Circadian variation in physiological responses to exercise on a stationary bicycle ergometer

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The responses of six healthy male subjects to submaximal and maximal exercise on a stationary bicycle ergometer have been investigated over a 24-hour period. Measurements were made on each subject at approximately three-hourly intervals and they included minute ventilation at a carbon dioxide output of 1.5 l min^{-1} ($\dot{V}_{E1.5}$), tidal volume at a fixed $\dot{V}_E$ of 30 l min^{-1} (V_{T30}), oxygen intake ($\dot{V}_{O_2}$) at a work load ($\dot{W}$) of 150 W ($\dot{V}_{O_{2150}}$), tympanic temperature (T_{ty}) and cardiac frequency at a $\dot{V}_{O_2}$ of 1.5 l min^{-1} ($f_{H1.5}$). The experiments were conducted in three parts: on the first occasion two subjects were measured during exercise; on the second occasion a further four subjects were observed in a similar way but starting from a baseline of zero load, and the measurements also included an estimate of cardiac output ($\dot{Q}$) using a rebreathing technique. Finally the maximum aerobic power output ($\dot{V}_{O_{2max}}$) was measured in three of the subjects in early morning and late evening. Diet and habitual physical activity were held constant between the exercise test on all three occasions.

The results show that in the first two subjects $f_{H1.5}$ and T_{ty} had a rhythmic pattern of variation with time of day whereas $\dot{V}_{E1.5}$, V_{T30} , and $\dot{V}_{O_{2150}}$ remained fairly constant. The variation in $f_{H1.5}$ was associated with T_{ty} ; the two variables reached a minimum at $\sim 0500 \text{ hr}$ and a maximum at $\sim 1200 \text{ hr}$. These results were confirmed on the remaining subjects but the changes in $f_{H1.5}$ and T_{ty} were shown to be more variable and reduced in magnitude. Further, if the changes were calculated from a baseline of zero load, it was shown that the absolute changes observed in $f_{H1.5}$ and T_{ty} were not due to the exercise per se but to changes in the basal level from which each subject operated. In addition it was shown that $\dot{V}_{O_{2max}}$ and $\dot{Q}$ remained constant and were independent of the time of day.

It is concluded that provided the exercise test conditions are rigidly standardized and subjects exercise from a controlled baseline there is no evidence for circadian variation in the change of responses to work at submaximal or maximal effort.

There is a growing volume of literature on the effects of circadian rhythms on the physiological performance of man at rest, during sleep, and while engaged in various physical activities (see Kleitman (1949) and Mills (1966) for general review) but to our knowledge no comprehensive study has been undertaken of the effects of time of day on physical work output and exercise tolerance. Many authors have noted changes of body temperature and cardiac frequency at rest (Conroy and Mills, 1970) and have presented data on athletic performance at two or

more different times during the day (Conroy and O'Brien, 1973; Wahlberg and Åstrand, 1973) but no detailed study of the responses to submaximal and maximal exercise throughout a 24-hour period has been attempted.

In the present investigation six healthy male subjects have been studied during work on a stationary bicycle ergometer at three-hourly intervals throughout a day and the following night. A preliminary report on the first two subjects measured has already been given (Crockford and Davies, 1969).

Material and methods

The six subjects were required to attend the laboratory at 0800 am in the postabsorptive state. Their physical characteristics are given in Table 1. The experiments were

TABLE 1
PHYSICAL CHARACTERISTICS OF THE SIX SUBJECTS

Subject	Age (yr)	Height (m)	Weight (kg)
GWC	35	1.74	74.5
CTMD	35	1.78	73.9
SR	21	1.64	62.0
AL	32	1.73	75.4
MP	30	1.80	81.0
MB	32	1.77	69.0
Mean	30.8	1.74	72.6
±SD	±5.2	±5.4	±6.5

