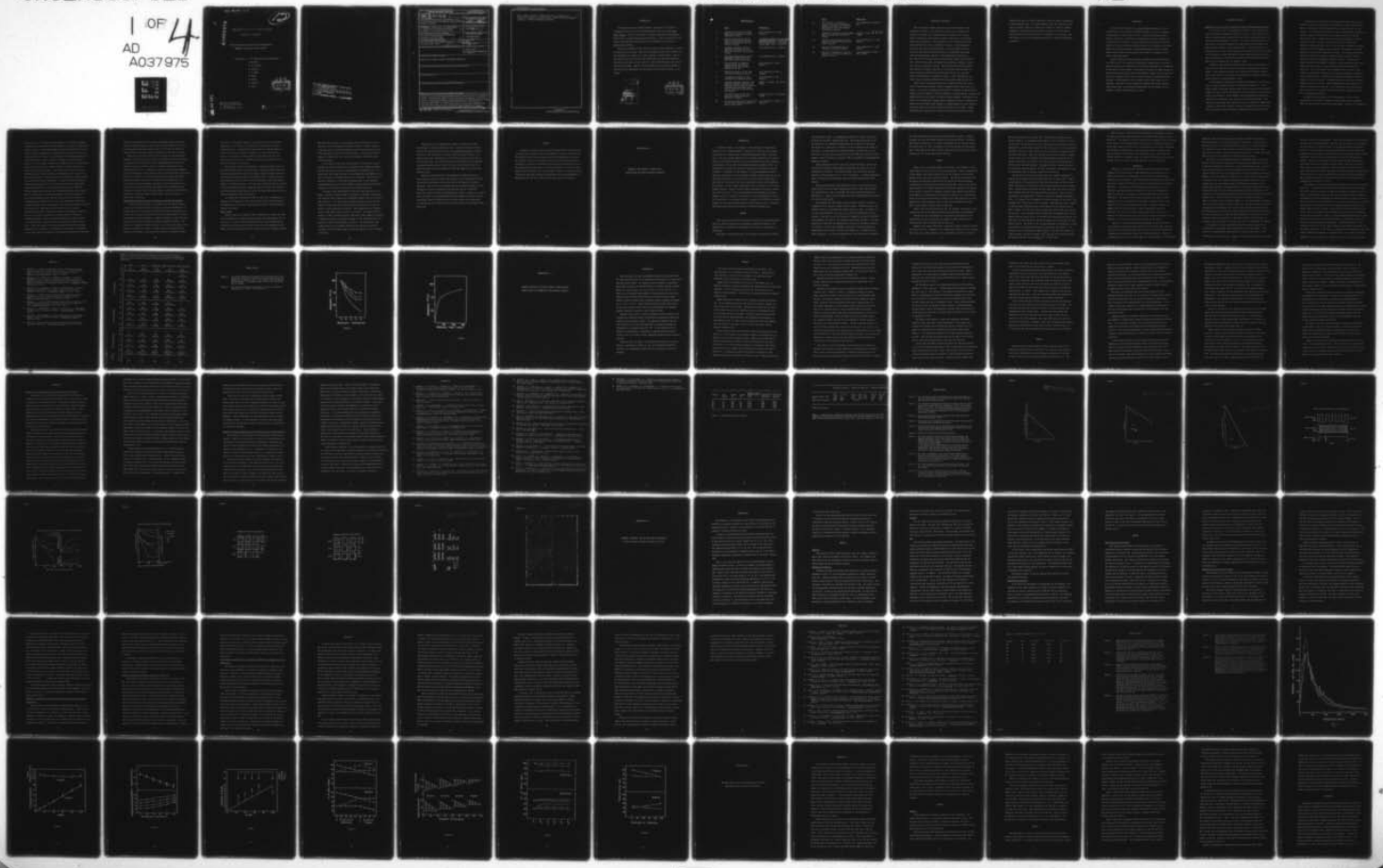
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FINAL REPORT ON A. F. O. S. R. GRANT 72 - 2362

(June 1972 - July 1976)

THE INVESTIGATION OF METABOLIC AND CARDIOVASCULAR RESPONSES TO FATIGUING STATIC EFFORT

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The research reported covers several approaches to the problem of isometric fatigue based on the working hypothesis that muscular fatigue is metabolic in nature. Obtained data support several important conclusions--at tensions of 70 percent maximum voluntary contraction fatigue is metabolic while at lower tensions some degree of transmission failure occurs, the integrated electromyogram per se is not a good measure of muscular fatigue but the frequency of the power spectrum may be; fatigue induced by isometric contractions is peripheral and does not involve central nervous fatigue.

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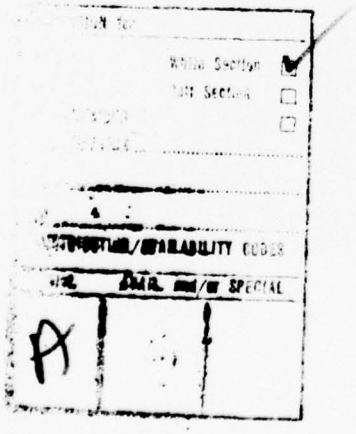
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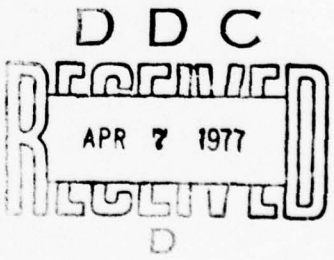
Other studies reported striking alterations in endurance in different circumstances and alterations of some of the physiological responses. Further elucidation is needed.

INTRODUCTION

The enclosed series of reports provide a description of research investigations carried out in this laboratory under the aegis of Air Force Grant 72-2362. There are 15 reports of separate experimental investigations either wholly or partly supported under the grant. Some of these reports have already been published and the others will be published in a variety of physiological journals.

The list of studies and the journals in which we have published, or intend to publish, is given below. They are not presented in the order in which they were performed, but rather in a sequence related to subject matter. This is artificial in the sense that all the reports deal with the theme embodied in the title of the grant, so that there is a clear link between any one investigation and any other. However, for the purposes of the narrative summary of our results, the presentation of the material in the present sequence is convenient.





INVESTIGATIONS

	Title	Publication
1.	Metabolic constituents of human muscle after fatigue and during subsequent recovery.	to be submitted to J. Appl. Physiol.
2.	Glycogen depletion in specific types of human skeletal muscle fibers in intermittent and continuous exercise.	in Metabolic Adaption to Prolonged Physical Exercise, H. Howard and J.R. Poortmans (Ed.), Birkhauser Verlag Basel, 1965. p. 402-415.
3.	Strength, endurance, and the amplitude and frequency of the EMG during isometric contractions in man.	to be submitted to J. Physiol.
4.	The relationship between electromyographic activity and local blood flow during contractions.	to be submitted to J. Physiol.
5.	The development of isometric tension during asynchronous stimulation of fast and slow muscles in the cat.	to be submitted to Amer. J. Physiol.
6.	Isometric endurance in fast and slow twitch muscles in the cat.	to be submitted to Amer. J. Physiol.
7.	A computerized method for the stimulation of mammalian muscle.	to be submitted to Amer. J. Physiol.
8.	Isometric strength, endurance, and the blood pressure and heart rate responses during isometric exercise in healthy men and women, with special reference to age and body fat content.	Europ. J. Physiol. 360, 49-61, (1975)
9.	Insulative power of body fat on deep muscle temperatures and isometric endurance.	J. Appl. Physiol. 39, 639-642, (1975).
10.	The effect of deep muscle temperature on the cardiovascular responses of man to static effort.	to be submitted to Europ. J. Physiol.

	Title	Publication
11.	The influence of posture on isometric strength and endurance, forearm blood flow, and the blood pressure and heart rate response to isometric exercise.	to be submitted to Aerospace Med.
12.	Respiratory responses to simultaneous static and rhythmic exercises in humans.	Clinical Science, ~~40~~ 49, 427-432, (1975)
13.	Cardiovascular responses to acute exposure to 2900 m during rest and static exercise.	to be submitted to J. Appl. Physiol.
14.	The effect of handgrip span on isometric exercise performance.	to be submitted to J. Appl. Physiol.
15.	The lack of influence of reactive hyperemia on exhausting rhythmic or static exercise.	to be submitted to Europ. J. Appl. Physiol.

RELEVANCE OF RESEARCH

One of the major problems which faces Air Force personnel is the development of fatigue. The problem of fatigue and its attendant reduction of efficiency were recognized early and gave rise to a great deal of mission-oriented personnel research, particularly in the United States and Great Britain. The main impetus in this research field came during World War II and has continued ever since. In considering the problem in the light of the Armed Forces, a greater amount of the research has been directed towards the field of experimental psychology than towards physiology, and most of the physiological studies have been aimed at the fatigue induced by prolonged and usually heavy physical work. That work has almost invariably been rhythmic or dynamic in character, such as in walking or cycling. Much less attention has been paid to the influence of isometric exercise or to the effects this may have, not only on muscular coordination and efficiency, but also as a possible source of contribution of psychomotor fatigue. These considerations can raise a host of possible difficulties for both ground staff and air crew.

Static effort is notoriously the kind of muscular effort which gives rise to early muscular fatigue, which is cumulative and is also slow in recovery. It is easy to envisage the difficulties raised for the ground staff--those men who are engaged in lifting, handling or carrying parcels, packages, machinery parts or other objects can become quickly fatigued. Even with the arm held in the perpendicular, holding objects weighing as little as 20 pounds can induce muscular fatigue, while holding or carrying objects in other arm positions will reduce the critical weight which gives rise to fatigue. Repair and maintenance personnel will encounter many situations likely to induce

fatigue while most of a pilot's activity is static in nature, exacerbated by gravitational loads. It is worth observing that the conditions giving rise to muscular fatigue are likely to be greatest at times of military emergencies, when the pace of work and its duration will inevitably be prolonged and, as in the early days of a campaign in new territory, when the emphasis will be on the energetic operation of supply and maintenance procedures.

BACKGROUND

The work carried out under A. F. Grant 72-2362 represents a variety of approaches to the problems of isometric fatigue. Some of it represents a continuation of earlier lines of work, to extend and clarify previous findings, while other investigations represent new lines of development in our approach to the problem. All such studies have relevance to practical issues, but some studies were designed primarily in the practical vein while others were designed primarily to provide physiological data of a fundamental nature, without which we cannot hope finally to elucidate the problems of muscular fatigue.

Muscular fatigue has been variously attributed, by different workers to a failure of 1) the contractile mechanism, 2) transmission at the neuromuscular junction, 3) transmission over the muscle membrane or 4) transmission in the central nervous system. The evidence concerning the large increase in blood pressure during static effort predominantly supports the view that it is driven by a chemical reflex from the muscle; however, the possibility that some part of the response is due to central nervous drive cannot yet be excluded. The heart rate and respiratory responses share common features which suggest that the controlling mechanism may also be shared, but the evidence to define these mechanisms is poor.

ABSTRACT OF RESULTS

Explorations into the cause of fatigue and related physiological responses

At the start of our 4 year program we decided to test a working hypothesis that muscular fatigue was metabolic in nature. We pursued the hypothesis by analysing muscle biopsy tissues for their constituents before and after fatigue (Investigations 1 and 2). We learned that the changes in the constituents of muscles depended on the type of exercise undertaken, and, with isometric exercise, on the tension exerted. Following isometric contractions there is only a modest depletion of glycogen and ATP in the muscles, at all tensions. Creatine phosphate is almost completely depleted and lactate concentration is very high in the muscles following fatigue at 30-50% MVC but not at tensions that are higher or lower.

Similarly, quite different concentrations of those constitutents occur when very heavy rhythmic exercise occurs either continuously or intermittently. These differences appear to be related to the different types of muscle fiber involved. The matter is complicated, as indicated in the two detailed reports of investigations 1 and 2.

At this point, we decided to discontinue investigations, for the mean time, on muscle biopsies from man. The principal reasons are: 1) The biopsy sample is too small (usually about 15 mg) to permit a full battery of analyses so that in any one experiment we must set priorities in the constituents to be measured. 2) Not enough is yet known about the distribution and function of different fiber types in man in different muscles. This decision was made along with another one, to try to develop an animal model in which we could induce isometric fatigue in a fashion imitative or voluntary contractions; this development is described later in this narrative.

It appeared from the results from our biopsy material that while some metabolic events may cause fatigue at 30-50% MVC, it seemed unlikely that those same events can be held responsible for fatigue at higher or lower tensions. In thinking about the ways in which we might explore these matters further, without the direct evidence from biopsy material, we decided that the best avenue available was to use the electromyogram as a method to assess muscular activity, to be compared with the related muscle blood flows (Investigations 3 and 4). While scattered evidence is available concerning the EMG in response to static effort, the analysis of surface EMG had not, we felt, been adequately explored. Nor had any workers systematically pursued this procedure in investigations of muscular fatigue induced by sustained, sub-maximal isometric tensions. The appropriate studies required the development of devices and procedures whereby we could analyze the surface EMG in a more sensitive manner than had been done heretofore. The outcome proved to be rewarding since we believe it has yielded a method by which fatigue can be assessed accurately, irrespective of the tension exerted. Furthermore, we believe the method can be used to forecast, from a few seconds of recording, how long it will take to induce fatigue at any given tension. Further exploration of the validity of our belief in this method is required. If it does prove to be valid, then it may also prove to be a device worth using in practice although at present it is a complicated procedure.

We believe that the report of our Investigation 3 to be of great significance in the study of fatigue, not only because of the procedures used, but also because of the results they yielded. Several of the important

conclusions are: 1) It appears that at tensions of 70% MVC the fatigue is metabolic in nature while at lower tensions, some degree of transmission failure occurs, 2) The integrated EMG increases with tension and with the length of time the contraction is held and does not, by itself, provide a good yardstick of fatigue 3) The frequency of the power spectrum of the surface EMG provides a good yardstick of fatigue always starting and ending at the same values, irrespective of tension, and 4) Fatigue induced by isometric contractions is solely peripheral in nature and does not involve central nervous fatigue. From this study there is so much new information, some of which we found to be surprising, that it is not yet possible at this time to interpret it all with precision. Further studies are called for and will be undertaken. One aspect that we have begun to explore (Investigation 4) is the relationship between the surface EMG and muscular blood flow. At low isometric tensions, up to 10% MVC, in which fatigue does not occur, the integrated amplitude shows a change which is, essentially, a square wave when the contractions begin and end. The forearm blood flow, however, takes some time to increase to a steady-state, presumable due to a lag in the production of the local vasodilator substances and the increase in blood pressure; these two effects are offset by the compression of local vessels due to increased intramuscular pressure. Curiously, the blood flow immediately after the start of an isometric contraction at tensions from 10 to 40% MVC is virtually unchanged. During a sustained contraction to fatigue, there is a rapid increase of blood flow at first, becoming a slower increase later. Since the increase of integrated amplitude of the EMG is linear throughout the contraction, the implication is that there is recruitment of motor units whose blood supply is poorer than those which are functional

early in the contraction. The intimate relationship between the blood flow and continued function of motor units, and the anatomical variations in blood supply to different kinds of muscle fiber, make it clear that further study of this subject will be rewarding in the study of fatigue.

While these and other studies were in progress, we had successfully developed, for the first time, a method of inducing isometric contractions in animals at any tension desired and of maintaining that tension until fatigue occurred in a manner similar to voluntary contractions in man (Investigations 5, 6, 7). Furthermore, these contractions were induced at motor unit frequencies within the range found in voluntary human contractions. There is no need, here, to reiterate the details of methods and results which are described in detail in the reports of investigations 5, 6, 7. It is clear that this development represents a major step forward in the study of muscular fatigue offering the opportunity of intimate studies of muscles in fatigue and of selecting muscles for study of very different composition of different types of muscle fiber. The implciations are obvious and far-reaching.

The influence of inherent factors on isometric strength and endurance

In a multi-factor analysis of the influence of the inherent factors of age, sex and body-fat content on isometric strength and endurance, it was no surprise to find that men are stronger than women (Investigation 8). In both sexes, strength declined with age while increased body fat content was related to increased strength. Isometric endurance, on the other hand, increased with age and decreased with increasing body-fat content. The increase in strength with body fat content is said to be due simply to the fact that muscles become trained to carry a greater weight and thereby increase their strength. The decrease in endurance, as body-fat content

increases, is attributable simply to the insulative power of increased subcutaneous fat, leading to a higher muscle temperature in the limb (Investigation 9). Increased muscle temperature has long been known to result in a decrease in isometric endurance. We have found that the deep muscle temperature in the forearms of thin subjects may be 4-6° C lower than that in fat men, a difference sufficient to account for the greater endurance of the thin men.

The increase in heart rate throughout a fatiguing contraction at 40% MVC was strikingly similar in men and women. Heart rate, which always increased during exercise, attained its highest magnitude during exercise in the subjects who had the highest resting heart rates. However, older subjects displayed a smaller increase in exercising heart rates than younger subjects. The blood pressure at the end of the 40% MVC was directly related to the resting blood pressure. Aging and body fat content both increased the resting systolic blood pressure in men and women; this aging effect was further exaggerated during the exercise.

In a later study (Investigation 10), we found that, in young men, no changes in the responses of heart rate occurred at any muscle temperature we examined but that at muscle temperatures below 20° C the blood pressure response was reduced.

Other studies

Finally, there are a number of other investigations in which the principal intention was to address practical issues (Investigatigations 11, 12, 13, 14, 15). In one of these (Investigation 11) it was established that strength was not altered in different postures but that endurance was 20% longer in the sitting position than in a semi-reclining or recumbent posture.

The matter has importance in deciding the posture of pilots of the new generation of fast and highly manueverable aircraft. Readier induction of fatigue, and its attendant problems of loss of manipulative skill and other capabilities occur in reclining postures. These must be balanced against the benefits of those postures in combating undesirable gravitational stresses.

In one study on respiration during isometric contractions, we have extended our earlier findings from resting men to men engated in rhythmic exercise and isometric exercise simultaneously (Investigation 12). Interestingly, the average increase in minute-ventilation was 20L/min at rest and at all levels of rhythmic exercise up to 100 Watts. The matter is of practical importance to individuals performing work in self-contained breathing apparatus with a finite volume of gas; the greater the isometric component is, the shorter the period the gas supply will last.

