to react to them could be a threat to life as was seen in the death from 'heat-stroke' of a British champion cyclist in a 'Tour de France' some years ago.

Three of the country's best track-cyclists were suspended during the 1970 South African Championships because it was alleged that they had taken amphetamines before their events. This unfortunate occurrence raises the question of whether the amphetamines are really able to improve the performances of athletes and, if they do, whether the improvement is due to an increase in the aerobic and/or anaerobic capacity for exercise or is in the realm of the individual's psyche. There is no unanimity in the scientific literature on this subject.

Boje,<sup>1</sup> and Smith and Beecher<sup>2</sup> claim that amphetamines improve the athlete's performance, but Haldi and Wynn<sup>3</sup> and Karpovich<sup>4</sup> could find no such improvement.

There is a similar lack of agreement on the physiological effects of the amphetamines. Lehmann *et al.*<sup>5</sup> found that the amphetamines did not improve  $\dot{V}O_2$ , heart rate and cardiac output. Segers *et al.*,<sup>6</sup> however, found an increase in heart rate and oxygen consumption at rest and 98 W (600 kgf m/min) exercise, and a paradoxical increase in blood lactate at rest but not after exercise. Margaria *et al.*<sup>7</sup> in a study of 3 partially trained students could find no significant effect of 10 mg of metamphetamine on  $\dot{V}O_{2,MAX}$ , maximum heart rate, time of performance or blood lactic acid. The findings of Pirnay *et al.*<sup>8</sup> on 6 trained subjects on a treadmill were in substantial agreement with those of Margaria *et al.*, except in the run to exhaustion where the blood lactic acid levels were significantly higher after the use of amphetamines. Unfortunately, the lengths of the runs to exhaustion were not given.

In view of the disagreements in the scientific literature on this subject there appeared to be a good case for

measuring the aerobic and anaerobic capacity of two champion track-cyclists, pedalling a bicycle ergometer, at different work-loads up to their maximum. We also investigated performance times and the same physiological parameters when these cyclists were carrying out a run to exhaustion at close to their maximum oxygen intakes after an average dose of one of the more powerful amphetamines (10 mg of methamphetamine) and after a placebo without their being aware of which of the two substances they had taken. This paper is a report of our findings in this regard.

### METHODS

Both subjects were champion cyclists and they were highly motivated. They were thoroughly familiarized with the procedures and the apparatus before the main study in a preliminary test of the procedures in which a placebo and 5 mg of dextro-amphetamines by mouth were used.

Subject A started the experiment at 8.00 a.m. and subject B at 1.00 p.m. on two consecutive days. Each subject rested for 1 hour on a deckchair in an air-conditioned room before resting observations of oxygen uptake, heart rate and blood lactate were taken.

The subjects were given oral doses of 10 mg methamphetamine solution or a placebo immediately before commencing to pedal on an electronically controlled constant-work-rate bicycle ergometer. They were not told whether they had received the drug or the placebo. Subject A was given the drug on the first day and placebo on the second, whereas the order was reversed for subject B.

The men worked at a particular work-rate for 3 minutes. Oxygen uptake, heart rate and blood lactate were determined for each work-rate during the time interval 2-3 minutes. They performed work at rates of 45, 136, 181, 203 and 226 W (2 000, 6 000, 8 000, 9 000 and 10 000 ft-lb/min) continuously without any rest pauses. This was followed 10-20 minutes later by maximal or near maximal work-loads of 294, 316, and 339 W (13 000, 14 000 and 15 000 ft-lb/min) and if possible at 362 W (16 000 ft-lb/min) to determine their maximum oxygen uptakes. They were given a 20-30-minute rest pause between each work-load. After the highest work-loads that each rider could manage they rested for 20-30 minutes.

Subject A and subject B then commenced working at 90% and 95% of their maximum oxygen uptakes respectively to test for endurance times. Oxygen uptakes and heart rates were monitored every 3 minutes till exhaustion. Blood lactates were taken at the start and just before exhaustion. The time till exhaustion was the duration of the experiment until the subject could no longer maintain his rate of work.