conducted in three parts. On the first occasion two subjects (GWC and CTMD) were studied during submaximal exercise at regular intervals over a 27-hour period. On the second occasion the remaining four subjects were similarly studied, and on the final occasion the maximal aerobic power of three of the subjects were measured at 0800 hr in the morning and 1800 hr in the evening of the same day. Throughout each experimental period attempts were made rigidly to standardize the diet and physical activity of each subject. The following routine was carried out: the subjects were measured sequentially on the bicycle ergometer. A standard progressive submaximal test was given to each subject at three-hourly intervals in which the work load was raised every 5 minutes. At least five work loads were performed, the aim being to span the whole range of the subjects' submaximal work capacity. In the first pair of subjects exercise was started at 50 W but in the last four subjects, who were studied on a separate occasion, a baseline of zero load was used. This enabled changes in exercise performance to be calculated (Davies and Crockford, 1971; Whipp and Wasserman, 1972). On finishing the bicycle test, the subject was allowed to eat a measured portion from a standard diet which was prepared in advance. The diet was so arranged that the food was equivalent to a 24-hour energy intake of 11 220 kJ, and each intake after exercise was equivalent to ~1420 kJ. The food contained 65% carbohydrate, 20% fat, and 15% protein, and care was taken to offer the subject as much variety as possible in small portions. A fluid intake of 25 ml, which if not water was accounted for in the calorie balance, was allowed. Following the exercise the subjects were allowed to rest or read or listen to the radio and to take light exercise (walk around, play table tennis, etc). The light exercise periods were not allowed to exceed 30 minutes of the total time between each definite bicycle ergometer test. Immediately before the beginning of the exercise test the subject voided his bladder.

During exercise oxygen intake ($\dot{V}O_2$) and pulmonary ventilation ($\dot{V}_E$) were measured using a standard open circuit technique (Davies and Shirling, 1967), and body core temperature (T_{ty}) was monitored from a thermistor placed close to the tympanic membrane. The thermistor was heavily insulated from the outside environment and was kept in situ throughout the 24 hours of the experiment. Cardiac frequency (f_H) was measured using a differential electrocardiograph amplifier and instantaneous ratemeter, and cardiac output was estimated in four of the six subjects using a CO_2 rebreathing technique (Jones *et al.*, 1967). In the event of an unsuccessful plateau $PvCO_2$ was estimated by extrapolation. No correction was made for the downstream phenomenon, arterialized blood P_{CO_2} was not taken, and cardiac output ($\dot{Q}$) was computed using a program devised by Godfrey (1970) assuming a normal dead space for each subject. Further details and discussion of the limitations of the method for measuring $\dot{Q}$ are given by Godfrey and Davies (1970) and Godfrey *et al.* (1971).

Maximal aerobic power ($\dot{V}O_{2\text{ MAX}}$) was measured using a continuous exercise test in which the subject started at approximately 90% of his maximal work level predicted from his previous submaximal responses. The criteria for maximal performance were that $\dot{V}O_2$ showed no further increase with increasing work load ($\dot{W}$) and plateau values of $\dot{V}O_2$ agreed within $\pm 5\%$ (Davies, 1968).

Results

The results collected on the first pair of subjects (GWC and CTMD) showed that $f_{H1.5}$ and T_{ty} varied with the time of day whereas $\dot{V}O_2$ at a fixed rate of work, $\dot{V}_{E1.5}$, and V_{T30} remained fairly constant. The variations in $f_{H1.5}$ and T_{ty} were associated ($r = +0.47$, $p < 0.001$); both variables reached a minimum at 05.00 hr followed by a gradual rise throughout the morning to reach a maximum between 14.00 and 18.00 hr. The rise in T_{ty} and in $f_{H1.5}$ was of the order 0.8°C and 14 beats min^{-1} respectively. These results were confirmed by observations on the remaining subjects during phase 2 of the study but the change in T_{ty} and $f_{H1.5}$ was shown to be more variable and reduced in magnitude (Fig. 1). In subject AL, T_{ty} rose sharply in the morning, reaching a maximum at 12.00 hr, remained fairly constant during the day, and then fell sharply in the night, whereas the T_{ty} in SR, MB and MP varied more rhythmically. In these three subjects, a T_{ty} minimum was reached at 05.00 hr and a maximum between 15.00 hr and 17.00 hr. The inter-subject variability of $f_{H1.5}$ was less than for T_{ty} ; $f_{H1.5}$ rose in the morning and fell during the night, but in contrast to the results on CTMD and GWC no well-defined maximum was observed (Fig. 1). The mean differences between day and night time $f_{H1.5}$ and T_{ty} values for the six subjects were 0.76°C and 7 beats min^{-1} respectively.