In another study (Investigation 13) we have found that even at the modest altitude of 2,900 m (9,500 ft) endurance of isometric contractions was reduced by 10% in subjects who customarily reside close to sea level at 160 m (400 ft). Also, heart rates and blood pressures at rest were elevated by 14 beats/min and 16 mm Hg and there was evidence of erratic behavior in these cardiovascular indices. Those changes were not redressed in the 3 days that our subjects spent at altitude. But subjects who were resident at 1066 m (3,500 ft) did not demonstrate those changes on transport to altitude; in short, they showed evidence of some acclimatization to an altitude at 2,900 m from residency at 1,066 m. The implications, that acclimatization may be markedly affected by the altitude of previous residency, call for further study of the acute responses of men to changes in altitude.

Investigation 14 was concerned with changes of isometric strength and endurance at different hand-grip sizes. Isometric strength is reduced by some 10% or more when the two poles of a handgrip dynamometer are moved only 0.6 cm (3/8 inch) wider or narrower than the optimal distance. The results showed that the endurnace of a 40% MVC was essentially the same at all hand span sizes. But when those data were transposed into the endurance at absolute tensions (as is usually the case in the practical scene) the optimal handspan size yielded endurance times 30% longer than at the other hand-span sizes.

Finally, in Investigation 15, we examined the validity of the much-quoted previous claims of Muller, that endurance can be increased by as much as ten-fold by performing strenuous exercise in the presence of reactive hyperemia. The matter was of striking practical importance because, if true, the benefits would be considerable and would open the way to potential manuevers to avoid or reduce the development of fatigue. However, as we expected on the basis of current physiological understanding of muscular function and fatigue, Muller's claims proved to be false; there was no improvement in endurance when the exertion occurred in the presence of an increased local blood flow.

SUMMARY

In summary, we believe that the work described briefly above has moved us significantly towards the goal of unveiling the cause(s) of fatigue and the mechanisms that control it and its associated physiological responses. The findings from the studies with specific practical goals show striking alterations in endurance in different circumstances and alterations of some of the physiological responses. The major developments, in our view, have resulted from the studies of a more fundamental nature. In these we believe that we have made major advances and contributions to the understanding of muscular fatigue and that we have set the scene for further advances.

INVESTIGATION 1

METABOLIC CONSTITUENTS OF HUMAN MUSCLE AFTER FATIGUE AND DURING SUBSEQUENT RECOVERY.

INTRODUCTION

In earlier studies of the changes of the metabolites in human muscle before and after fatiguing isometric contractions, relatively little change was found in the concentrations of adenosinetriphosphate (ATP) or glycogen [6,7]. The most striking changes were in the high concentrations of lactate and the nearly complete depletion of creatine phosphate (CP) after fatiguing contractions at 30% and 50% of the maximal voluntary contraction (MVC). At 20% and 80% MVC neither the increase in lactate nor the decrease in CP were so marked. Furthermore, in the interval of 11 minutes between successive isometric contractions, the CP was almost completely reconstituted but the lactate never recovered to its resting levels. On the basis of these data it was difficult to determine that any one metabolite could be held responsible for isometric fatigue, though lactate must be held in suspicion at the intermediate tensions. Clearly, the next logical experimental step was to examine the rates of recovery of the various metabolites by modifying the interval between a series of isometric contractions. In this investigation, 5 successive leg-isometric contractions were held to fatigue at 50% MVC with intervals between the contractions varying between 3 and 20 minutes; also, 2 successive contractions were held with an interval of 80 minutes between them.

METHODS

Three young, healthy males volunteered to take part in this investigation. They were medically examined and the purposes, methods and hazards of the experiment were explained in detail before they consented, in writing, to participate.

Each subject trained both legs in the isometric contractions at 50% MVC

for 10 consecutive days. The dynamometer consisted of a chair to the front of which was attached a tempered steel bar. Two strain gauges glued to the bar formed part of a Wheatstone bridge which fed an amplifier controlling the display on a large meter. Distortion of the bar displaced the needle on the meter. An ankle harness was attached through a universal joint to the free end of the steel bar; the subject sat in the chair with his ankle in the harness, and with the knee at an angle of 90°; he extended the leg horizontally against the harness.

After determining the MVC at the start of each experiment, the first of 5 consecutive isometric contractions was performed; the tension of all the contractions was 50% MVC. The interval between the contractions was kept constant in each experiment, at 3, 7, 11 or 20 minutes. In another experiment, only 2 contractions were performed, when the interval between them was 80 minutes.

Muscle biopsy specimens were obtained by needle (1); the specimens were frozen within 3-5 sec in liquid nitrogen and stored at -80°C until analysed for concentrations of ATP, CP, glycogen and lactate by methods previously described (5). Finger-tip blood samples were taken simultaneously and analysed for lactate concentration.

We considered that the number of muscle biopsies should be confined to 8 samples from one leg and 7 samples from the other. Therefore we had to establish priorities in deciding when samples should be taken. Our desire was to take them immediately before C_1, C_2, C_4 and C_5 and immediately after C_1, C_4 and C_5. But with a limit on the number of samples to be taken we followed this procedure only once, in the experiment with 11-min intervals. From past experience we knew that the samples before and after C_1 (provided the tension was constant, as here) were reasonably consistent in the concentration of metabolites; hence we chose to accept these samples as a "standard" for the other experiments. So, when the intervals were 3 min and 20 min, the samples

were taken immediately after C_4 and C_5 and just before C_2 and C_5. Finally, one sample was taken just before C_2 when the interval was 80 min. We decided that biopsy specimens were to be least illuminating when the interval between the contractions was 7 min; accordingly, we took no specimens in that experiment. Blood samples were taken from the finger pad just after postcontraction biopsies and just before precontraction biopsies.

RESULTS

Figure 1 shows the average changes in durations of the isometric contraction at 40% MVC from the first to the fifth contraction. These are reminiscent of the findings from earlier reports (6,8) of the influence of the interval between serial contractions on their duration. The shorter the interval was, the shorter the durations became, but by the fourth and fifth contraction, a steady-state had been achieved or closely approached. Since, in the steady-state condition, the interval between the contractions represents the capacity of the muscle to recover its isometric function, these values can be plotted, as in Figure 2, to demonstrate the processes of recovery. As in the previous study, the recovery curve assumed an asymptotic form with rapid early recovery slowing after some 10 minutes, until, in this case, 80 minutes later some 90% of total muscular capacity had been recovered.

Table 1 shows the concentrations of ATP, CP, glycogen and lactate in the resting state and at the various specified times throughout each experiment.

As expected, the concentrations of the metabolic constituents in the muscle after the first contraction were similar to those found in recent investigations, when the tension was the same (6,7).

Changes in the muscle constituents during the recovery of muscle function are shown in Table 1. Compared to the concentration found at rest, at 3.6 mmole kg^{-1}, there was a small reduction in the concentration of ATP as a result of

the first contraction to 2.9 mmole. kg^{-1}, values which were similar to our earlier findings. In succeeding muscle biopsies, little difference was seen in that level, and irrespective of the interval before the successive isometric contractions, the ATP never recovered to the resting level in these experiments. Similarly, there was a small reduction in the concentration of glycogen after the first contraction. While the glycogen stores were, in general, repleted to some extent in the rest periods and slightly further depleted by the successive contractions, at the end of the fifth contraction the glycogen store was never more than half depleted. Although there was a distinct reduction of the glycogen deposits through the final contraction, this appeared to have no relationship with the interval between the contractions.

At the end of the first contraction there was a marked accumulation of lactate, which reached an average concentration of 23.1 mmole. kg^{-1}. Similar concentrations of the molecule were found after the fourth and fifth contractions, irrespective of the length of the intervals between the serial contractions. During recovery the matter was more complicated; the rates of recovery were different after the first and the fifth contractions. After the first contraction, the accumulation of lactate in the muscle disappeared rapidly at first. For example, the concentration of lactate decreased to about half, some 12 mmoles. kg^{-1} in the first 3 min of recovery. Thereafter the rate of removal of lactate slowed, and after 20 min it was about twice the control level at about 4 mmoles. kg^{-1} and still had not reached the control value even after 80 min recovery. So the second contraction began with a concentration of lactate greater than the control value. At the end of the fourth recovery period, just before C_5, the concentration of lactate was higher than it was after the first recovery period. The amount of that increase appeared to be inversely related to the length of the interval between the contractions (see Table 1). The increase in the concentration of lactate from R_1 to R_4 when the interval was 3 min was small, from 12 to 14 mmoles. kg^{-1}, but when the interval was 20 min the increase was from 4 to 12 mmoles. kg^{-1}, a rise of 60%.

After the first, fourth and fifth contractions, the phosphagen stores in the muscle were always drastically reduced to similar levels, between 2 and 5 mmoles.kg^{-1}. The levels of CP after fatiguing exercise appeared to be unaffected by the length of the interval between contractions. In recovery periods, the CP increased rapidly at first and as time progressed it more nearly approached resting values, asymptotically. Like the concentrations of lactate, there was no difference in the levels of CP following C_4 and C_5. But unlike the lactate there was no evidence to show any systematic difference in the concentration of CP at the end of the first and fourth recovery intervals.

DISCUSSION

Clearly, in the search for a metabolic cause of muscular fatigue, changes in the concentration of any metabolite to be singled out as a sole cause must bear a relationship to the duration of isometric contractions seen in Figure 1. The second of the five successive contractions was never as long as the first one, even when the interval was as long as 80 minutes. The duration of the second contraction depended on the interval, varying from 68% of the duration of the first contraction when the interval was 3 minutes to 86% after 20 minutes and 92% after 80 minutes. The duration of the fifth contraction was shorter still, ranging from 44% of the duration of the first contraction with a 3-min interval to 75% when the interval was 20 min. It seems reasonable to assume, then, if we are to erect a causal relationship between a metabolite and isometric muscular fatigue, that there must also be a demonstrable relationship between the changes in the concentration of the metabolite and the known functional capacities of the muscle.

While it is true that during these experiments the ATP concentration after isometric exercise was never restored to its resting value, there was no clear-cut relationship either after the first or the fifth contractions, irrespective of the interval between the serial contractions. These are circumstances which do not correlate with the observed capacity of the muscles.

Similarly, there was no obvious pattern relating the depletion of glycogen with the duration of the fatiguing isometric contractions. Further, unlike fatiguing rhythmic exercise where the glycogen deposits are totally depleted (4) isometric exercise did not reduce the muscle's glycogen by more than half even at the end of the fifth successive contraction. It seems that neither ATP nor glycogen can be blamed for isometric muscular fatigue.

The case for creatine phosphate being the responsible agent is more promising. At the point of fatigue the CP is almost totally depleted at the end of all the contractions, irrespective of the intervals between them. The fact that the concentrations of CP are all similarly low at the end of the contractions would seem to fit one requirement of an agent responsible for fatigue. Further, the recent evidence of Edwards et al (2) shows that the initial rate of recovery of CP after isometric fatigue is extremely rapid and it is conceivable that the concentrations that we found several seconds after the contractions represent the reconstitution of CP before the samples were frozen. At the end of the first rest period (just before C_2) the concentration of CP increased as the rest period increased in duration but never reached the original resting value. This fact would fit the need of our suspect metabolite to behave in concert with the endurance times of C_2. The same pattern of events is true of the concentrations of CP just before C_5. But the difference between the concentrations of phosphagen before the second and fifth contractions in any one experiment was small and inconsistent, whereas the differences in durations of these contractions was large and clearly dependent on the duration of the interval between the contractions. This fact is hard to reconcile with the possibility that the changes in concentration of CP are responsible for fatigue.

The changes in lactate concentration, however, seem to answer all the requirements in correlation with the durations of the contractions. First, there was a comparably high concentration of lactate at the end of all the contractions in each experiment. Second, the control, resting level of lactate

was never restored in any experiment. Third, the concentrations at the start of C_2 were lower, in each experiment, than they were just before C_5. And finally, the concentration of lactate decreased as the interval between contractions increased. On these general scores, the accumulation of lactate during the fatiguing contraction and its time-related failure to dissipate before the next contraction begins fulfills the requirements of an agent responsible for fatigue. The rates of dissipation of lactate before C_2 and the durations of that contraction were not linearly related; further, that lack of linearity with respect to C_5 was accentuated. There is, however, no obvious need for that relationship to be linear, particularly if recent evidence is substantiated, that different fiber types, associated with selectively different metabolism, are predominantly recruited at the tension used here from fast-twitch fibers, as suggested by Gollnick, et al. (3).

The findings in this study are slightly different from those of our earlier study (6). Previously when the tension was 50% MVC and the interval between the serial contraction was also 11 minutes, we observed no differences in the level of lactate before the second and fifth contractions whereas in similar circumstances here the lactate was some 40% higher before the fifth contraction than it was before the second contraction. Also, in our previous study, in those circumstances, the repletion of CP in 11 minutes was complete before C_2 and almost complete before C_5 whereas in this study the CP was reconstituted only to about 60% of the resting value, although again there was little difference in the values found before C_2 and C_5. The most reasonable explanation of these differences seems to be that in the two studies, the proportion of fast and slow fibers in their muscles was different. The known differences in the biochemical make-up of the two types of fibers could thereby well account for the changes described. If this is so, it emphasizes the need either to take into account individual differences or to ensure that in such studies, the biopsy samples of muscle are examined for their proportion of fast and slow fibers.

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Table 1. Average concentrations (mmoles. Kg^{-1} wet muscle) of constituents of muscle and plasma of the subjects at rest and at varying times after isometric contractions (C) and recovery intervals (R) in different experiments.

		ATP	CP	Glycogen	Muscle Lactate	Blood Lactate
	Rest	3.6 (3.0-4.9)	18.1 (15.5-20.7)	92 (82-103)	2.1 (1.8-2.2)	0.9 (0.6-1.4)
3 min intervals	C_1	--	--	--	--	1.7 (1.5-1.8)
	R_1	2.5 (2.2-3.1)	5.1 (2.6-7.8)	68 (50-84)	12.1 (7.5-19.8)	2.1 (2.0-2.3)
	C_4	2.9 (2.1-3.8)	2.0 (1.4-3.0)	74 (70-74)	22.5 (16.3-28.7)	4.2 (3.3-4.8)
	R_4	2.6 (1.6-2.9)	6.2 (1.5-8.8)	62 (41-73)	14.2 (13.2-16.1)	4.9 (3.3-6.7)
	C_5	2.3 (1.8-3.1)	3.3 (0.2-8.6)	47 (22-70)	22.0 (19.9-24.0)	4.4 (3.2-6.2)
11 min intervals	C_1	2.9 (2.3-3.1)	5.0 (4.1-6.0)	77 (56-98)	23.1 (16.3-29.1)	--
	R_1	3.2 (3.0-3.3)	12.1 (8.5-18.0)	82 (5-108)	6.9 (5.5-8.2)	2.3 (1.7-3.2)
	C_4	2.9 (2.4-3.6)	3.6 (0.9-4.7)	63 (40-99)	19.6 (18.3-22.1)	2.9 (2.0-3.6)
	R_4	3.2 (2.6-3.8)	15.6 (13.1-18.8)	72 (46-93)	12.8 (0.0-14.0)	3.7 (1.9-5.3)
	C_5	2.2 (1.7-3.1)	1.9 (0.8-2.9)	63 (37-78)	22.7 (16.3-27.4)	3.8 (2.9-4.7)
20 min intervals	C_1	--	--	--	--	--
	R_1	2.9 (2.0-3.7)	13.9 (9.2-16.5)	77 (78-84)	4.1 (3.0-5.5)	1.4 (0.9-2.4)
	C_4	2.9 (2.6-3.1)	7.6 (6.0-8.0)	63 (55-74)	20.0 (14.1-27.5)	2.3 (2.2-2.4)
	R_4	3.1 (2.6-4.1)	14.7 (5.9-19.2)	68 (46-84)	12.2 (6.5-15.5)	2.7 (2.2-3.8)
	C_5	2.3 (2.2-2.4) 2.1/3.8	5.1 (3.6-7.6) 9.6/17.0	44 (42-45) 4.6/2.1	20.3 (180-18.6) 35/80	3.1 (2.1-3.2) 1.9/1.7
80 min interval	C_1	--	--	--	--	--
	R_1	3.0	13.6	85	4.2	1.8

FIGURE LEGENDS

Figure 1: The average duration of isometric leg contractions (of 3 subjects) at a tension of 50% MVC when the intervals between the successive contractions were 3 (+), 7 (■), 11 (▲), 20 (●) and 80 (×) minutes. The average length of the first contraction was 71 seconds.

Figure 2: The recovery of the muscle's capacity to exert an isometric contraction at 50% MVC; data from Fig. 1.