The time after administration of the drug when observations were taken and the length of the rest pauses were approximately the same on both days of the experiment.

### Analytical Procedures

Oxygen uptakes were determined by collecting expired air into a Douglas bag via tracheal tubing and a Collins

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J valve. Duplicate samples of the expired air were used to determine  $\text{CO}_2$  content on a Beckman LB 1 infrared medical gas analyser and  $\text{O}_2$  content on two paramagnetic oxygen analysers (Beckman Model E2). The volume of expired air was measured in a chain compensated gasometer. From these measurements oxygen usage at STPD was calculated.

Heart rates were counted with an electrocardiograph.

Blood for lactate determinations was taken from the fingertip after the hand had been immersed in a water-bath at  $40^\circ\text{C}$ . Lactate concentrations were determined by the method of Barker and Summerson with modifications by Hullin and Noble.

#### RESULTS

The heights, weights and ages of the two men are given in Table I.

The test doses of the amphetamine and the placebo were given just before the subjects started to pedal the bicycle at the lowest work-load. According to Gilman and Goodman<sup>9</sup> the effects of ingested amphetamines are apparent  $\frac{1}{2}$ -hour after ingestion and persist for about 3 hours. Half

TABLE I. PHYSICAL CHARACTERISTICS

Subject	Weight (kg)	Height (cm)	Age (years)
A	74.00	179.2	21
B	70.80	172.4	19

an hour after the test doses were administered the men were pedalling at 294 W (13 000 ft-lb/min) and if there was any effect of the amphetamines it should have been apparent at that work-load and also at the higher work-loads. The maximum work-loads were achieved at between 75 and 115 minutes after the test dose was taken and the run to exhaustion at between 105 and 165 minutes after the test dose was ingested.

#### Submaximum Exercise

In Table II and Figs. 1-3 are given the  $\text{VO}_2$ , heart rates and pulmonary ventilations. Table II also includes the blood lactic acid values at submaximum work-loads after the placebo and after the amphetamine had been taken. The amphetamine effect should have been apparent at work-loads of 294 W (13 000 ft-lb/min) and above, but it is clear from these results that there is no difference in these parameters of exercise between the effects of the placebo and the amphetamine.

#### Maximum Exercise

These results are also given in Tables II and III and in the same illustrations. It is clear from these results that there is no difference between the effects of the placebo and the amphetamine on  $\text{VO}_{2\text{MAX}}$ , maximum heart rate and maximum ventilation.

There was, however, one important difference between the responses of these subjects after administration of the test doses. Both men were able to work at maximum effort for longer periods after the amphetamine and subject A completed the full period of 3 minutes of exercise at 362 W (16 000 ft-lb/min) which he could not do after the placebo. This is reflected in the high value of blood lactic acid, after amphetamine, of 16.6 mmol/litre of subject A after 3 minutes at 362 W (16 000 ft-lb/min) compared with 11.6 mmol/litre after  $1\frac{1}{2}$  minutes on the placebo. Un-