The results shown in Fig. 1 indicate the absolute changes of $f_{H1.5}$ and T_{ty} during exercise with time of day but from these data it is not possible to ascer-

FIG. 1. Absolute changes in f_H 1.5 , T_{ty} , and $\dot{V}O_{2\ 150}$ with time of day. Individual and mean (---) values for six subjects. T_{ty} represents the aural temperature recorded at the end of 20 minutes' continuous submaximal test. They may not be taken as representative steady state values of T_{ty} which usually require 45 minutes of exercise to establish due to the high thermal capacity of the body at the onset of work.

tain whether they reflect a genuine circadian variation in submaximal exercise performance or whether they are merely a consequence of a change in the physiological baseline from which each subject was

FIG. 2. Changes in exercise tympanic temperature (ΔT_{ty}), cardiac frequency at given $\dot{V}O_2$ of $1.5\ l\ min^{-1}$ (Δf_H), minute ventilation at given $\dot{V}O_2$ of $1.5\ l\ min^{-1}$ ($\Delta \dot{V}_E$), and oxygen intake at given workload of $150\ W$ ($\Delta \dot{V}O_2$) measured from a baseline of zero load and cardiac output at given $\dot{V}O_2$ of $1.5\ l\ min^{-1}$. Mean $\pm$ SD data for four subjects. The bars at the bottom of the figure indicate the mean $\pm$ SD of the times during which the measurements were taken.

operating. In subjects CTMD and GWC it was not possible to answer this question since the first workload performed by each subject was $50\ W$ but in the second series of experiments on four subjects the measurements were repeated from a baseline of

TABLE 2
RESPONSES TO MAXIMAL EXERCISE MEASURED IN THREE
SUBJECTS AT 0800 HR AND 1800 HR ON THE SAME DAY

Subject	0800 hours			1800 hours		
	$\dot{V}E_{max}$ ($l\ min^{-1}$)	$\dot{V}O_{2\ max}$ ($l\ min^{-1}$)	$f_{H\ max}$ (beats min^{-1})	$\dot{V}E_{max}$ ($l\ min^{-1}$)	$\dot{V}O_{2\ max}$ ($l\ min^{-1}$)	$f_{H\ max}$ (beats min^{-1})
MB	166.48	4.58	174	155.39	4.36	179
AL	145.01	3.71	184	150.62	3.75	180
SR	130.34	3.14	188	106.78	2.90	188
Mean	144.27	3.81	182	137.60	3.67	182
SD	± 18.18	± 0.73	± 7	± 26.79	± 0.73	± 5

pedalling against zero load. In addition, cardiac output, and at a later stage in three of the subjects, maximal aerobic power were measured. The data for submaximal exercise are shown in Figure 2. It will be seen that $\Delta\dot{V}O_2$ for given $\dot{W}$ and $\dot{V}_E$ remain unchanged throughout the period of the study. Calculating the results from a baseline of zero load also obliterates the variation in T_{ty} previously observed and markedly reduces the rise in f_H . Cardiac output for a given $\dot{V}O_2$ remains constant during the 24 hours of the experiment.

Maximal performance

The responses to maximal exercise measured in the early morning and late evening are shown in Table 2.

The mean maximal cardiac frequencies were identical during the two periods of the day; $\dot{V}O_{2\max}$ and $\dot{V}_{E\max}$ were 0.14 l min^{-1} and 6.7 l min^{-1} lower during the evening but none of these differences was statistically significant.

Discussion

The initial experiments on two healthy male subjects (CTMD and GWC) were designed to evaluate the responses to submaximal exercise in relation to time of day, with diet and habitual activity held constant. They were repeated on a further four subjects during phase 2 of the investigation. The results show that both the circulatory and thermal responses to work vary with time of day during a 27-hour period but the periodicity and magnitude of the changes vary for each subject (Fig. 1). This gave rise to a large intersubject variability for both $f_{H1.5}$ and T_{ty} . The average cardiac frequency and tympanic temperature were 7 beats min^{-1} and 0.76°C higher in the day than the night. These changes were observed against a background of metabolic constancy (Fig. 1): $\dot{V}O_{2150}$, $\dot{V}_{E1.5}$, and $\dot{V}_{T30}$ remained constant throughout the investigations and were independent of the time of day. These results agree closely with the observations of Klein, Wegman, and Brüner (1968) and the recent report of Wahlberg and Åstrand (1973). The latter authors found an unchanging aerobic cost of work but a significant ($P < 0.05$) increase in f_H of 4 beats min^{-1} at 100 W (approximately equivalent to a $\dot{V}O_2$ of 1.5 l min^{-1}) during the day (15.00 hr) compared with the night (03.00 hr) time. However, these changes are small and in our experiments no account was taken of the possible confounding influence of change in basal level from which each subject was operating during exercise. In addition, though the changes in f_H at a given $\dot{V}O_2$ gave rise to a change in predicted maximal aerobic power ($\dot{V}O_{2\max}$), no direct measurements of this latter parameter were made in our investigation, and it is unclear whether the changes in f_H would be reflected in comparable changes of $\dot{Q}$. Therefore in