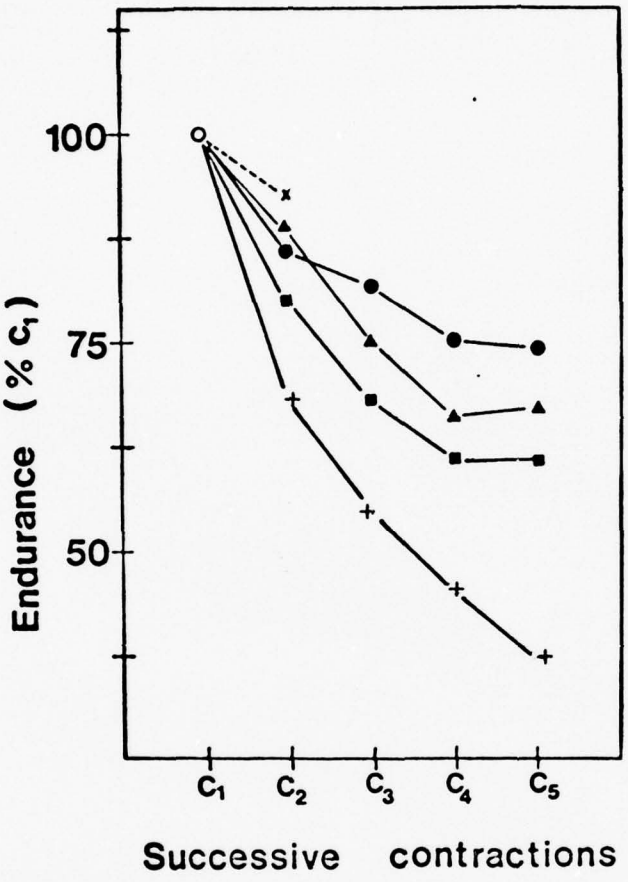

100
75
50
Endurance (% c_1)
C_1
C_2
C_3
C_4
C_5
Successive contractions

FIGURE 1

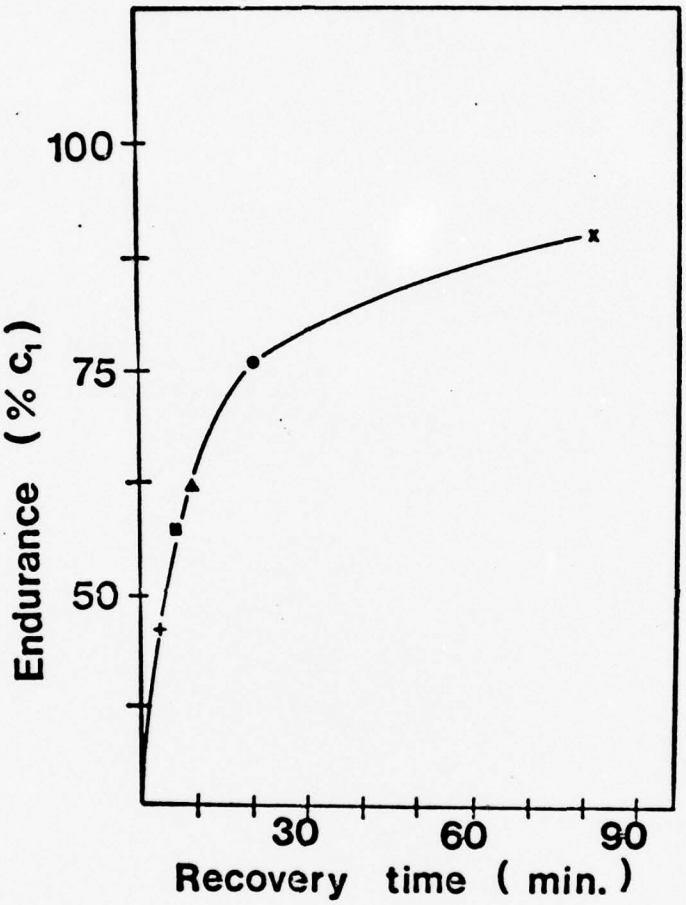


FIGURE 2

INVESTIGATION 2

GLYCOGEN DEPLETION IN SPECIFIC TYPES OF HUMAN SKELETAL MUSCLE FIBERS IN INTERMITTENT AND CONTINUOUS EXERCISE.

INTRODUCTION

Within the past few years considerable progress has been made toward our understanding of some of the fundamental characteristics of motor units and their muscle fibers. For example, specific metabolic, circulatory and dynamic properties of skeletal muscles of different animals including humans are closely related (2, 4, 5, 8, 19, 21, 23, 24, 28, 32). In spite of our increasing understanding of these properties we know little about how these different types of motor units are used by an intact animal in normal movements such as walking, running, swimming and jumping (1, 9, 10, 12, 16, 17). These studies do however provide some evidence of how types of muscle fibers may be used differentially by assessing glycogen depletion in specific types of muscle fibers.

Repeated short bursts of activity separated by short periods of rest (intermittent exercise) present certain unique physiological demands and responses from the human organism. One important finding is that the work intensity can be kept very high without a glycogen breakdown as pronounced as in continuous work (29, 30). It was therefore felt of interest to study whether a difference in glycogen depletion pattern could be found in the muscle fibers comparing intermittent and continuous exercise.

Moreover, since fat seems to be an important substrate for skeletal muscle in intermittent exercise (6, 13), it was thought worthwhile to determine the intramuscular lipid stores and the pattern of Oil Red O staining.

METHODS

Four healthy medical students participated in the study. Some characteristics of the subjects are given in table 1. Subject RG was only included in one part of the experiment as he experienced some discomfort after the biopsies in the first study.

Oxygen uptake was measured by collection of the expired air in a balanced spirometer, and the gas analyses were performed with the Schollander technique. ECG for counting of the heart rate was recorded on a one channel electrocardiograph. Blood lactate was determined with an enzymatic technique (20).

Muscle biopsies were taken with the technique described by Bergström (3). Local anesthesia was used in the skin and an incision through the skin was made with a knife blade. Thereafter, the needle was introduced in the lateral portion of the quadriceps muscle at an appropriate depth of 3 cm, where the biopsy was taken. All muscle biopsies were analyzed as tissue sections (histochemistry) and homogenates (biochemistry). In each subject a total of 9 muscle biopsy samples were taken and analyzed for total content of glycogen, lactate, creatine phosphate, ATP and glycose-6-phosphate (20).

For the histochemical analyses serial fresh-frozen 10μ tissue sections were cut at -20°C, placed on a cover glass, dried at room temperature and placed in one of several incubation media. Reduced nicotinamide adenine dinucleotide diaphorase (NADH-D) activity was determined by the method of Novikoff et al. (25) and myosin adenosine triphosphatase (Myo ATPase) activity by Guth and Samaha's (18) modification of Padykula and Herman's method (26). Wattenberg and Leong's (31) method for menadione-linked alpha-glycerophosphate dehydrogenase (α GPD) was used. Malate dehydrogenase

(MDH) activity was demonstrated with an incubating medium consisting of 110 mg of malic acid, 10 mg NAD, 15 mg NBT and 10 ml of 0.2M Tris buffer at a pH of 7.4. The final pH of the medium was adjusted with 10 N NaOH. Tissue sections were incubated for 30 min. Phosphorylase activity was demonstrated with the technique of Meijer (22). Fat was stained with Oil Red O using the technique described by Pearse (27).

Glycogen was stained using PAS (27) in 20μ thick sections. Control sections digested with α amylase demonstrated the specificity of the stain for glycogen.

The pattern of glycogen content was assessed by rating the PAS staining intensity from 4 (high) to 1 (none). A subjective rating for a given biopsy represents the mean of the values for all of the individual fiber ratings. The subjective rating of the PAS stain was checked by a photometric analysis of the PAS stained sections with a sensing probe of a multi-range light meter (Science Mechanics Model) placed into the camera tube of the triocular head on a Zeiss standard RA Model microscope. Using this system the split beam optics allowed observation of the tissue section being analysed. With the tissue in focus and the light source at a constant setting, the base iris was adjusted to include a group of 8-10 fibers for representative readings. The light meter was zeroed at 50 when the light passed through a clear area of the slide and coverslip. The tissue was then moved into the light beam and a reading taken on an area which was representative of the whole tissue staining intensity. The results were plotted on a semilog scale so that the transmitted light reflected the concentration of PAS staining in the section.

The validity of the PAS staining reaction intensity as a measure of glycogen concentration in muscle fibers was thus demonstrated in two ways. First, tissue sections preincubated in a diastase solution prior to the routine procedures prevented any staining within the muscle fibers. Secondly,

a photometric analysis of the tissue sections stained with the PAS reaction was correlated with glycogen values obtained from homogenates of the same muscle from which the tissue sections were taken. Figure 1 demonstrates the relationship of glycogen values derived spectrophotometrically from homogenized tissue and photometrically of tissue sections stained with PAS ($r = -0.76$).

The correlation ratio of the subjective evaluations of PAS staining intensity of tissue sections of human biopsies and photometric readings was -0.77 (fig. 2). The accuracy of the subjective evaluations of human muscle is underestimated because the photometric readings were taken from up to 10 fibers for a representative area of each biopsy whereas subjective ratings were done on individual fibers. A more precise assessment of the accuracy of the ratings is shown in figure 3, which graphically relates glycogen content with subjective rankings based on the intensity of PAS staining of 10 slides of unknown origin with respect to the subject or treatment ($r=-0.86$).

The subjects were studied 2-3 times with submaximal and maximal exercise in the weeks prior to these experiments. The purpose was to acquaint the subjects with the different exercise procedures that were going to be used and also to determine their maximal oxygen uptake (table 1). The experiment consisted then of three different exercise periods. Each time the total work output was the same for each subject and the tests were performed with at least one week interval.

In the first experiment (intense-continuous) the subjects performed at a work load demanding approximately 120% of maximum $\dot{V}O_2$ until exhaustion, which occurred within 4-6 min. After a rest period of 20 min duration the work was resumed and this procedure of rest and work was continued until the total work time was 20 min. Biopsies and blood samples were

obtained at rest, after the first exercise period was terminated (work time 4.75) and after 20 min of work (fig. 4, arrows).

In the second experiment (intense-intermittent) the subjects performed intermittent exercise for 40 min. The ratio between rest and exercise was 1:1 with 10 sec rest and 10 sec work period at the same work load as in the first experiment. Muscle biopsies from the quadriceps muscle were taken at rest, after the same total work output as after the first work bout in experiment one (work time 9.50) and after 40 min of intermittent exercise (fig. 4, arrows). Blood samples from a fingertip were obtained when biopsies were taken. Heart rate and oxygen uptake were determined so that both the exercise and "recovery" level could be calculated.

In the third experiment (moderate-continuous) the subjects performed the same total work output but with continuous exercise for 40 min. The work load was then half of what was used in the first and second study (approximately 60% of maximum $\dot{V}O_2$). Biopsies and blood samples were obtained at rest, after the same total work output as after the first work bout in the first experiment (work time 9.50) and at the end of the 40 min work period (fig. 4, arrows). Heart rate and oxygen uptake measurements were performed after 10 and 40 min of work. Total work output in all three was the same and averaged 29,967 kpm (subject RG not included).

RESULTS

The observed mean oxygen uptakes, R-values and heart rates for the different conditions were the expected for the used work loads (table 2). The chemical determination of muscle glycogen demonstrated a reduction of almost 100 mmoles in the intense-continuous exercise (fig. 5). The

depletion was only one third of this in the intense-intermittent and the moderate-continuous exercise. Muscle and blood lactate concentrations reached 22 mmoles/kg and 11 mmoles/l, respectively, in the intense-continuous experiment. In the intense-intermittent exercise the blood and muscle lactate concentrations were also increased but only to half of the concentrations observed in the intense-continuous work. In the moderate-continuous exercise only a small increase in muscle and blood lactate concentration was observed during the exercise.

The energy rich phosphates were most markedly depleted in the intense-continuous work (fig. 6). At the end of the last exercise period ATP and CP values were as low as 2.8 and 3.9 mmoles/kg, respectively. This corresponds to only approximately 1/6 of the resting value. In the intense-intermittent exercise not so marked depletion occurred, and in the moderate-continuous work the reduction of the phosphagen store was very minor ($\sim$ 20%).

Generally speaking the metabolic response to intermittent exercise was somewhere in between what is found in intense- and moderate-continuous work. It is noteworthy, however, that the glycogen reduction in the intermittent exercise was not higher than in the moderate-continuous exercise. The chemical determination of muscle triglyceride concentration revealed no significant pattern for reduction in any of the three exercise conditions.

In most tissue sections of control samples there was no noticeable difference in PAS staining intensities among the different fiber types. This is consistent with the observations made by Gollnick et al (17) when resting muscle glycogen values were high as in this paper. Two of four of the samples taken after approximately 5 min of intense-continuous exercise showed some glycogen loss while no loss was evident in any of

the biopsies taken after about 5 min of total work time during an intense-intermittent exercise. Samples taken after the completion of the intense-intermittent exercise and the moderate-continuous exercises, though similarly depleted of glycogen quantitatively, were much less depleted than the samples taken after intense-continuous work. Also, the level of glycogen depletion was similar in the initial and final samples of the moderate-continuous exercise. The mean per cent glycogen loss as determined by histochemical procedures were 40, 12, and 15 for post exercise samples after intense-continuous, intense-intermittent and moderate-continuous work, respectively. These relative values agree with those determined from homogenates of the same biopsy samples (fig. 5) in that there was 3-4 times as much depletion after the intense-continuous work than after the other two work programs.

In each of the subjects there was more glycogen loss from the myosin ATPase dark fibers (presumably fast-twitch) after intense-continuous work than after a moderate-continuous work (fig. 7). Glycogen loss resulting from the intense-intermittent work tended to fall between the intense-continuous and moderate-continuous work with respect to glycogen depletion within ATPase dark fibers (fig. 7).

Similar results were found when glycogen was related to NADH-D activity. However, a more consistent trend in the selective involvement of specific fiber types was more obvious when the glycogen loss was related to the NADH-D activity of a fiber. A clear difference within each subject between the intense-continuous and moderate-continuous work sessions are illustrated in figure 8. More glycogen was lost from the NADH-D light fibers after intense-continuous than moderate continuous work. The intense-intermittent work resulted in a selective glycogen loss with respect to a fiber's NADH-D activity that fell between the

selectivity resulting from the other two types of work (fig. 8). The type of fiber from which most of the glycogen is lost in a muscle is necessarily dependent on the percentage of each fiber type found in the muscle sample analyzed. In fact, the total muscle biochemical characterization of rested or exercised muscle is greatly dependent on the type of fibers which make up a sample. Figure 9 illustrates a remarkable consistency within subjects in the fiber properties with respect to either myosin ATPase or NADH-D activity.

Fibers which showed some glycogen loss were also lightly stained with the phosphorylase preparations. From all of the samples studied, 97% of the phosphorylase light fibers also demonstrated glycogen depletion. On the other hand it was not uncommon to find fibers with some glycogen loss that failed to clearly demonstrate some loss of phosphorylase activity. A similar phenomenon has been observed in stimulated guinea pig skeletal muscle (8). The relationship demonstrated between glycogen loss and myosin ATPase staining intensity (fig. 2-5) are essentially identical to that found when compared with α-GPD

No change in the lipid content (Oil Red O in frozen sections) could be attributed to any of the exercise regimens. Practically all myosin ATPase light and NADH-D dark fibers stained heaviest with Oil Red O. Fibers that stained light to moderate with Oil Red O were fast-twitch fibers with only rare exceptions.

Figure 10 illustrates serial sections of a muscle sample taken after 40 min of moderate-continuous work. The muscle fibers are characterized according to their oxidative capacity (a,b), contractile properties (c,d), lipid content (e), glycolytic capacity (f) and the alterations in phosphorylase (g) and glycogen (h) due to exercise.

DISCUSSION

Selective Glycogen Depletion After Various Types of Movements

The greater glycogen loss after intense-continuous compared to intense-intermittent and moderate-continuous work as found in this study is consistent with previous work (29). The intense-continuous exercise routine was also characterized by the most dramatic increases in muscle and blood lactate and decreases in ATP and CP (fig. 5 and 6). These changes show clearly that the degree of muscle biochemical change induced by exercise is not determined solely by work intensity or duration. The results do demonstrate that duration and ratio of the rest and work period along with the work intensity determine the relative importance of glycogen as an energy source.

A major new finding is that fast-twitch fibers provide a relatively greater porportion of the glycogen utilized by exercising muscles when the movements are more intense. Thus, the data supports the notion that fast-twitch muscle fibers are more involved in the more intense movements. Gollnick et al. (16) reported a greater amount of depletion in fast-twitch fibers than slow-twitch fibers after six 1-min bouts of work (energy production equivalent to 150% of their aerobic power). However, from this study one could argue that the idea of selectivity of glycogen depletion with respect to fiber types did not occur in a strict sense because depletion patterns reflected differences in the proportion of fast and slow fibers. That is, after three 1-min exercise bouts approximately three times as much glycogen was lost from the FT as was from ST fibers but there were about three times as many FT fibers in the samples analyzed. Likewise, after the 6th 1-min exercise bout, approximately twice as much glycogen was lost from FT fibers but there

Figure 5

was almost twice as many FT fibers within the samples analyzed. In this study one can see from fig. 9 that the difference in the selective glycogen depletion among the three different work routines was not affected by differences in the proportion of fast and slow fibers among the samples analyzed (cf. also fig. 7).

When the PAS staining intensity was related to the NADH-D rather than ATPase activity of a fiber, a clearer although similar pattern of differences emerged in selective glycogen depletion resulting from the three different exercise routines (fig. 7 and 8). This is to be expected since NADH-D more accurately reflects the long term frequency of a fiber's contractions which is governed by the susceptibility of the muscle unit's motoneurons to activation (5, 19, 24, 32). In an individual the fibers with the higher NADH-D activity seem to be slow twitch and vice versa; consequently selective fiber involvement can be related to the speed of a muscle fiber. There are some fibers in human muscles that are fast-twitch as well as having relatively high NADH-D activity as is common in many laboratory animals (7) and in some highly trained individuals (15). It is logical and indeed the results of this study support the idea that NADH-D activity reflects a fiber's firing susceptibility more precisely than myosin ATPase. Strong evidence for this concept has been demonstrated in acutely and chronically exercised guinea pigs (2) and bushbabies (11).

As was observed in this study, Gollnick et al. (15) demonstrated a greater loss of glycogen in slow-twitch fibers after moderate exercise (74% of $\dot{V}O_2$ max) than after intense exercise. Similar results have been observed in bushbabies after a slow-continuous run on a treadmill compared to repetitive jumping (12). The fact that the glycogen depletion pattern after the intense-continuous and intense-intermittent work were not the same suggest that factors other than the nature of the motor unit recruitment are determining the pattern of glycogen depletion. It appears that

during intense-intermittent work muscle glycogen was spared relative to the intense-continuous work and that the glycogen sparing effect was related to the oxygen availability during that type of work.

There have been reports of intramuscular lipid loss due to exercise. The absence of any alteration in triglyceride content of the muscle sample and the Oil Red O staining properties as a result of exercise in this study does not preclude the possibility that muscular lipids were actually affected (1, 6). Rather low resting triglyceride levels were found in most samples and the muscle triglyceride values varied markedly. Also, the specificity of the histochemical stain for lipids is somewhat limited. At room temperature only liquid and semi-liquid lipids would be stained since coloring is based solely on the solubility of colorant in the lipid.

Validity of Glycogen Depletion as a Reflection of Motor Unit Recruitment

The validity of the PAS stain for muscle glycogen has been open to question. However, the correlation ($r = -0.76$) of the spectrophotometric determination from homogenized muscle and photometric assessment from frozen sections prepared from the same muscle samples demonstrates the validity of the technique (fig. 1). Furthermore the accuracy of the subjective ratings of PAS staining intensity as a reflection of muscle glycogen is strongly supported by the correlations in figures 2 and 3.