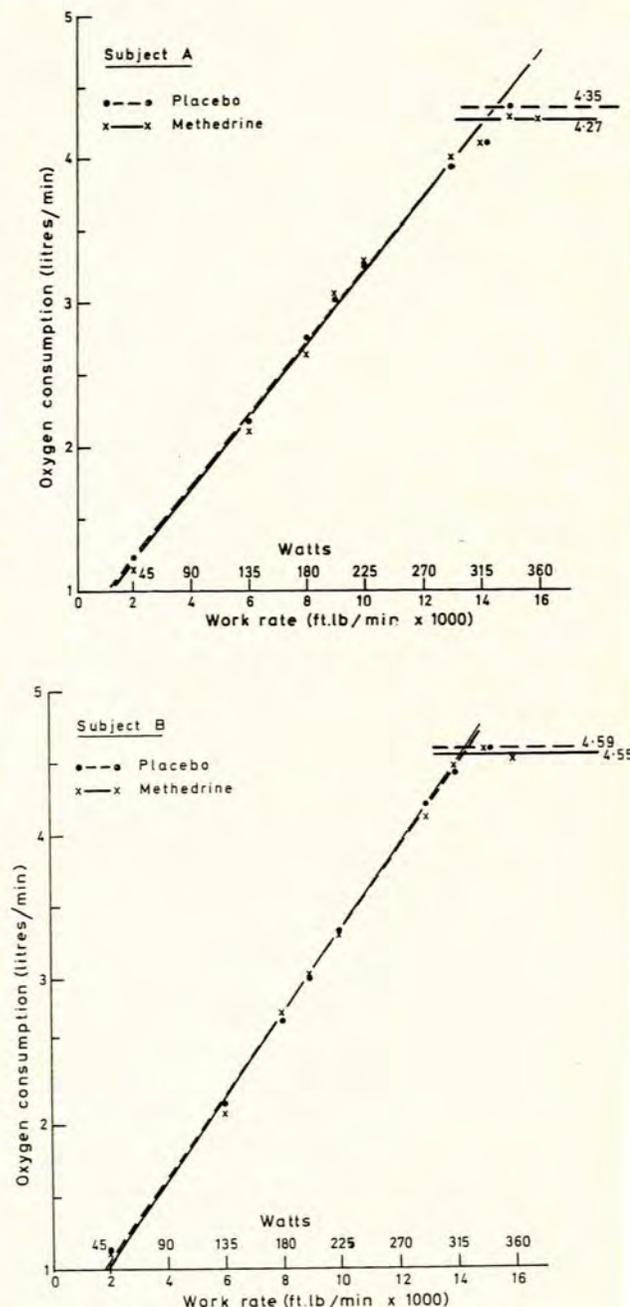


Fig. 1. The influence of amphetamine on oxygen consumption at different work rates.

fortunately, it was not possible to obtain satisfactory blood samples from subject B after maximum effort.

#### Exercise to Exhaustion at 90-95% of $\text{VO}_{2\text{MAX}}$

The results of the run to exhaustion at 90-95% maximum oxygen intake are also given in Table II. The main finding was that both men were able to pedal for longer periods after the amphetamine than after the placebo. The increase after amphetamine compared with the placebo was 61% in subject A and 29% in subject

TABLE II. ANALYSIS OF FINDINGS

Subject A	Test	Work-rate		Duration of exercise (min)	Period (min) of observation after adm. of drug/placebo	Heart rate (beats/min)	V <sub>E</sub> (litre/min)	VO <sub>2</sub> (litre/min)	Lactate (mmol/litre)		
		ft-lb/min	Watts								
Day 1: 10 mg methamphetamine given (Methedrine)	Submaximal work-loads	Rest	0			64	7.9	0.30	1.69		
		2 000	45	3	4-5	96	25.7	1.14	1.30		
		6 000	136	3	8-9	121	37.8	2.10	1.38		
		8 000	181	3	11-12	140	49.4	2.62	2.03		
		9 000	203	3	15-16	152	59.1	3.05	3.11		
		10 000	226	3	19-20	160	69.6	3.28	4.70		
		13 000	294	3	38-39	174	95.5	4.00	6.75		
		14 000	316	3	60-61	183	105.3	4.09	8.60		
		15 000	339	3	83-84	190	119.8	4.28	14.31		
		16 000	362	3	115-116	189	119.9	4.26	16.55		
	Maximal work-loads					Max.	Max.				
		90% VO <sub>2</sub> .MAX.		16' 31"		190	4.27				
		Endurance time					152-153	86.8	3.70	8.71	
							155-156	184	94.4	4.01	—
							158-159	189	101.4	4.06	—
					161-162	195	103.6	4.07	—		
Day 2: Placebo given	Submaximal work-loads	Rest	0			64	8.2	0.32	2.03		
		2 000	45	3	2-3	109	23.8	1.22	1.62		
		6 000	136	3	6-7	129	42.1	2.17	1.77		
		8 000	181	3	10-11	149	53.3	2.75	2.83		
		9 000	203	3	14-15	152	63.1	3.01	3.85		
		10 000	226	3	18-19	165	69.4	3.24	4.99		
		13 000	294	3	39-40	171	96.3	3.93	6.23		
		14 000	316	3	63-64	181	113.3	4.09	8.90		
		15 000	339	2' 34"	85-85' 34"	184	125.8	4.35	11.55		
		16 000	362	1' 35"	No observations						
	Maximal work-loads					Max.	Max.				
		90% VO <sub>2</sub> .MAX.		10' 17"		184	4.35				
		Endurance time					154-155	164	89.7	3.81	7.53
							157-158	182	102.7	4.03	—
							160-161	183	106.8	4.01	11.45