the second series of experiments, we repeated the exercise studies from a baseline of constant pedalling against zero load and included measurements of $\dot{Q}$ using a rebreathing technique. In the final experiments we made direct measurements of $\dot{V}O_{2\max}$ in three of these four subjects in the early morning and late evening. The data from these experiments show that $\dot{Q}$ at a given $\dot{V}O_2$, and $\dot{V}O_{2\max}$ remained constant (cf Wahlberg and Åstrand, 1973) and are independent of the time of day (Fig. 2; Table 2). Further, calculating the f_H and T_{ty} data from a baseline of zero load obliterates variations in circulatory and thermal responses previously observed (Fig. 1).

These results taken together are important and, contrary to our previous expectation (Crockford and Davies, 1969), suggest that provided conditions are standardized, measurements taken from fixed baseline exercise performance remain the same throughout a given 24-hour period. The observed changes in absolute f_H and T_{ty} must be due to some underlying basal circadian rhythm and not to the response to exercise *per se*. What therefore is the nature of this underlying rhythm which affected our earlier results? The answer may lie in our observations of $\dot{V}O_{2150}$, $\dot{Q}$, and $\dot{V}O_{2\max}$ in the first two and third stages of our study respectively. It will be noted that these three variables remain constant irrespective of whether they are calculated in absolute or relative (Δ) terms. This is in contrast to what has been found for subjects who have been allowed to sleep during the night (Conroy and Mills, 1970). Under these conditions $\dot{V}O_2$ shows a marked fall during the somnambulant periods. The constancy of $\dot{Q}$ and the absolute changes in f_H imply mathematically (but not necessarily biologically) a small rhythmic change in basal cardiac stroke volume with time of day, which in turn (again by implication from our first series of experiments) must be associated with changes in T_{ty} . Provided posture and the effective muscle mass performing the work remain fairly constant, as in the present experiments which involved upright two-leg work on a bicycle ergometer, there is some common agreement (Bevegård and Shepherd, 1967) that a change in stroke volume usually implies a displacement of blood to the periphery, possibly to subserve the requirements of thermoregulation. Indeed, Kaneko, Zechman, and Smith (1968) have shown that rhythmic changes in peripheral blood flow do occur. They observed that arm blood flow measured by venous occlusion plethysmography reaches a maximum in the later afternoon or early evening which corresponds with our circulatory observations. Thus one is led to the conclusion that the changes in f_H we originally observed must be thermogenic and not metabolic in origin.

A change in T_{ty} can only result from an increase in the dissipation or conservation of body heat. Several

authors (Mills, 1966) have noted a rhythmic change in skin temperature (T_s), the curve relating to time of day being the mirror image of that found to T_{ty} . In a previous study (Crockford, Davies, and Weiner, 1970) we also noted a rise in T_s during the night but a maximum in the T_{ty} at sweat onset during the day. Taken together all these data and those of the present investigation suggest that variations in heat loss mechanisms, particularly the interaction between skin, blood flow, and sweat onset, may be more important than heat production in regulating the rhythmic basal changes in observed f_H and T_{ty} . In exercise these factors will be operative, but our data merely indicate that they will give rise to changes of absolute f_H and T_{ty} of the same order as those seen during baseline exercise during which no external work is performed. Thus in practical terms, particularly with reference to circadian variation of performance, they will have little bearing. Aerobic power output and physiological response to a given change in work output during exercise on a stationary bicycle ergometer remain constant and independent of the time of day.

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