All muscle fibers in humans have similar glycogen concentrations in rested muscle according to this study and Gollnick et al. (17), and cannot account for the difference in the glycogen remaining among the fiber types after exercise. The selective glycogen depletion in fast-twitch, low oxidative fibers following a fast-continuous work load may not be reflecting a selective utilization of those types of muscle fibers but may simply be a manifestation of the metabolic and vascular properties

associated with that fiber. That is, the small number of capillaries and low mitochondrial content of the fiber yields a very inefficient utilization of glycogen compared to higher mitochondrial content fibers. When muscles are required to work maximally, one may not have the luxury of recruiting an ideal population of motor units having the most desirable properties for maximum efficiency of a particular movement. Motor units of all types may be recruited simultaneously even though all are not especially adept at working under that set of conditions at maximal efficiency. It has been demonstrated in guinea pigs that supramaximal stimulation of whole muscles either directly or indirectly results in a more rapid loss of glycogen in the low oxidative rather than the high oxidative fibers (8). Consequently, maximal voluntary recruitment during maximal muscular efforts could cause glycogen depletion patterns identical to that induced by electrical stimulation. This criticism of glycogen loss being dependent on metabolic and vascular properties is not valid for the slower or less intense exercise since the high oxidative fibers are depleted in spite of their greater oxidative capacity and decreased dependence on glycogen (9).

Other potential drawbacks to the interpretation of glycogen depletion as a reflection of motor unit recruitment patterns is the apparent differences in efficiency of slow and fast muscles to produce tension or perform work in isometric and isotonic contractions (14). Further, little is known of the pattern of nerve impulses that reach a muscle in normal movements in intact individuals. Differences in patterns of impulses delivered to a muscle without differences in total impulses over a time period could undoubtedly alter the nature of a muscle's substrate utilization.

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Subject	Age years	Height cm	Weight kg	Maximal values		
				Oxygen uptake l/min	Heart rate beats/min	Work load kpm/min
MB	21	184	72	3.65	190	1650
RP	22	182	98	3.60	198	1550
WR	23	173	68	2.90	214	1220
RG	22	176	63	2.80	194	1220

Table 1. Characteristics of the subjects

	Intense-continuous		Intense intermittent			Moderate-continuous	
	0-2';	2'-4'45"	exerc.	rest	e+r	10'-12'	38'-40'
Oxygen uptake l/min	2.16	3.2	2.38	2.16	2.24	1.92	1.98
R	0.84	0.89	0.94	0.91	0.92	0.92	0.89
Heart rate beats/min	168[1]	198[1]	151-174			134	156

[1]End of the period

Table 2. Oxygen uptake, respiratory exchange ratio (R) and heart rate in the three experiments [intense-continuous work bouts (20 min), intense intermittent work (40 min) and moderate-continuous work (40 min)] with a total work output of 29,467 kpm.

FIGURE LEGENDS

Figure 1: The correlation between biochemically determined glycogen content and the log-plot of the photometric light meter reading from the PAS stained sections.

Figure 2: The correlation between the photometric log-plot and the subjective rating of PAS sections. Biopsies 1, 4 and 7 are resting samples; 2, 5 and 8 are during the exercise and 3,6 and 9 are after exercise. 1, 2, 3 are from intense-continuous activity; 4, 5, 6 from intense-intermittent and 7, 8, 9 from moderate-continuous activity.

Figure 3: The correlation between the ranking of PAS sections and the biochemical glycogen content.

Figure 4: This graphically represents the three work loads over time with the biopsy points indicated by arrows.

Figure 5: Glycogen and lactate levels are graphed for the biopsies, taken in connection with moderate (M)-continuous, intense (I)-intermittent and intense (I)-continuous work.

Figure 6: ATP and CP levels in various biopsy samples.

Figure 7: The major squares represent only those fibers showing some glycogen depletion. They have been divided into light and dark myosin ATPase fibers. The numbers in the corner of the squares are the percentages of glycogen depletion contributed by the ATPase light fibers.

In subject RP the marked depletion of glycogen from the ATPase dark fibers during moderate continuous work may be explained by the fact that he mainly had this fiber type in his muscle (>90% myofibrillar ATPase dark fibers).

Figure 8: The fiber contribution of glycogen depletion based on the intensity of NADH-D stained sections. The major squares represent 100% of those fibers with some glycogen depletion. The portion of each square occupied by a given NADH-D intensity represents the glycogen loss.

Figure 9: The fiber populations for the after-exercise biopsies. The bars total 100% and the numbers are the number of fibers of that biopsy.

Figure 10: Serial sections of MB after moderate-continuous exercise. a) NADH-D, b) MDH, c) myosin ATPase, alkaline pre-incubation, d) myosin ATPase, acid pre-incubation, e) Oil Red O, f) alpha-GPD, g) phosphorylase and h) PAS.

Figure 1

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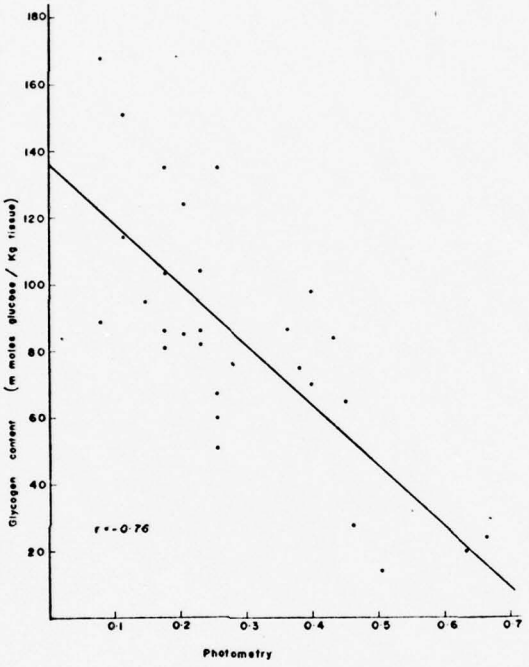


Figure 2

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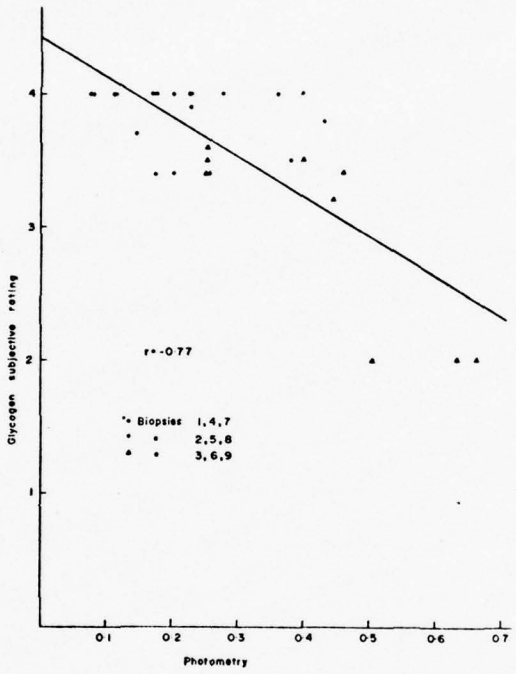
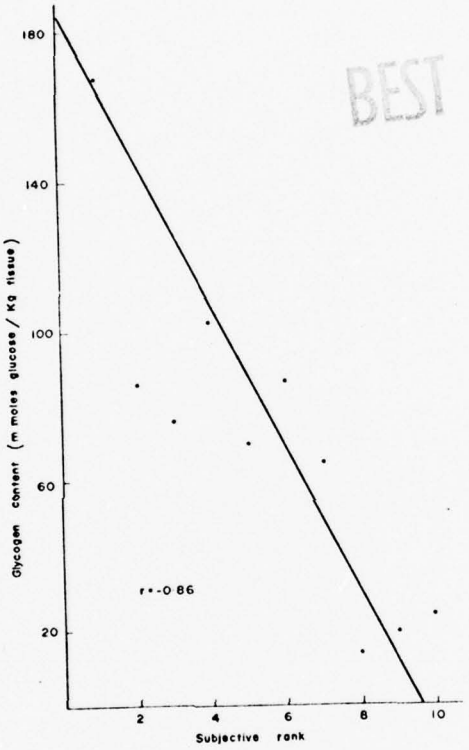


Figure 3



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Figure 4

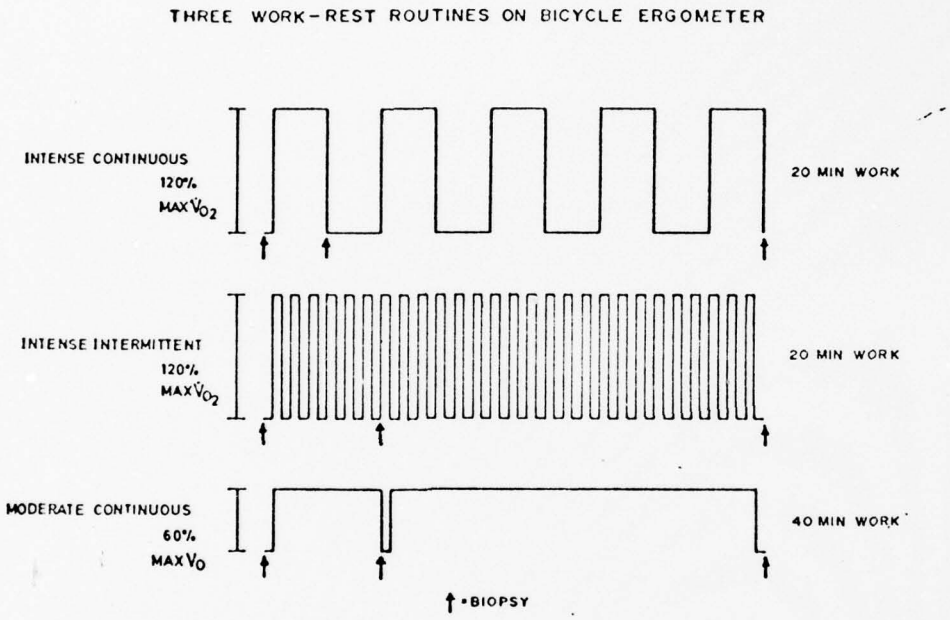
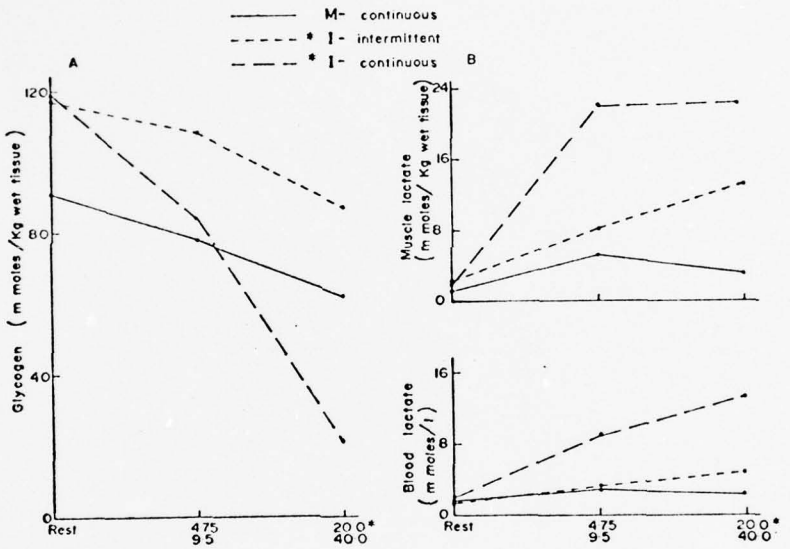

THREE WORK-REST ROUTINES ON BICYCLE ERGOMETER
INTENSE CONTINUOUS
120%
MAX $\dot{V}_{O_2}$
20 MIN WORK
INTENSE INTERMITTENT
120%
MAX $\dot{V}_{O_2}$
20 MIN WORK
MODERATE CONTINUOUS
60%
MAX V_O
40 MIN WORK
↑ = BIOPSY

Figure 5

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Muscle glycogen, lactate and blood lactate before, during and after each exercise routine



Biopsy time (minutes of accumulated work time)

Figure 6

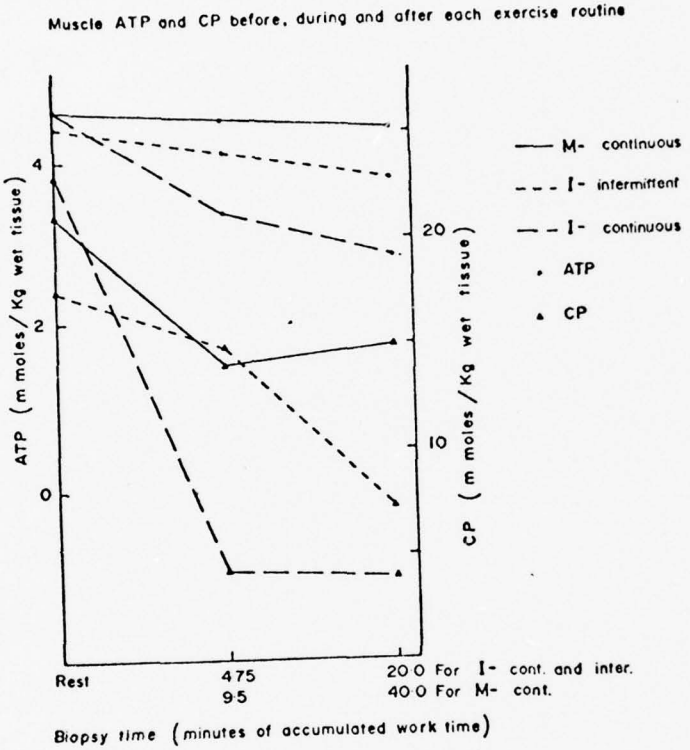

Muscle ATP and CP before, during and after each exercise routine
M- continuous
I- intermittent
I- continuous
ATP
CP
ATP (m moles/Kg wet tissue)
CP (m moles/Kg wet tissue)
4
2
0
20
10
Rest
4 7 5
9 5
2 0 0 For I- cont. and inter.
4 0 0 For M- cont.
Biopsy time (minutes of accumulated work time)

Figure 7

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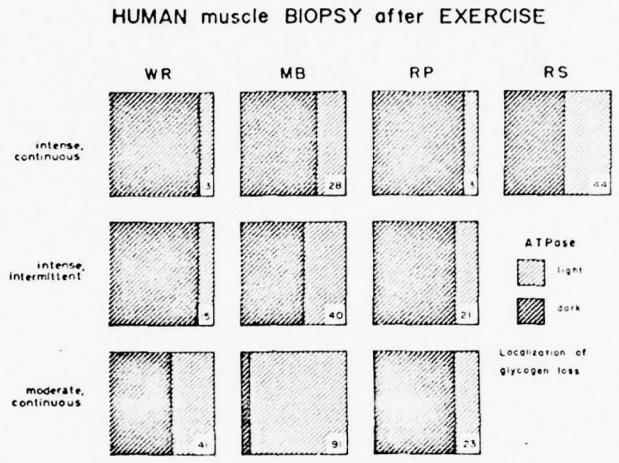


Figure 8

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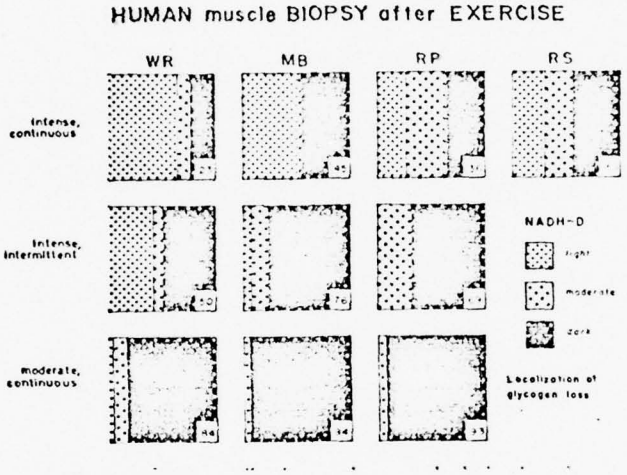
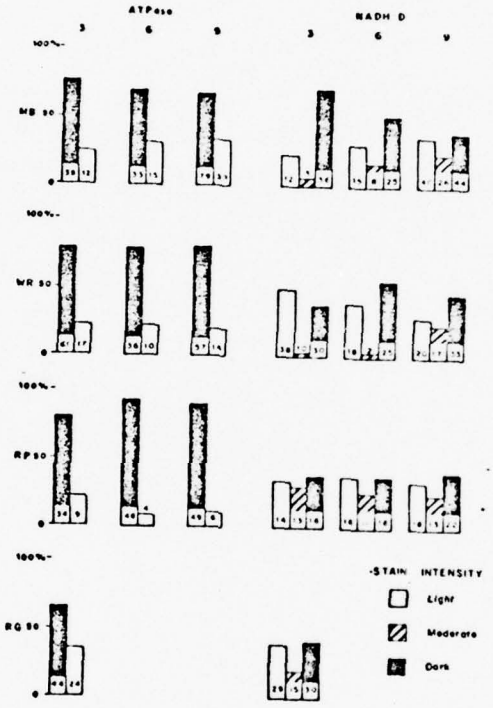


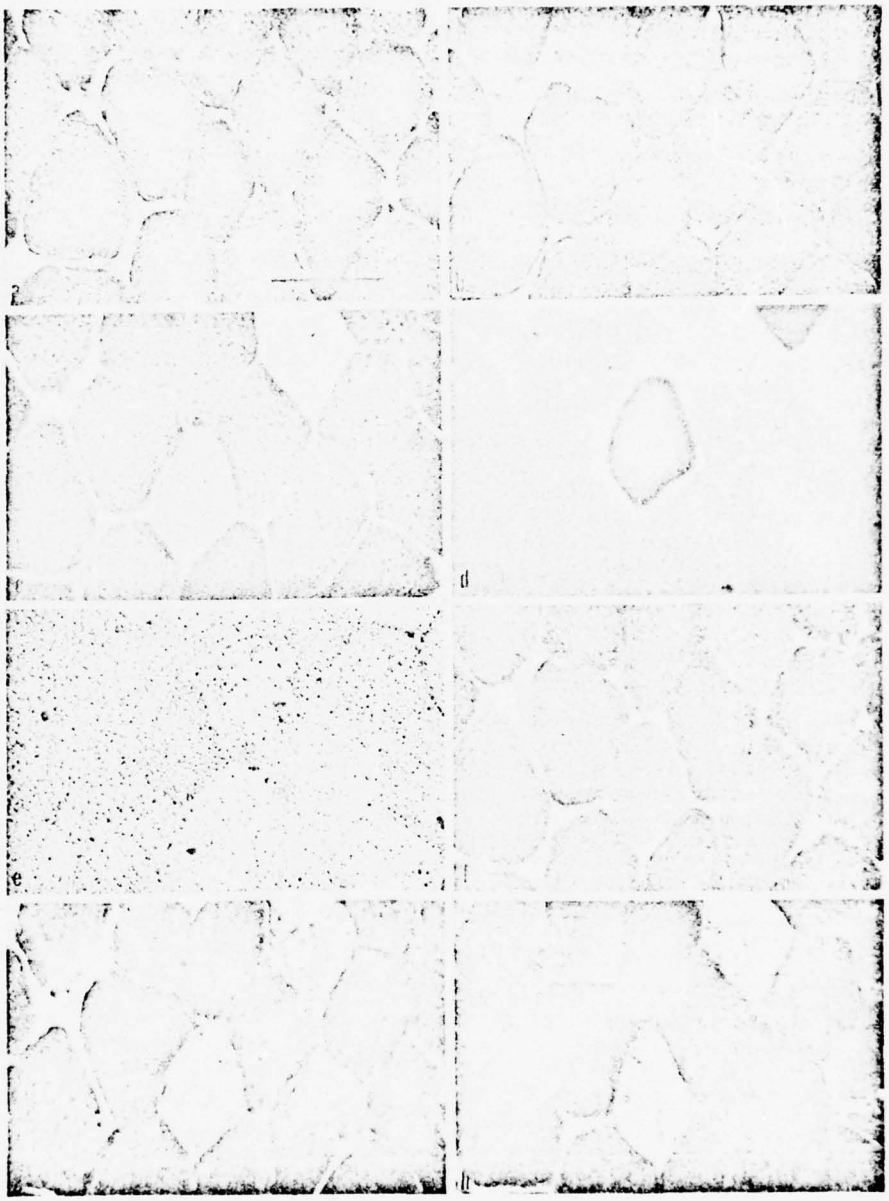
Figure 9

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Figure 10



INVESTIGATION 3

STRENGTH, ENDURANCE, AND THE AMPLITUDE AND FREQUENCY OF THE EMG DURING ISOMETRIC CONTRACTIONS IN MAN.