Subject B	Test	Work-rate		Duration of exercise (min)	Period (min) of observation after adm. of drug/placebo	Heart rate (beats/min)	V <sub>E</sub> (litre/min)	VO <sub>2</sub> (litre/min)	Lactate (mmol/litre)		
		ft-lb/min	Watts								
Day 1: Placebo given	Submaximal work-loads	Rest	0			68	9.3	0.36	1.93		
		2 000	45	3	2-3	98	30.1	1.13	2.14		
		6 000	136	3	6-7	128	50.5	2.13	—		
		8 000	181	3	9-10	146	58.8	2.70	3.26		
		9 000	203	3	13-14	154	74.2	2.98	3.63		
		10 000	226	3	17-18	164	75.6	3.33	4.38		
		13 000	294	3	29-30	176	116.3	4.20	7.61		
		14 000	316	3	43-44	184	131.8	4.42	12.79		
		15 000	339	3	73-74	188	139.5	4.59	16.72		
		16 000	362	2' 5"	No observations						
	Maximal work-loads					Max.	Max.				
		95% VO <sub>2</sub> .MAX.		8' 20"		188	4.59				
		Endurance time					104-105	188	130.3	4.27	15.82
							107-108	191	126.3	4.36	18.48
								76	10.2	0.36	1.93
Day 2: 10 mg methamphetamine given (Methedrine)	Submaximal work-loads	Rest	0			76	10.2	0.36	1.93		
		2 000	45	3	2-3	102	29.4	1.10	1.82		
		6 000	136	3	6-7	129	50.0	2.07	1.85		
		8 000	181	3	10-11	140	62.5	2.76	2.18		
		9 000	203	3	14-15	150	62.2	3.01	2.72		
		10 000	226	3	17-18	156	68.4	3.28	3.85		
		13 000	294	3	30-31	172	103.1	4.11	6.39		
		14 000	316	3	46-47	179	123.9	4.47	11.46		
		15 000	339	3	69-70	186	139.7	4.58	15.31		
		16 000	362	2' 40"	88-88' 40"	193	141.0	4.51	—		
	Maximal work-loads					Max.	Max.				
		95% VO <sub>2</sub> .MAX.		10' 45"		190	4.55				
		Endurance time					115-116	184	123.5	4.20	18.35
							118-119	191	133.5	4.44	—
							121-122	194	130.8	4.35	—

The heart rates, minute ventilation, VO<sub>2</sub> and blood lactic acid values in subject A were all higher at the point of exhaustion (after 16 min 21 sec) after amphetamine had been taken than at the point of exhaustion

(after 10 min 17 sec) after the placebo had been administered. The results were not so clear-cut in subject B. Only the heart rate at the point of exhaustion (after 10 min 45 sec) after the amphetamine was taken was higher

TABLE III.  $\text{VO}_2$  MAX AND MAXIMUM HEART RATE OF THE TWO SUBJECTS

Subject	Maximum oxygen usage (ml/kg/min)		Maximum heart rate (beats/min)	
	Methamphet.	Placebo	Methamphet.	Placebo
A .. ..	57.1	59.2	190	187
B .. ..	64.2	64.9	190	188
Average ..	60.6	62.1	190	186

than the value at the point of exhaustion (after 8 min 20 sec) after the placebo was ingested. This may be due to the relatively smaller difference in the time to exhaustion in subject B: 10 min 45 sec compared with 8 min 20 sec.

*Blood Lactic Acid Concentrations versus Oxygen Consumption*

Blood lactic acid concentrations are plotted against  $\text{VO}_2$  for the different work-loads for subjects A and B in Fig. 4. These figures show that the levels of  $\text{VO}_2$  at which the concentrations of lactic acid increase above control values are no different after either the placebo or the amphetamine. The increase occurs at between 50 and 54% of maximum  $\text{VO}_2$ . However, the maximum values of blood lactic acid are higher after the amphetamine because, as indicated above, subject A was able to continue to pedal the bicycle ergometer at the higher work-loads for a longer period after the amphetamine.

*Subjective Responses*

Subject A said that he felt as if he recovered quicker between work-loads on the day he was given the drug. Subject B reported no subjective sensations.

DISCUSSION

As all the important measurements were made between 75 and 165 minutes after the ingestion of the amphetamines, it is a safe assumption that these measurements were made during a period when the subjects were under the influence of the amphetamine.

*Submaximal Effort*

We were not able to detect any difference between measurements of  $\text{VO}_2$ , heart rate, minute ventilation and blood lactic acid concentration of the subjects on amphetamines as compared with the placebo at submaximum work-loads. This result is in agreement with that of Lehmann *et al.*<sup>5</sup> but is contrary to the findings of Segers *et al.*<sup>6</sup>

*Maximum Effort*

$\text{VO}_2$  MAX, maximum heart rate and maximum minute ventilation were similar after administration of both the placebo and the amphetamine. This accords with the findings of Margaria *et al.*<sup>7</sup> and of Pirnay *et al.*<sup>8</sup>