INTRODUCTION

The complexity of the waveform of the surface electromyogram makes it difficult to establish precisely its relationshiop to the activity of the underlying muscles. However, certain features of the surface EMG and its response to isometric function are known.

A clear-cut relationship has been established between the force of brief isometric contractions and the average rectified surface EMG as long as the muscles are kept at constant length (10, 12, 21, 27, 33). Also, continued strenuous activity results in an increase in the amplitude of the integrated surface EMG (7, 8, 9, 22, 23). This increase has been attributed to the recruitment of additional motor units or to the higher discharge frequencies in previously recruited units as the muscle fatigues (10).

But it is not only the amplitude of the surface EMG that can vary during sustained activity. A variety of attempts of varying degrees of sophistication, have been made to analyze the frequency of the surface EMG. Mainly, these evaluations have been concerned with the duration of the carrier wave or the Piper rhythm (7, 11, 30, 31). More sophisticated analyses have involved selective frequency amplification (5, 24, 32, 35) or Fourier analysis of the surface EMG (4). In general, these various analytical procedures show that there is little or no relationship between the frequency of the EMG and the tension generated but that there is a reduction in frequency of the carrier wave and its components in prolonged isometric contractions. The decrease in frequency has been attributed to either an increase in the wave duration of the individual motor unit action potentials or a differential fatigue in fast twitch as opposed

to slow twitch motor units (20).

Most of the experiments described above have dealt with the amplitude or frequency of the surface EMG during non-fatiguing contractions of uncontrolled length and uncertain tension. Further, only on rare occasions has any one study examined the relationship between strength, endurance, and EMG at more than one tension. The present report is of a systematic study of the relationship between isometric strength and endurance and the amplitude and frequency of the surface EMG.

METHODS

Subjects

The subjects in these experiments were 3 male and 3 female volunteers whose ages, heights and weights are listed in Table 1. All subjects were fully informed of the experimental procedures and were physically examined before being accepted as volunteer subjects.

Strength and endurance

Isometric strength and endurance were measured on a portable handgrip dynamometer similar to the one described previously by Clarke, Hellon and Lind (6). Isometric strength (MVC) was assessed as the larger of 2 brief (3 sec) maximal efforts; 3 min were allowed between these contractions. The variation in the MVC never exceeded $\pm$ 3% from day to day. The target tensions for the submaximal contractions were set in terms of the MVC established on each day. In many of the experiments described below, the subjects were asked to maintain a submaximum tension for 3 sec, or continuously until they could no longer maintain a given target. In other experiments, they maintained a continued maximum effort at 100% MVC or after a fatiguing

contraction during which the tension fell rapidly; the contraction was ended when the tension reached a pre-determined level.

Training

All the subjects were trained in hand-grip contractions 3 days per week for 4-6 weeks. Each day, after establishing their MVC, the subjects performed 5 successive contractions to fatigue at a tension of 40% MVC; 3 min were allowed between contractions. This procedure was repeated until the variation in endurance for at least 3 days was reduced to less than $\pm$ 5%.

EMG

The arm was scrubbed, and washed with acetone. The surface EMG of the forearm was measured from adhesive silver/silver chloride disc electrodes (American Hospital Supply no. 65375-030) with an active surface area of $2cm^2$. Two bipolar electrodes were placed approximately 8 cm apart over 1) the medial and 2) the lateral surfaces of the forearm. The D.C. resistance between the electrodes and the skin was always below 5000 ohms and the capacitance lay between 0.04 and 0.05μF. Care was taken to ensure that electrodes were placed in the same spot each day. The amplifier for the EMG had a differential input impedence of 10^8 ohms and a flat frequency response from D.C. to 4000 Hz. The raw EMG was recorded on a Sangamo-Tanberg series 100 FM tape recorder. Two types of analysis were performed on the recorded data. First, the EMG was digitalized and half-wave rectified and then integrated (amplitude) over 1½ sec intervals in a LINC computer. Second, the frequency of the full-wave EMG was analyzed by calculating a full wave fast Fourier transform (FFT) on the digitalized EMG data. For the purpose of this analysis, the 1.5 sec EMG sample was subdivided into 6 serial 250 ms intervals. The FFT was then calculated over each of these intervals from a fundamental frequency of 4 Hz through

the first 126 harmonics, thereby establishing an analysis of the amplitude of frequency components of the EMG from 4-508 Hz. Finally, all six power spectra were averaged to give the average frequency power spectrum over the 1.5 sec sampling period as shown in Fig. 1. This figure represents the analysis of the EMG which was sampled early and late in a fatiguing contraction at a tension of 40% MVC in one subject. To simplify the analysis, these spectra can each be represented by a single average frequency, 143 and 122 Hz, respectively, from mathematical calculations of the center of gravity of the power spectra. In the same manner, then, data presented under "Results" refers only to the average or "center frequency" of the power spectrum calculated as described here.

For the brief (3 sec) contractions, the EMG was sampled over the middle of the 3-sec interval. Due to the variability of the length of the fatiguing contractions between subjects performing exercise at any one tension, the data was sampled over 1.5 sec intervals at the onset and at 20, 40, 60, 80 and 100% of the duration of the contractions. For sustained maximum effort (i.e. with rapidly falling tension) the EMG was sampled at set time periods as described under "Results".

Statistical analysis of the data involved the calculation of means and standard deviations.

Experimental procedures

In the first two experiments we investigated the relationship of the amplitude and the center frequency of the EMG to 1) brief isometric contractions at tensions varying from 5% to 100% MVC and 2) contractions held to fatigue at submaximum tensions from 25% to 70% MVC. The remaining experiments were intended to examine some of the mechanisms concerning the changes of the amplitude and frequency found in the first 2 experiments.

The experimental procedures for those experimetns are described in the appropriate sections of the Results. In all experiments, the subjects sat quietly with their arms bared to the shoulder, with their elbows held at an angle of 90°; the environmental temperature was kept constant at 25 ± 1° C. A minimum of 24 hours was allowed between experiments on any one subject.

RESULTS

Brief isometric contractions

Five subjects participated in these experiments to examine the relationship between isometric strength and the amplitude and the center frequency of the surface EMG. After measuring the MVC, 3-sec contractions were performed at 10, 20, 40, 60, 80 and 100% MVC; 3 min were allowed between contractions. Each subject performed this procedure in replicate. The results are shown in Fig. 2. Analysis of the data showed that although the amplitude of the EMG was greater on the lateral surfaces of the forearm, the pattern of response of the amplitude and the frequency to the brief tension (and for endurance in subsequent series of experiments) was the same on both surfaces of the arm. Therefore, the data from both surfaces of the forearm were pooled. Each point in Fig. 2 represents the average $\pm$ S. D. of the EMG recorded from the 5 subjects on 2 different occasions. As has been reported by others, we found a linear relationship between the amplitude of the EMG and the tension exerted in brief isometric contractions. It was noteworthy that the data relating strength and EMG amplitude on any one subject was as linear as that of the mean. But there was a large inter-subject variation in the absolute amplitude of the EMG; the co-

efficient of variation was 28%. There was a surprisingly high coefficient of variation (14%) for the results on any one subject in spite of the care taken in preparing the skin and in ensuring that the electrodes were always placed in the same spot each day. However, this large variation was markedly reduced by normalizing the EMG amplitudes in terms of the EMG amplitude during the MVC at the start of each experiment. This maneuver resulted in a reduction of the coefficient of variation for the group to only $\pm$ 4.6%. All the data from other experiments reported below have been treated in this way.

In contrast to the direct relationship between increasing tension and the amplitude, the center frequency of the surface EMG was remarkably constant between subjects and was independent of the tension exerted, averaging 152.5 $\pm$ 4.8 Hz for tensions of 10, 20, 40, 60, 80 or 100% MVC. Two lower tensions (1 and 5% MVC) were examined in 2 of the subjects, and they also showed no difference in the center frequency from any of the other tensions. Unlike the amplitude, the center frequency had a low variability in day-by-day experiments.

Sub-maximum tensions held to fatigue

The amplitude and center frequency of the power spectra during fatiguing isometric contractions at tensions of 25, 40, 55 and 70% MVC are illustrated in Fig. 3. As in the previous experiment, each point illustrates the average results obtained during 2 endurance contractions performed on 2 separate days for each of the same 5 subjects examined in the first experiment.

The average endurance times of the contractions $\pm$ S.D. for these 5 subjects were 353.6 $\pm$ 92.7, 138.8 $\pm$ 26.8, 70.0 $\pm$ 14.9, and 38.4 $\pm$ 7.9 sec for tensions of 25, 40, 55 and 70% MVC respectively. At the onset of the contraction, there was a linear relationship between the amplitude and the

tension exerted, as expected from the earlier results. As the contraction continued, there was an approximately linear increase in the amplitude of the EMG which was nearly parallel for all 4 tensions examined. Thus, at any time during a fatiguing contraction, the amplitude of the EMG was a function of at least 2 variables: 1) the tension exerted and 2) the degree of fatigue in the muscle. In the upper panel of Fig. 3 is the change in the center frequency for all 4 tensions. The center frequency was constant for all 4 tensions, falling in linear fashion from an average of 153 Hz to 116 Hz, at the point of fatigue.

Figure 4 shows the data represented in Figs. 2 and 3, as well as additional data from a further experiment. In the bottom panel of Fig. 4, the solid line represents the average amplitude for brief maximum contractions held to fatigue at 25, 40, 55 and 70% MVC; the solid points at the tip of each arrow shows the amplitude at fatigue. The increase in amplitude during these fatiguing contractions was about 30% at all tensions.

In the upper panel of Fig. 4 the solid line shows the center frequencies of the EMG for brief contractions. The arrows and the points show the decrease and the final center frequency at fatigue at the 4 tensions; the reduction was always by the same amount, some 25% at all tensions.

In addition, our subjects held a sustained maximal effort, during which the tension fell rapidly and linearly; the contraction ended when the tension had fallen to 70% MVC. The average duration of this contraction was 14.4 sec. During that time, the amplitude fell linearly and in parallel with the tension, and reached the same value as that found at the start of a fatiguing contraction at 70% MVC. The center frequency, however, fell rapidly from 153 to 116 Hz within 5 sec and remained at that level for the remainder of the contraction.

To pursue the concept of maximal effort, but in different circumstances we conducted the following experiments. Two subjects each held fatiguing contractions at 40% and 70% MVC. After they had reached the point of fatigue at the original target tension, the subjects went on to exert a continued maximum effort until the tension had fallen by another 15% MVC (i.e. to 25% and 55% MVC respectively). Figure 5 shows that during the regular fatiguing contractions, while the tension remained constant, the amplitude increased linearly and the center frequency decreased linearly in the same fashion as described in Figs. 2 and 3. After the 70% MVC, the tension during the sustained maximum effort fell linearly to 55% MVC in an average time of 18 sec, whereas after the 40% MVC, the tension did not fall linearly, and took 27 sec to reach 25% MVC. As the tension fell, so did the amplitude, in parallel. The center frequency, however, remained at the same value as that found at the point fatigue where the target tensions of 40% and 70% MVC could no longer be held.

It is worth noting that in this procedure, when the tensions had reached 25% and 55% MVC respectively, the EMG amplitude had decreased to the levels found at the end of a contraction sustained to fatigue at those tensions (compare with Fig. 3).

Changes in strength and its associated EMG during fatiguing sub-maximum contractions.

At set intervals during sustained, fatiguing contractions at 25, 40, 55 and 70% MVC, 3 subjects exerted brief maximal efforts. Figure 6 shows the results obtained at all 4 tensions. In each case, there was a linear reduction of strength throughout the fatiguing contraction; also, the center frequency fell linearly throughout the contraction and was unaffected by the brief maximal efforts. The changes in amplitude were markedly different,

however, depending on the tension exerted continuously to fatigue. In all cases the amplitude increased throughout the sustained sub-maximal tensions in the manner described earlier (Fig. 3). But, in response to the successive brief maximal efforts during the sustained sub-maximal contractions, the amplitude showed variations from the extremes of a linear fall throughout the contraction at 25% MVC to no change at all throughout the contraction at 70% MVC.

The changes in strength, amplitude, and center frequency were also measured at intervals during the 20 min after each of these fatiguing contractions. Strength always took longer than 7 min to recover to the control level, whereas amplitude and center frequency had recovered within 3 min and 1 min respectively.

Changes in EMG during successive fatiguing contractions

Three subjects performed 6 successive contractions to fatigue at 40% MVC. On separate occasions, the interval between the contractions was 15 sec, 1, 3, 7, or 20 min. When the interval was 3 min or longer there was no difference in the amplitude or the center frequency throughout the 40% MVC; hence the results in experiments with intervals of 7 and 20 min have been omitted from Fig. 7. The values of both the amplitude and the center frequency at the start of the contractions are shown as open symbols and those at the end of the contractions are represented by closed symbols. When the interval between the successive contractions was 3 min, the amplitude at the start of each contraction was the same and had increased to the same amount at the point of fatigue. But when the interval was 1 min, and more so when it was 15 sec, the second and later contractions began with a markedly higher amplitude than in the first contraction. Also, the amplitude at the end of the second and subsequent contractions was slightly

but progressively higher ($P=<0.01$) as the interval between the contractions decreased to 1 min and 15 sec. The center frequency always started at the same value in the successive contractions, 152 Hz, except when the interval between contractions was only 15 sec. In those circumstances the second and subsequent contractions began with a center frequency reduced to 142 Hz. The center frequency was always at the same value, 116 Hz, at the end of each contraction.

The influence of circulatory occlusion on the EMG during fatiguing isometric contractions.

Five subjects performed two successive contractions. Before the first contraction, the circulation to the arm was occluded by a pneumatic cuff inflated to 300 mm Hg. The cuff remained inflated during a contraction to fatigue at 40% MVC, a rest period of 30 sec and a subsequent sustained maximal effort, held for 15 sec. In the second contraction, the tension started just below 40% MVC and fell steadily; the average tension was 34% MVC for the 15 sec contraction.

Figure 8 shows the changes in amplitude and center frequency during these contractions. In the first contraction, the amplitude increased, but only by some two-thirds of the increase found when there is a free circulation (compare with Fig. 4) while the center frequency fell to the same value found with a free circulation. Thirty seconds later, when the second contraction started, the amplitude was about half-way between the values found at the start and the end of the first contraction; thereafter the amplitude fell, as tension fell. The center frequency, at the start of the second contraction, showed a slight recovery (6%) from its level at the point of fatigue of the first contraction. Within 3 sec the center frequency had fallen again to its lowest value and remained at that level throughout the remainder of the second contraction.

DISCUSSION

As reported by others, (2, 10, 12, 21, 27) we found a linear relationship between the amplitude of the halfwave rectified and integrated surface EMG and muscular force for a brief isometric contraction. The higher EMG amplitude required to obtain these tensions has been attributed to the additive effects on the surface EMG of muscle fiber recruitment, found predominently at lower tensions, and an increase in the frequency of firing of previously recruited motor units, usually found during contractions performed at higher tensions (27). However, the frequency of the surface EMG was independent of the tension exerted and was presumably independent of the frequency of firing or recruitment in the motor units as well. These results agree with those of Kaiser and Peterson (15) who also found the frequency of the surface EMG to be independent of the EMG amplitude, tension exerted, or the frequency of firing of motor units for brief contractions of undefined strength in the M. orbicularis oris, M. tibialis anterior and M. biceps brachii muscles in man.

During fatiguing isometric contractions, the amplitude of the surface EMG increased almost linearly, by about 30%, to fatigue for any of the 4 submaximal tensions examined. However, at fatigue, the amplitude of the surface EMG was still directly related to the tension exerted. Thus, with the exception of the contractions performed at 70% MVC, the integrated EMG amplitude at fatigue was substantially less than that recorded for a brief MVC.

In its simplest interpretation, the increase in EMG amplitude during the fatiguing contractions for any of the 4 submaximal tensions examined could be attributed to a compensatory increase in either the frequency of

firing of previously recruited motor units or to an increase in recruitment to maintain the target tension in the face of fatiuging muscle fibers. However, except for the contractions at 70% MVC, the total integrated electrical activity at fatigue was less than that for a brief MVC. At 70% MVC, the evidence supports the view that fatigue is caused by biochemical events in the muscle fibers and not by failure of transmission either at the neuromuscular junction or at the membranes of the muscle fibers. When the contractions are held at tensions of 55% MVC or less, fatigue appears to involve some failure of the excitation mechanism. The decrease in maximum strength during contractions at 25, 40 and 55% MVC was substantially greater than the decrease seen in the maximal electrical activity. We are forced to conclude that a substantial degree of mechanical or contractile fatigue must be present at those tensions. The greater proportion of electrical failure during fatiguing contractions performed at lower tensions seems to indicate that the proportion of mechanical contractile failure at fatigue is directly related to the tension exerted, becoming the predominent or the sole cause of fatigue for isometric exercise performed at 70% MVC.