The new finding in our study is

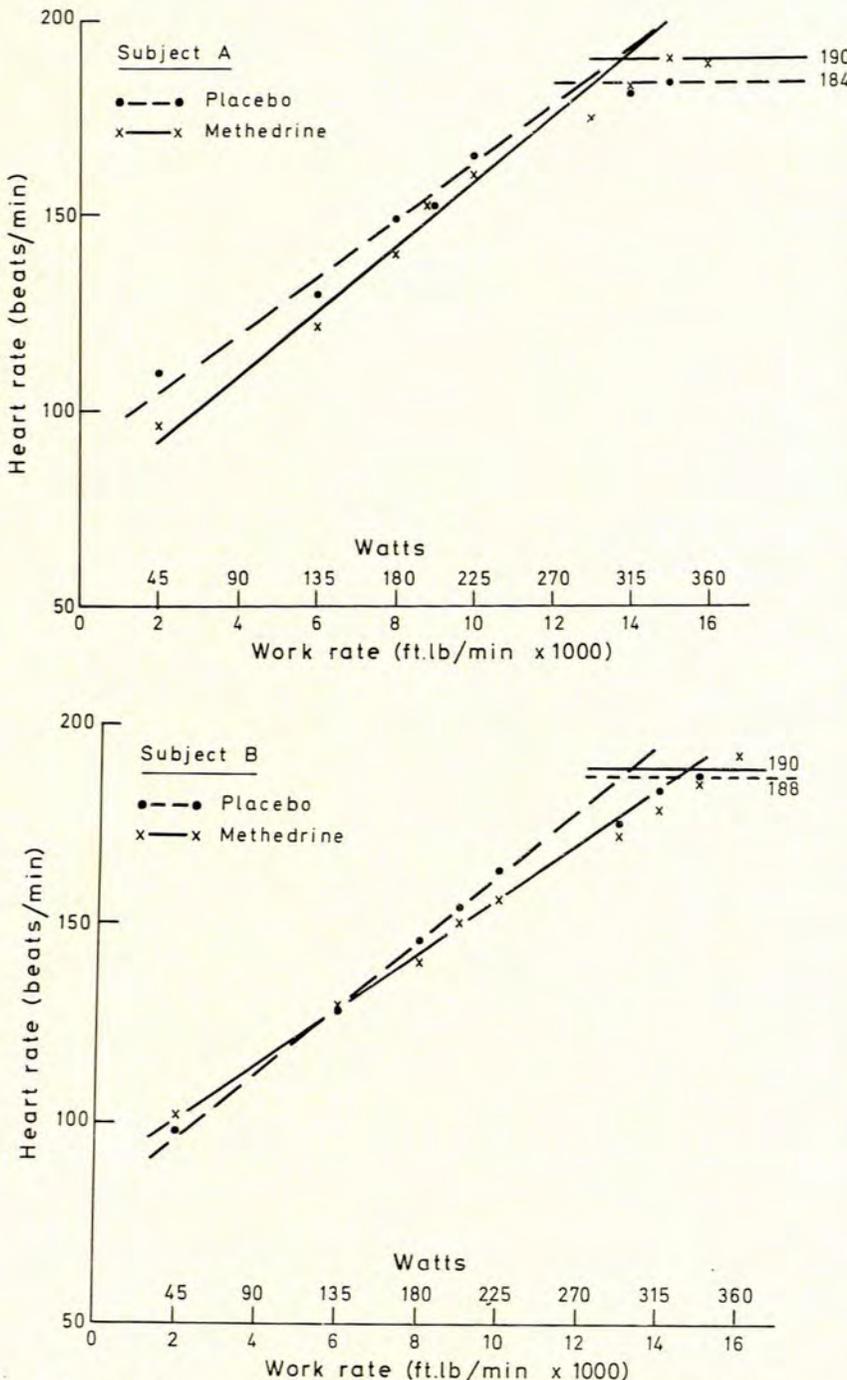


Fig. 2. The influence of amphetamine on heart rate at different work rates.

that the subjects were able to complete a longer period of pedalling the bicycle ergometer at 362 W (16 000 ft-lb/min) after taking the amphetamine, than they were able to do after taking the placebo. The greater length of time at maximum effort after ingestion of the amphetamine was reflected in a higher blood lactic acid in subject A; unfortunately, a sample of blood was not obtained after maximum effort of subject B, due, probably, to the intense vasoconstriction of fingertip blood-vessels at maximum effort.

*Run to Exhaustion at 90-95% of  $V_{O_2\text{MAX}}$*

Both the men were able to pedal the bicycle ergometer for longer periods at 90-95% of  $V_{O_2\text{MAX}}$  after ingestion of the amphetamine than after the placebo. In the case of subject A, where the increase in time to exhaustion was 6 minutes (61%) after taking the amphetamine, higher heart rates,  $V_{O_2}$ , minute ventilations and blood lactic acid values were observed compared with the placebo, but not so in subject B where the increase in time to exhaustion due to the amphetamine was only 2 minutes (29%).

Pirnay *et al.*<sup>8</sup> also found higher blood lactic acid levels after a run to exhaustion in the men given amphetamines, but, unfortunately, they did not give the lengths of time the men exercised before they reached the point of exhaustion and this information is obviously important in this regard.

*Relationship between Physiological Findings and Performance*

These studies have shown unequivocally that the ingestion of amphetamines does *not* increase the athlete's capacity for aerobic exercise. The athlete is, however, able to continue to exercise for a longer period at maximum effort and, judged by the higher blood lactic acid levels, has a greater capacity for anaerobic exercise after ingestion of amphetamine. It is this ability to increase the anaerobic capacity that, undoubtedly, results in the better performances of swimmers and runners, reported by Smith and Beecher<sup>2</sup> after the use of amphetamines.