We were surprised to find that the maximum force for brief contractions fell linearly during fatiguing contractions at all tensions that we examined. While the amplitude of the EMG during such contractions decreased linearly during fatiguing contractions at 25% MVC, it did not fall as fast as the maximal strength of the muscles, thereby implicating some degree of failure of electrical transmission as the contraction progressed. As the tension increased, progressively lower reduction in the amplitude of the EMG were seen in response to brief maximal efforts during the sustained sub-maximal effort, until, at a tension of 70% MVC, no failure of electrical transmission was apparent.

The exact location of failure in electrical transmission remains unknown. A number of possibilities have been suggested including pre-synaptic failure (17), neuromuscular failure (3, 34) and a failure of the muscle fiber membrane to propagate an action potential (1). Although transmission fatigue in the central nervous system has been suggested by some, the evidence put forward by Merton (26), by Stephens and Taylor (33), and in this investigation (see Figure 11) points to the peripheral nature of muscular fatigue.

Stephens and Taylor (33) reported that, during sustained maximal effort, the tension fell linearly with time for the first minute, during which there was a parallel fall in EMG amplitude, suggesting to them that electrical failure was the causative agent for fatigue over that period of time. And, although Merton (26) was unable to detect electrical failure under similar circumstances, in a more recent paper (25) he found that the firing frequencies of the adductor pollicus during maximal effort can reach frequencies in excess of 100 Hz, frequencies which have been shown to cause rapid electrical failure (3, 34).

In summary, then, at any point in time, the EMG amplitude is a compound variable influence by 1) the tension exerted, 2) the degree of fatigue developed during that exertion, and 3) the previous degree of fatigue developed in the muscle. The mechanism of muscular fatigue appears to have a tripartite relation with the tension exerted. It is a combination of failure in biochemical events and in transmission, dependent on the tension exerted. At high tensions, the failure appears to be biochemical in nature, and as the tension is reduced a progressively greater proportion of transmission failure appears to occur. This evidence must be given appropriate

concern in future considerations of the role of recruitment and rate coding of motor units involved in sustained contractions at varying levels of sub-maximal tensions.

As reported by others we found a decrease in EMG frequency in fatiguing muscle, (4, 5, 13, 14, 15, 18, 20, 23, 24, 28, 29). But whereas the amplitude of EMG was a function of a number of variables, the center frequency of the EMG power spectra proved to be an excellent index of muscle fatigue. The center frequency was linearly but inversely related only to the degree of fatigue for both sub-maximum tensions held to fatigue for contractions involving maximum effort. The mechanism of this phenomenon has been attributed to an increase in the duration of the motor unit potentials (20). Subsequent work by Mortimer, et al. (28) has shown that both lactic acid or a related reduction in pH, but not anoxia alone, can cause such an increase in the duration of motor unit action potentials. However, Karlsson, et al. (16) and Lind, et al. (19) have clearly shown that both intracellular and extracellular lactate remain elevated and pH remains reduced (19) for some 10 min following fatiguing static effort. Further, the absolute level of muscle lactate is not the same at fatigue for contractions performed at a wide range of sub-maximal tensions, whereas the center frequency of the EMG is identical at fatigue for all tensions. Finally, our experiments show that for serial fatiguing contractions the frequency of the surface EMG recovers in less than 1 min. These findings, along with those reported above, suggest that lactate cannot be the causative agent of muscular fatigue.

Although the results from the present investigation shed no further light on the causative agent for fatigue it seems reasonable to suggest that the agent is biochemical in nature, released in the muscle during

isometric contractions, since occlusion of the forearm prevents recovery of the center frequency of the EMG. Whatever the factor may be which is responsible for this effect, that factor must increase rapidly in concentration during exertion and must be cleared rapidly ($\frac{1}{2}$ time = 15 sec) from the muscle following the cessation of contraction. Whatever the factor may be, it causes the center frequency of the EMG to decrease to the same point irrespective of the tension exerted and thereby provides a good non-invasive tool by which to assess muscular fatigue.

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Table 1. GENERAL CHARACTERISTICS OF SUBJECTS

Subject	Sex	Ht. (cm)	Weight (Kg)	Age (yrs)
JP	M	187.9	118.2	27
MC	M	184.8	68.9	24
SL	M	190.5	98.1	23
CW	F	167.6	61.3	28
DB	F	168.9	56.7	24
RM	F	177.8	61.4	26

FIGURE LEGENDS

Figure 1: Showing the average frequency histogram of the surface EMG sampled over a 1.5 second period early (———) and late (....) in an isometric contraction of 40% MVC held to fatigue. The center frequency of the power spectrum early in the contraction was 143 Hz and late in the contraction was 122 Hz.

Figure 2: This figure shows the relationship between the center frequency of the power spectrum (upper part), the integrated amplitude (lower part), and tension exerted in brief, 3-sec isometric contractions. Each point represents the mean $\pm$ S.D. for 2 contractions on each of 5 subjects.

Figure 3: Showing the integrated amplitude (lower panel) and the center frequency (upper panel) of the surface EMG throughout the duration of fatiguing isometric contractions at 25, 40, 55 and 70% MVC. Each point represents the mean of 2 experiments on the 5 subjects.

Figure 4: Showing the data presented in Figs. 2 and 3. The solid lines represent the relationship between the integrated amplitude (lower part) and the center frequency (upper part) at the start of contractions at various isometric tensions. The arrows point the direction of change of the integrated amplitude and the center frequency to the values reached at fatigue as sustained, sub-maximal tensions. Also shown by arrows are the directions of changes in the integrated amplitude and the center frequency of the surface EMG when a maximal effort was maintained until the tension had fallen to 70% MVC.

Figure 5: Showing the average results from 2 experiments on 5 subjects who held sub-maximal isometric tensions of 40 and 70% MVC to fatigue and thereafter sustained a maximal effort until the tension had fallen to 25 and 55% MVC respectively. The tension (△) and the integrated amplitude (□) and the center frequency (●) of the surface EMG are shown. It should be noted that the abscissa first represents normalized duration of the sub-maximum tension to fatigue and thereafter represents a reduction of tension which has no absolute or relative time relationship.

Figure 6: The subjects exerted their maximal effort at various periods throughout contractions held to fatigue at sub-maximal tensions (lower panels) varying from 25 to 70% MVC. In the upper panels are shown the integrated amplitudes of the EMG throughout these experiments. The results are the mean of 2 experiments on 3 subjects.

Figure 7: Showing the average integrated amplitudes (lower panel) and center frequencies (upper panel) at the start (open symbols) and end (closed symbols) of 6 successive contractions (C_1 to C_6) at a tension of 40% MVC with intervals of 15 sec. (0), 1 min (▱) and 3 min (△) between the contractions.

Figure 8: Illustrated here is the integrated amplitude (lower panel) and center frequency (upper panel) of the surface EMG recorded during 2 successive fatiguing contractions at a tension of 40% MVC when the arterial blood supply to the arm was arrested. In the second contraction (o), which began 15 sec after the first (●) had ended, the center frequency was only 6% higher than at fatigue and quickly fell to and remained at the value found with fatigue. The integrated amplitude had not returned to its original value, and fell throughout the second contraction.

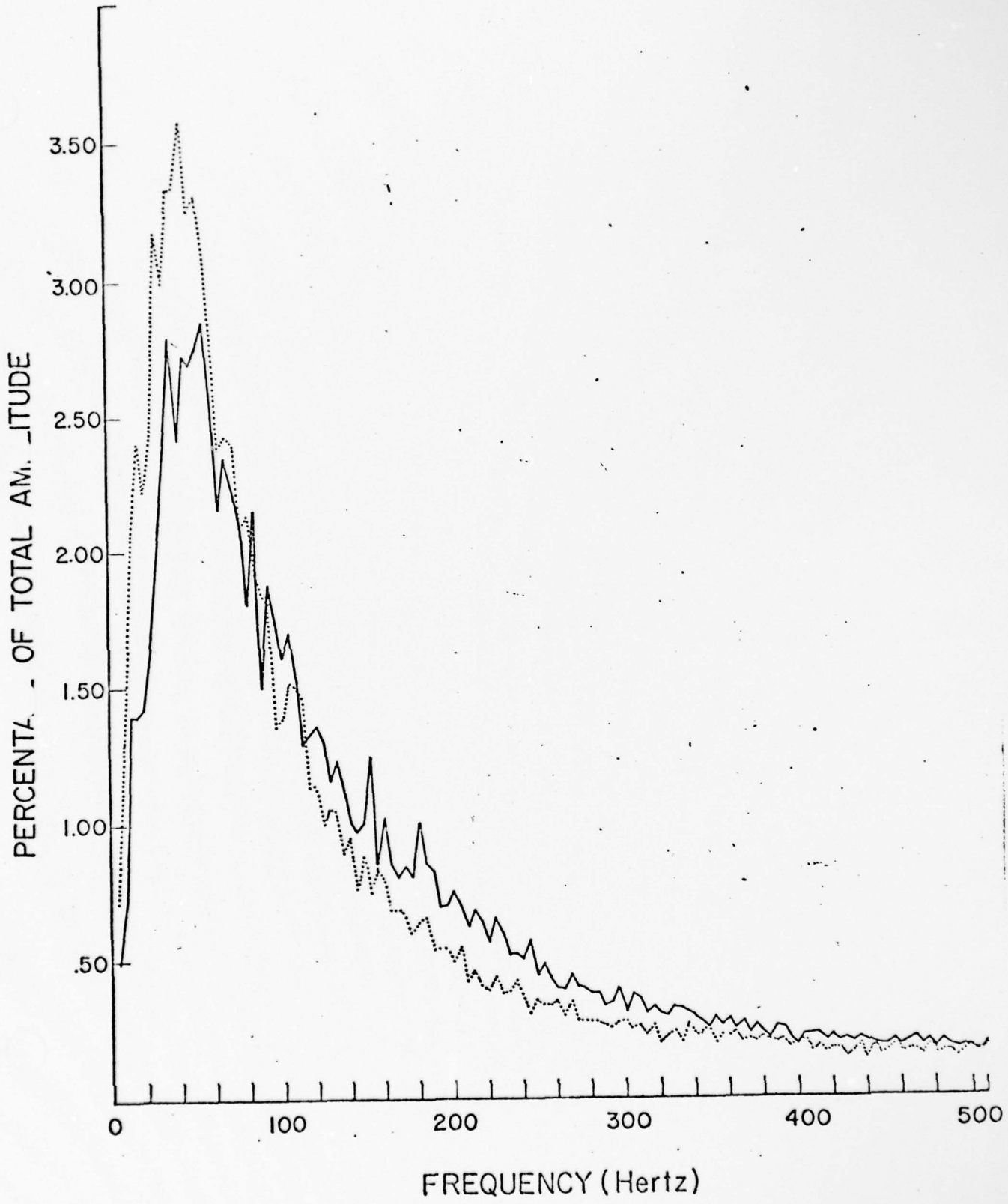

3.50
3.00
2.50
2.00
1.50
1.00
.50
PERCENTA - OF TOTAL AM. ITUDE
0
100
200
300
400
500
FREQUENCY (Hertz)

FIGURE 1

brief maximal efforts. The changes in amplitude were markedly different,

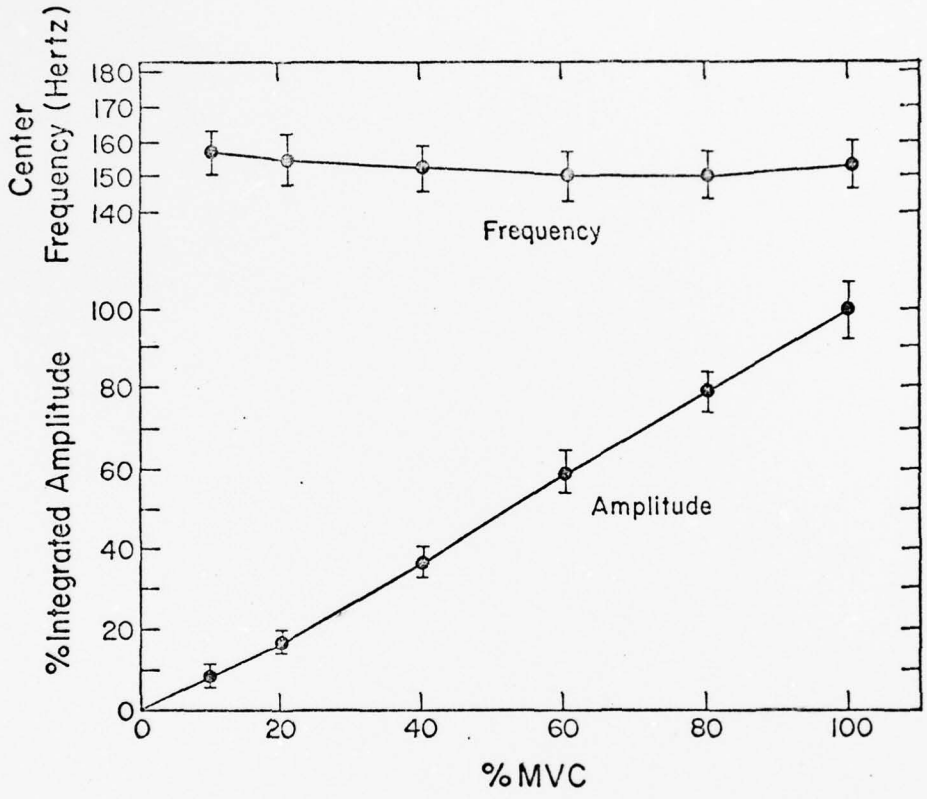


FIGURE 2

amplitude at the end of the second and subsequent contractions was slightly

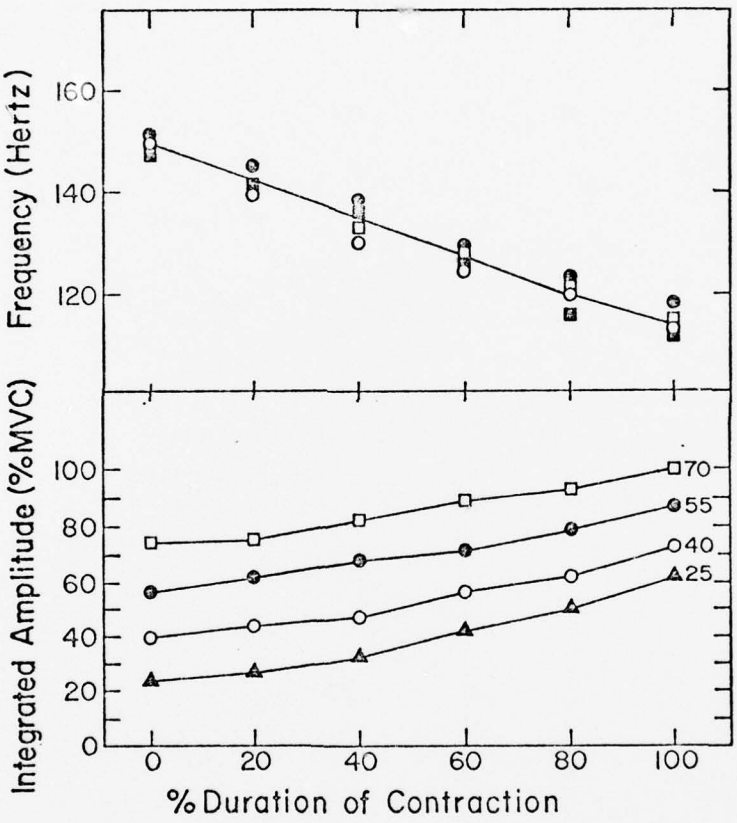


FIGURE 3

fallen again to its lowest value and remained at that level throughout the remainder of the second contraction.

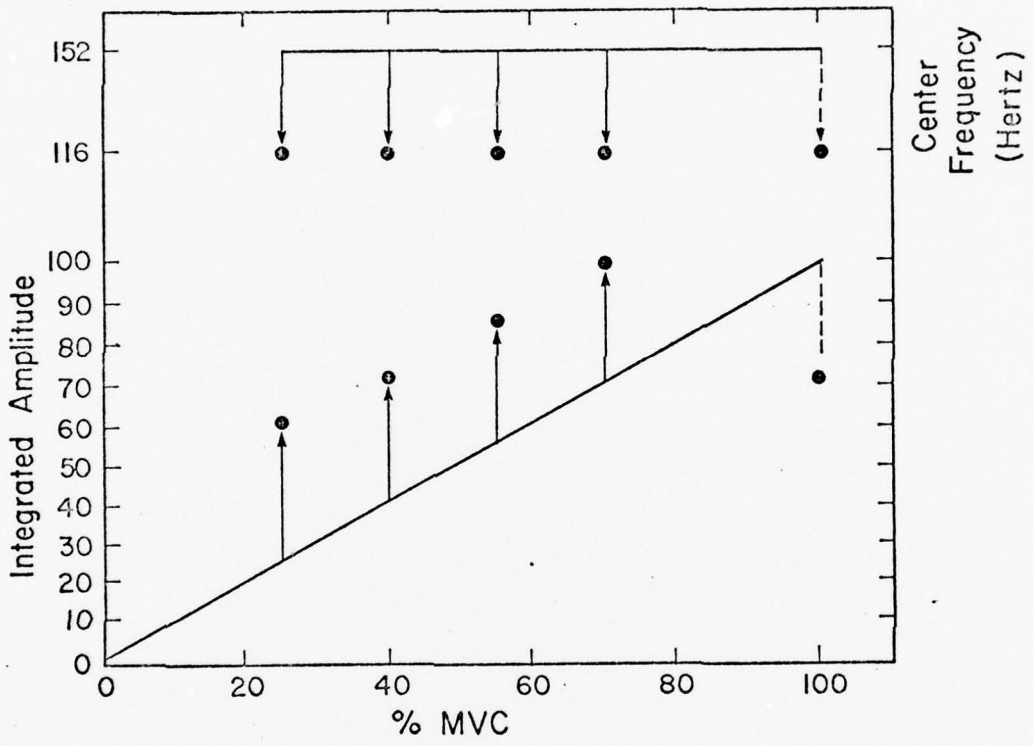


FIGURE 4

could be attributed to a compensatory increase in either the frequency of

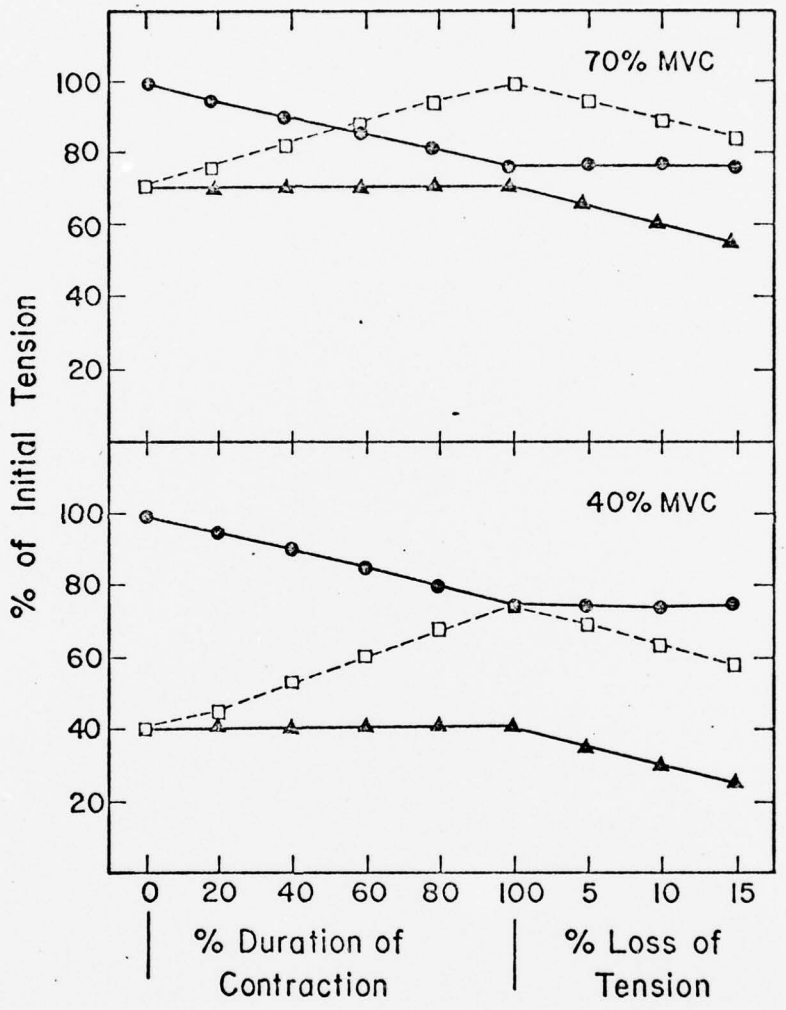


FIGURE 5

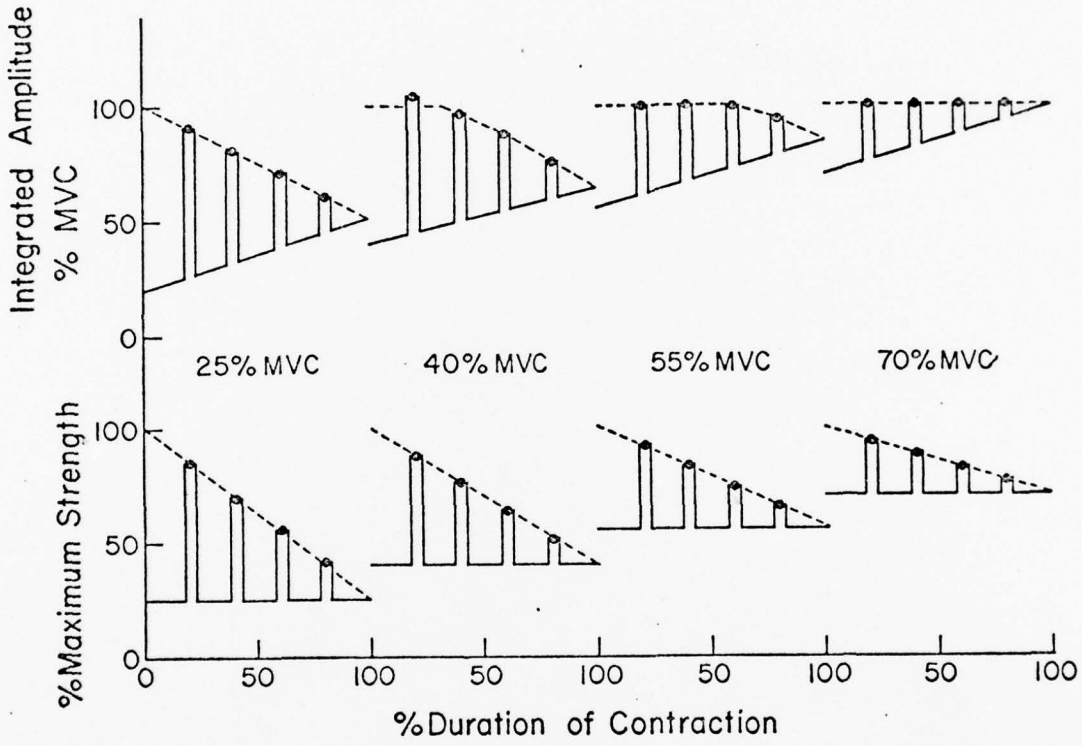

Integrated Amplitude
% MVC
100
50
0
25% MVC
40% MVC
55% MVC
70% MVC
%Maximum Strength
100
50
0
0
50
100
50
100
50
100
50
100
%Duration of Contraction

FIGURE 6

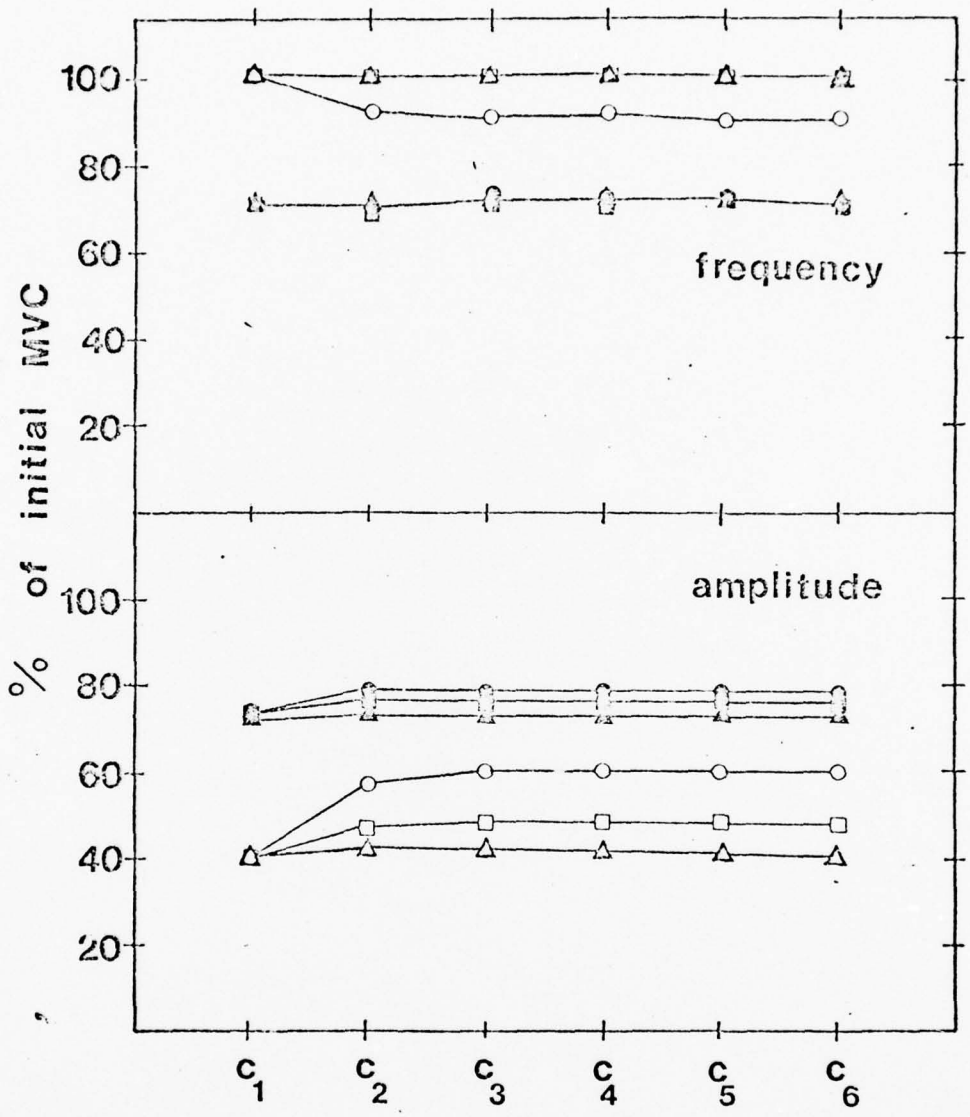

100
80
60
40
20
% of initial MVC
frequency
amplitude
100
80
60
40
20
C1
C2
C3
C4
C5
C6

FIGURE 7

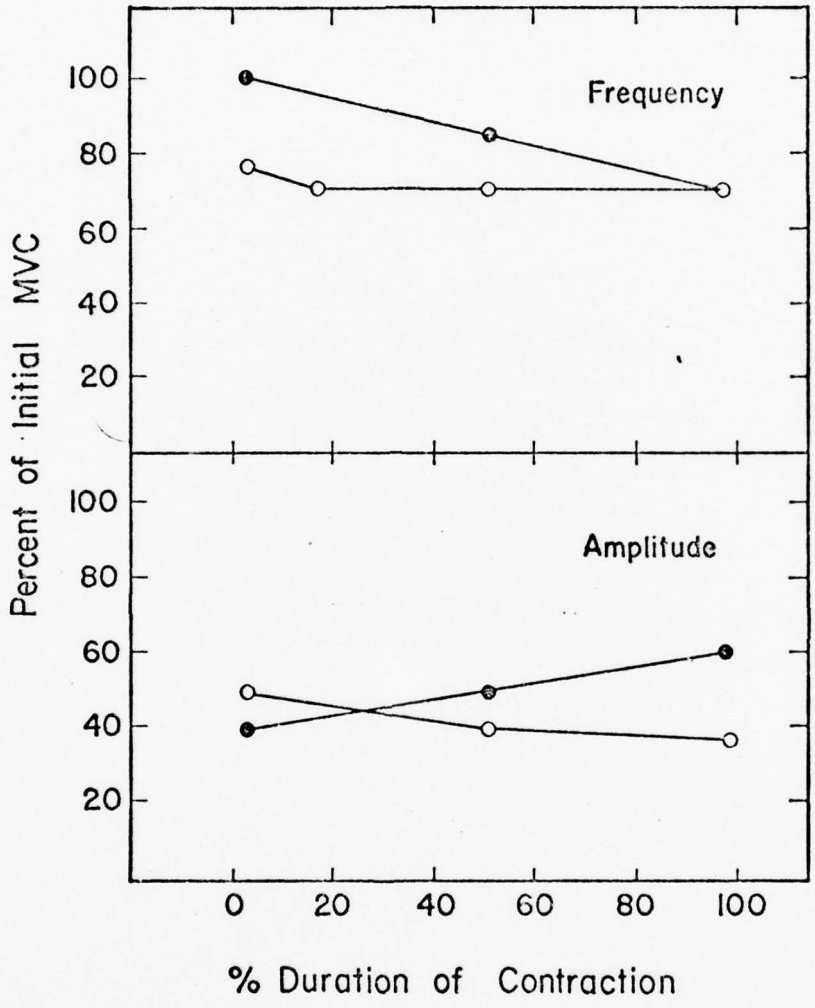

Frequency
Amplitude
Percent of Initial MVC
100
80
60
40
20
0
20
40
60
80
100
% Duration of Contraction

FIGURE 8

INVESTIGATION 4

THE RELATIONSHIP BETWEEN ELECTROMYOGRAPHIC ACTIVITY AND LOCAL BLOOD FLOW DURING CONTRACTIONS.

INTRODUCTION

In our search to understand the nature of muscular fatigue, too little attention has been paid to the electromyogram and the relationship between it and other physiological events in the muscle. In the past, Edwards and Lippold (3), and many others since, have shown that in the calf muscles, a linear relationship exists between the integrated amplitude of the EMG from surface electrodes and the isometric tension exerted provided that the muscle's length remained constant. After muscular fatigue, Edwards and Lippold (3) showed that the relationship between tension and the integrated amplitude of the EMG was still linear but at any given tension the integrated amplitude was higher. In recent reports, Milner-Brown and Stein (12) and Maton (11) have shown a direct relationship between electromyograms obtained simultaneously from both surface and needle electrodes. Also, Lind and Petrofsky (8,9) have presented evidence to correlate the findings of these and other authors in showing the inter-relationships between motor unit function and the development of the maintenance of sub-maximum tensions to fatigue.

Little attention has been paid to the relationship between the electromyogram and the blood flow through muscles. Lind, Taylor, Humphreys, Kennelly and Donald (10) used the electromyograph as a means to identify the existence of muscular activity in other limbs while the "test" limb was active. They concluded that the blood flow in the "inactive" limbs increased only in the presence of electromyographic activity. After the present investigation had begun, the view put forward by Lind, et al. (10) was disputed by Eklund, Kaijser and Knutsson (4). Eklund, et al. claimed that blood flow in the contralateral arm is always increased during isometric contraction

of muscles in the test arm whether or not electromyographic activity was present. They also claimed that "stray" electromyographic activity occurred in their experiments with no increase in local blood flow and that the extent of that "stray" activity could be increased 8-10 fold before it gave rise to an increase in blood flow. This suggestion was startling, since it refuted the view held since Gaskell (5) that any muscular activity resulted in local increase in blood flow due to metabolic factors.

The present experiments were designed to examine the relationships between the electromyogram and the blood flow in both arms during isometric contractions in one of them. In addition, since the report by Eklund, et al., we have paid particular attention to the blood flow in limbs in which some EMG activity occurred, irrespective of whether that activity was intended.

METHODS

Subjects

Twelve healthy men and women volunteered to act as subjects. The methods and procedures to be used were carefully explained to them. They were medically examined, including a treadmill stress-test (ECG) and a pulmonary function test; each subject signed a statement of informed consent before taking part in the investigation.

Forearm blood flows were measured by the Whitney (14) mercury-in-rubber strain-gauge plethysmograph. The electromyogram was recorded from silver/silver chloride electrodes placed over the muscles of the forearm. The

position of the electrodes was carefully measured to permit replacement of the electrodes on the same place in repeated experiments. The output from those electrodes was recorded simultaneously: 1) as a raw electromyogram on tape for later processing and 2) on a Honeywell 1560 UV recorder, after integration. A hand-grip dynamometer similar to that described by Clarke, et al. (1) was used in these experiments; specially sensitive amplification was provided to allow the accurate control of low isometric tensions.

Half of the subjects were trained in the use of the hand-grip dynamometer and the other half of the subjects were untrained.

In any one experiment, the MVC for the subject was assessed as the largest of three contractions (each lasting 3 sec) with a 3-min interval between them. After a further 3 min of rest, a series of brief contractions (3 to 5 sec) were made at minute intervals at tensions varying from 1% to 80% MVC. There followed a period of 5-min rest, after which the subject performed a series of contractions at 1, 3, 5, 7 and 10% MVC each held for long enough (1 to 3 min, depending on the tension) to establish a steady-state blood flow. After another 5 min rest period, the subject completed a fatiguing contraction at 20, 25 or 30% MVC. Within 2 minutes, he repeated the series of contractions at 1, 3, 5, 7 and 10% MVC. The surface EMG was recorded at all tensions, including the maximal effort.

RESULTS

For each subject, there was a linear relationship between the brief isometric contractions at tensions between 1% and 80% MVC and the integrated surface EMG (Fig 1). It is quite clear that for any one subject the fraction

of the tension applied could be interchangeably represented by the resultant integrated action potential.

Figure 2 shows the blood flow through the forearm in one subject throughout one experimental sequence. Similar results were obtained on all the other subjects. After one minute's rest, the subject exerted serial contractions of 1-minute duration at 1, 3 and 5% MVC and of 2-minute duration at 10% MVC, with a 1-minute interval between each contraction. At each tension, the forearm blood flow rose to reach a steady-state level which was higher than the resting value and which was graded with the tension exerted. During the rest periods, the blood flow always returned to or close to the resting level before the next contraction.

Figure 3 shows results from a different subject but from a similar experiment. In this case the open symbols represent the first forearm blood flow measured after the tension was exerted, within 3 seconds of the start of the contraction, while the closed symbols represent the steady-state blood flow after 1 to 3 min of contraction, depending on the tension exerted. Two discrete curves were obtained, each showing a direct relationship between blood flow and isometric tension. Similar results were obtained from all subjects.

Figure 4 shows the relationship between blood flow and the integrated action potentials during isometric contractions at tensions between 1% and 40%. The open circles represent the blood flow within 3 seconds of the start of each contraction (in the case of tensions of 25% and 40% MVC the contractions were held for 10-15 seconds). The closed circles represent the integrated EMG at tensions of 1% to 10% MVC when steady-state levels of blood flow had been reached. The triangular symbols in Fig 4 show the

relationship between the integrated EMG and blood flow throughout a fatiguing contraction at 30% MVC; because of arm tremor the blood flows could be measured for only the first two-thirds of the contraction.

The results in Fig. 4 show that the blood flow early in an isometric contraction increased with tension up to 10% MVC, but then did not increase further with tension up to 40% MVC. The steady-state blood flows at tensions up to 10% MVC were associated with increased levels of integrated EMG which had also reached a steady-state. But during the fatiguing contraction at 30% MVC the blood flow increased rapidly at first and then more slowly whereas the integrated EMG increased in an approximately linear fashion throughout the contraction, in the same way as has been described elsewhere (8).

In experiments where the EMG and forearm blood flow was measured on one arm while the other arm performed hand-grip contractions, six of our subjects were able to perform hand-grip contractions in one arm with no EMG activity in the other arm for the bulk (80% or more of the duration of a contraction held to fatigue) of the experiment. The other six subjects were unable to perform a contraction in one arm without some EMG activity in the "resting" arm; the EMG activity in the "resting" arm of these subjects was directly related to the forearm blood flow, in experiments similar to those illustrated if Figs. 3 and 4. Figure 5 illustrates the results from one subject, whose forearm blood flows and EMG's were measured during sustained contractions of 1-10% MVC, and in which the steady-state blood flows and EMG's are shown as closed circles. Also shown in Fig. 5, represented by open circles, are the integrated values for EMG and the forearm blood flows in a "resting" arm while the other arm was involved in a hand-grip contraction to fatigue at 30% MVC. Obviously, the amount of EMG activity was directly related to the increase in blood flow.