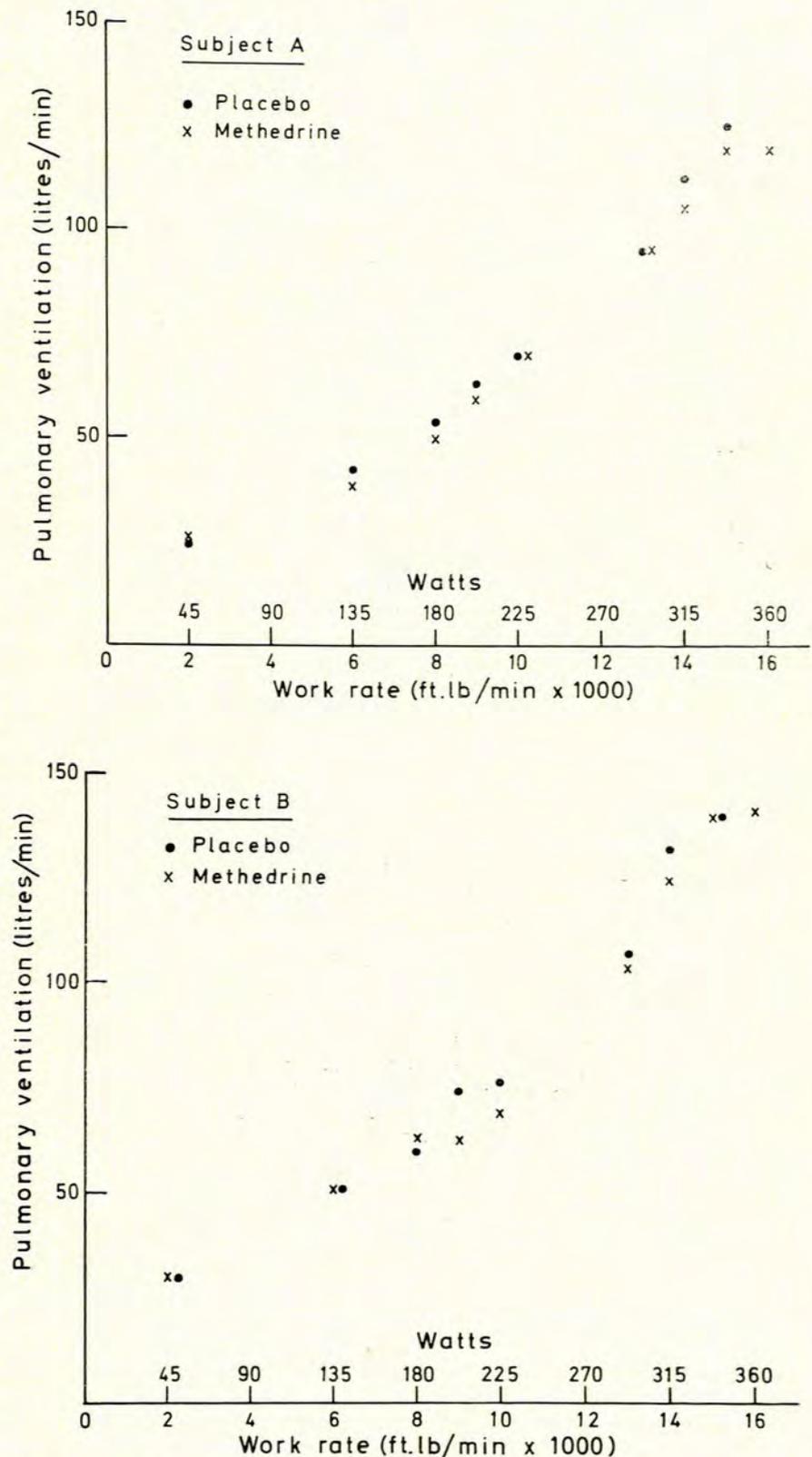


Fig. 3. The influence of amphetamine on pulmonary ventilation at different work rates.

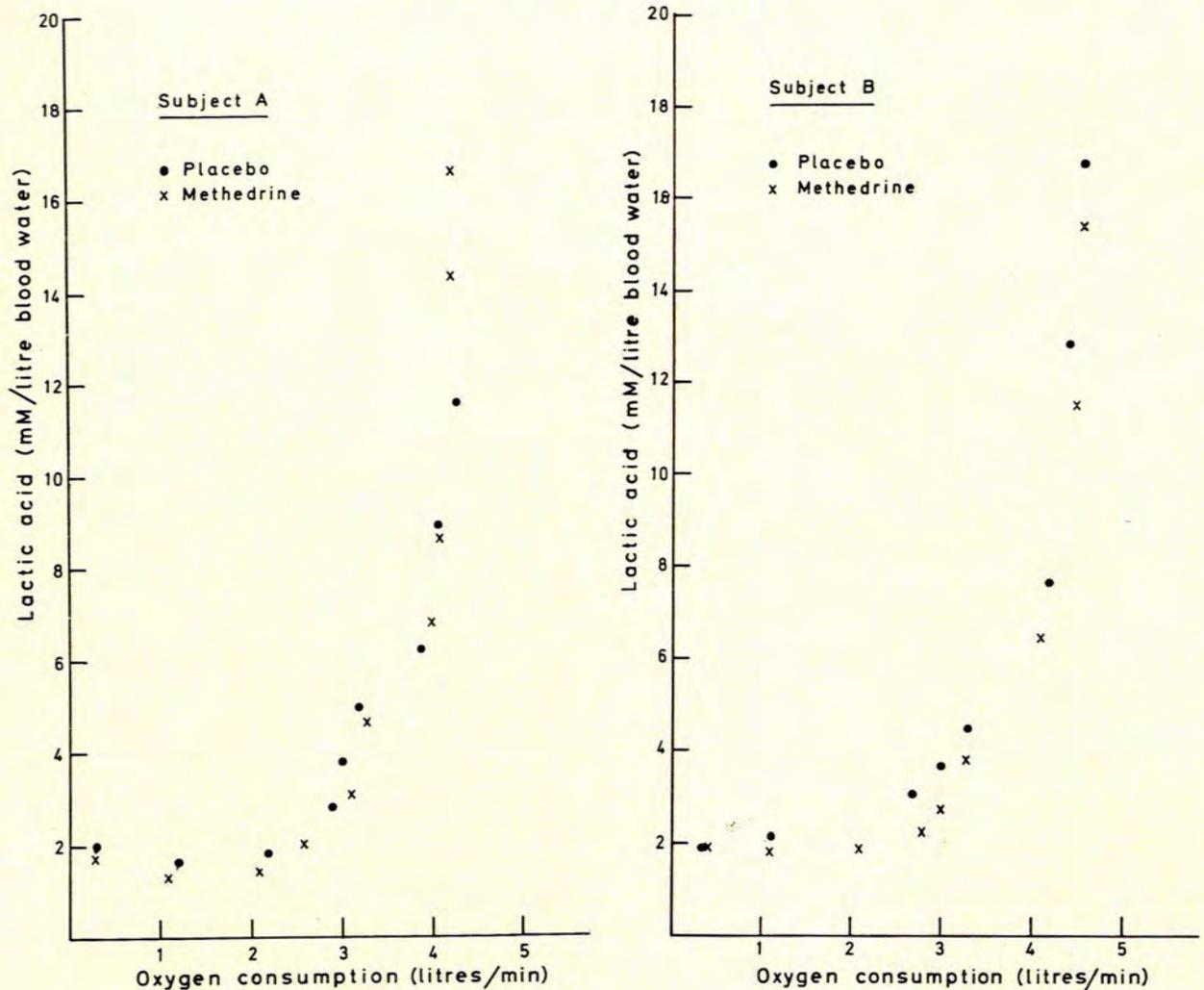


Fig. 4. The influence of amphetamine on blood lactic acid at different work loads.

Why these subjects were able to pedal the bicycle ergometer for longer periods after amphetamines, at close to maximum effort, is not clear. Whether it is a euphoria which makes the subject less conscious of the acute fatigue of maximum effort, or whether it is a change in the threshold of muscular pain which is associated with maximum effort, is not known.<sup>10</sup> While this enhanced ability to tolerate acute discomfort, and even pain, may not be dangerous in short events lasting up to an hour or so, the failure to be aware of and to react to these 'danger-signals' can be a threat to life in athletic events lasting some hours. The death from heart-stroke of a champion cyclist after taking amphetamines in the 'Tour de France' some years ago is a shocking example of this danger.<sup>1</sup>

We should like to pay tribute to the two track-cyclists for the fortitude they displayed during these arduous tests and to thank Prof. R. W. Charlton of the Department of Pharmacology of the University of the Witwatersrand for his interest and for supplying the amphetamines, and Mr C. Day of the *Rand Daily Mail* for helping to arrange these studies.

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