Three of the subjects in whom hand-grip contractions were able (until

fatigue was approached) to avoid EMG activity and the associated increase in the blood flow in the contralateral ("resting") arm,performed the same experiments when the contralateral arm was immersed in water at 40° C. In these circumstances, the forearm blood flow increased in the contralateral arm to values some 3-fold greater than in the test arm; the increase in forearm blood flows in these conditions is confined to skin vessels (2). In these experiments, the isometric contraction of the other arm results in an increase in mean arterial blood pressure (6, 10, 13). In these experiments, the mean arterial blood pressure increased by some 30 mm Hg while the blood flow in the "resting" arm did not increase over the 2 minutes in which the other arm contracted.

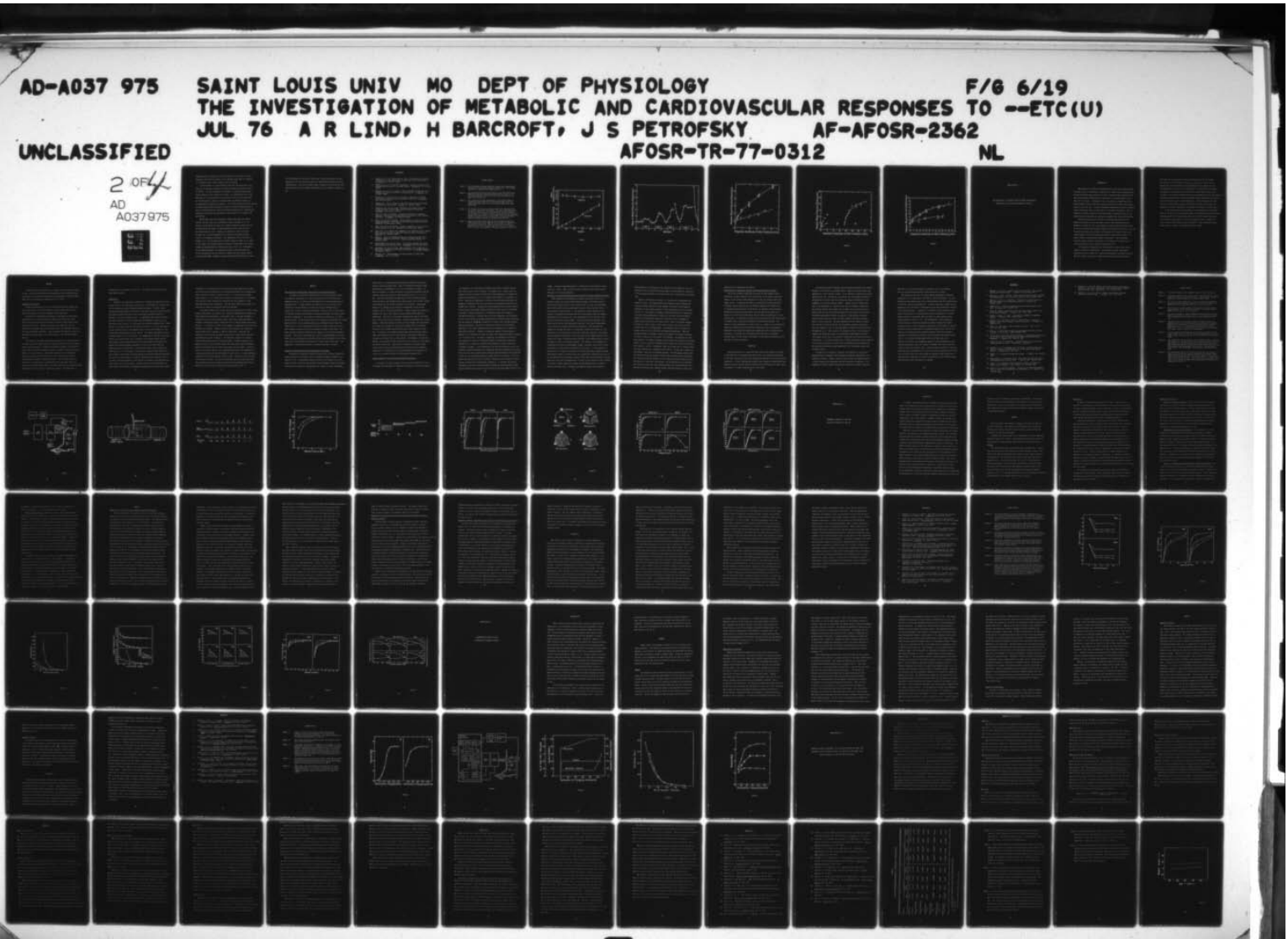
DISCUSSION

The present findings show that there is marked difference, with time, in the absolute relationship between EMG and forearm blood flow at low isometric tensions. Early in these contractions, the increase in blood flow was clear but much lower than the blood flows found in steady-state values. It has been clearly shown before (7) that the time taken to establish a steady-state blood flow is directly related to the tension exerted and may take several minutes to develop. Since the increase in blood pressure in such contractions follows a similar temporal pattern,it is tempting to believe that an important factor involved in the early change in blood flow is the dilatation of local vessels. The continued increase in blood flow towards a steady-state condition may be due to the increased perfusion pressure, possibly combined with a continuing development of vasodilatation. While the mechanism for local dilatation of blood vessels

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during exercise is believed to be solely metabolic in origin,it is worth keeping in mind that the rapidity of the response might make it worthwhile to re-consider that a neural component may be involved.

In this respect it is interesting to note that the blood flow at the start of an isometric contraction increases linearly with tensions from 1% to 10% MVC. In these conditions the influence of increased tissue hydrostatic pressure can be expected to be small. At tensions from 10% to 40% MVC there is no clear increase in the blood flow in the first few seconds of the contraction, despite an expected large and opposing increase in the hydrostatic intramuscular pressure. It is hard to believe that the increase in blood pressure found in isometric exercise can have increased enough in the few seconds involved to offset the presumed differences in intramuscular pressure, resulting in the same amount of blood flow at, for example, 10% and 40% MVC.

The evidence from these experiments supports the views put forward earlier (10) and refutes the contradictory views of Eklund, et al. (4). However, the data shown in their Fig. 2 showed a greater increase than can be accounted for by release of vasoconstrictor control which can do no more than double the flow. Thereby, the increase in blood flow shown in their Fig. 2 can be explained only in terms of cholinergic dilator-control or by metabolic dilatation. Our experiments differ from those of Eklund, et al. (4) (and agree with the earlier report by Lind, et al. (10)) in that half of our subjects showed no increase in blood flow of the contralateral arm during isometric contractions in the 'test' arm. Furthermore, in our remaining subjects who showed an increase in forearm blood flow in the contralateral arm, the increase in blood flow was directly related to the increased EMG. Eklund et al have stated that EMG activity can occur

in an arm without an increase in blood flow. This view violates the long-adopted view (5) that muscular activity is inevitably associated with local vasodilatation. Our results support those of Gaskell and all those who have come after him and are in direct contradiction of the findings of Eklund, et al.

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FIGURE LEGENDS

Figure 1: The relationship between isometric tension and integrated EMG during brief (10-15 sec) hand-grip contractions. The average results for 5 subjects are shown with S.D.

Figure 2: The forearm blood flow of one subject in one experiment where isometric hand-grip contractions were held for 1 min at 1, 3 and 5% MVC and for 2 min at 10% with 1 min intervals of rest after each contraction.

Figure 3: The forearm blood flows immediately (3 sec) after isometric contractions began (○) and in steady-state (▲) after the tension had been held for 1-3 min, plotted against the integrated EMG.

Figure 4: The forearm blood flow is plotted against the integrated EMG at tensions from 1% MVC to 40% MVC. The open circles represent the blood flow within 3 sec of exerting the various tensions. At low values of integrated EMG the closed circles represent the steady-state blood flows. At the higher values of the integrated EMG the triangles show the relationship between the EMG and blood flow during a fatiguing contraction at 30% MVC.

Figure 5: Showing the blood flow in one arm at the beginning (△) and after steady-state flows (●) had been reached in contractions at tension of 1-10% MVC. Shown, as open circles, are the blood-flows and EMG's from the same arm when it was "resting" while the other arm performed a fatiguing isometric contraction.

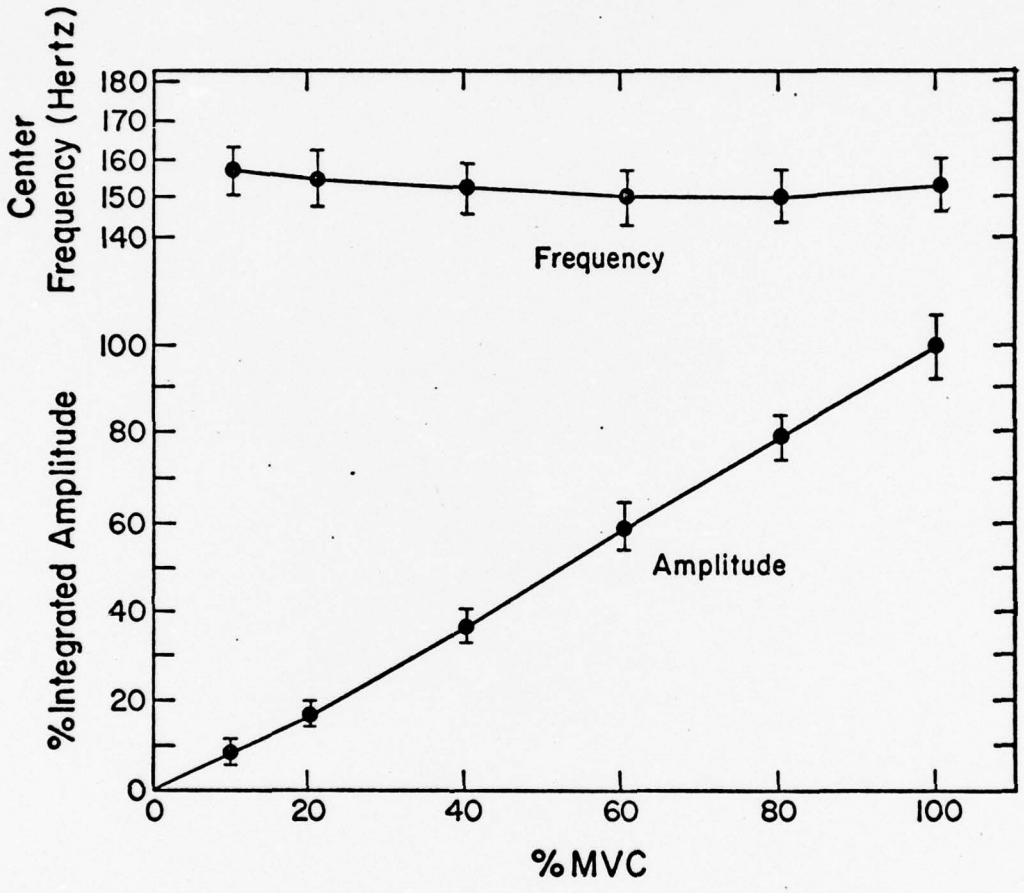

Center Frequency (Hertz)
180
170
160
150
140
Frequency
% Integrated Amplitude
100
80
60
40
20
0
Amplitude
0
20
40
60
80
100
% MVC

FIGURE 1

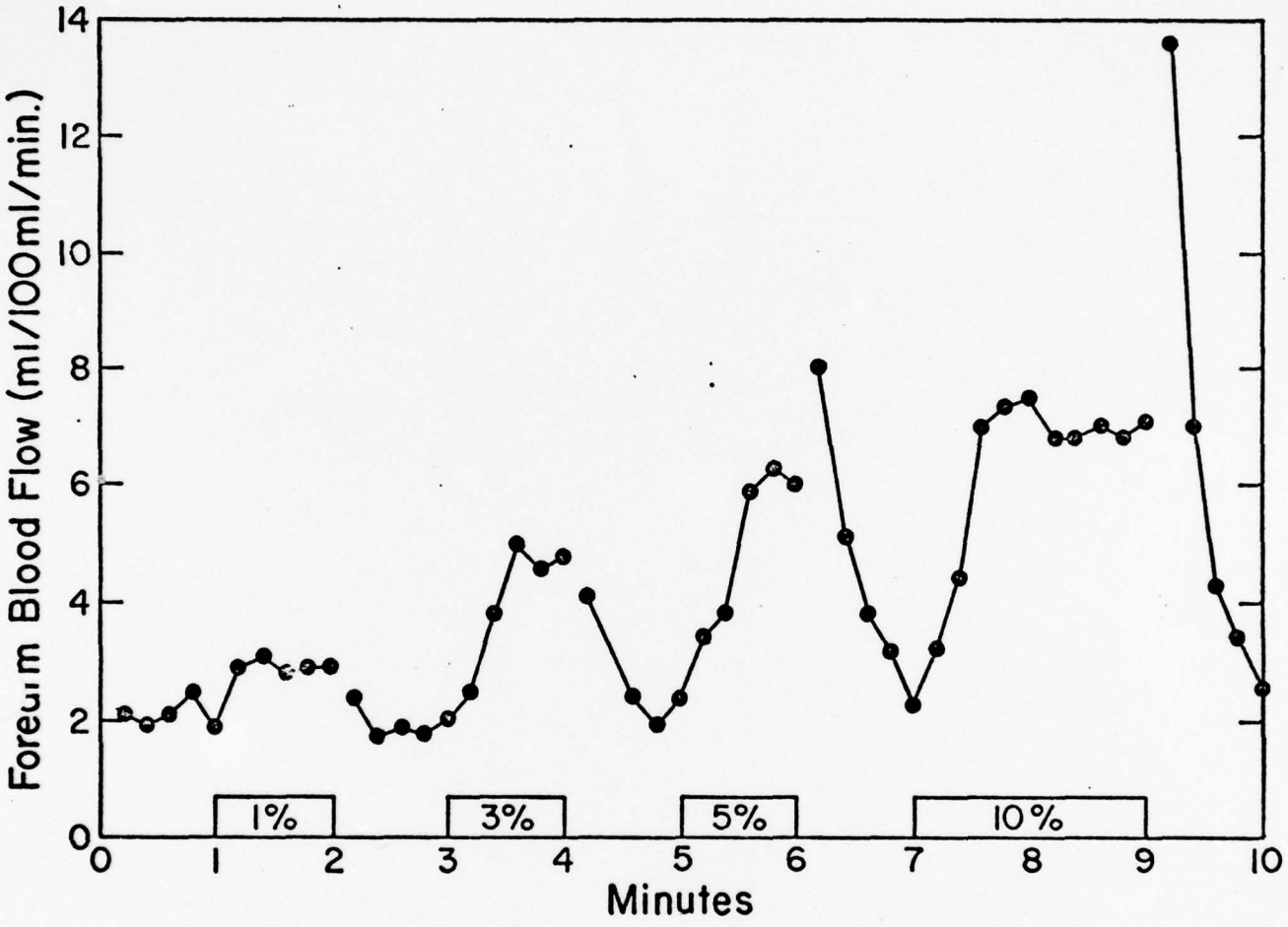

Forearm Blood Flow (ml/100ml/min.)
14
12
10
8
6
4
2
0
1%
3%
5%
10%
0
1
2
3
4
5
6
7
8
9
10
Minutes

FIGURE 2

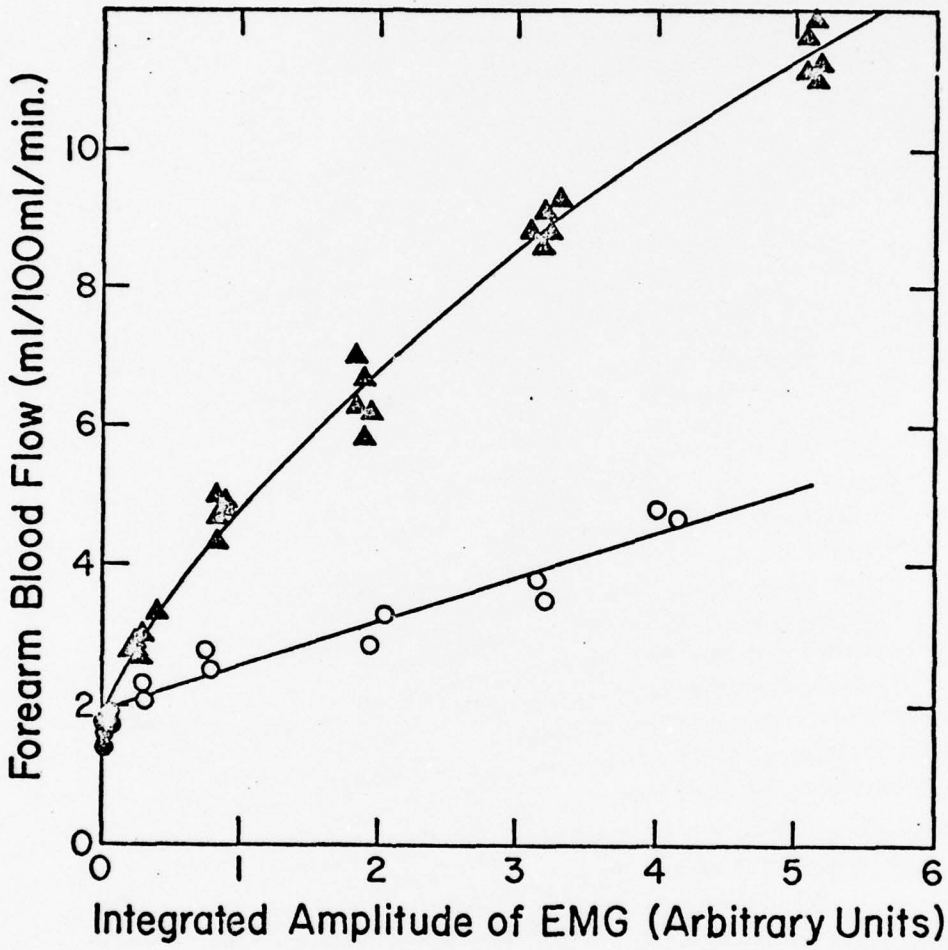

Forearm Blood Flow (ml/100ml/min.)
0
2
4
6
8
10
0
1
2
3
4
5
6
Integrated Amplitude of EMG (Arbitrary Units)

FIGURE 3

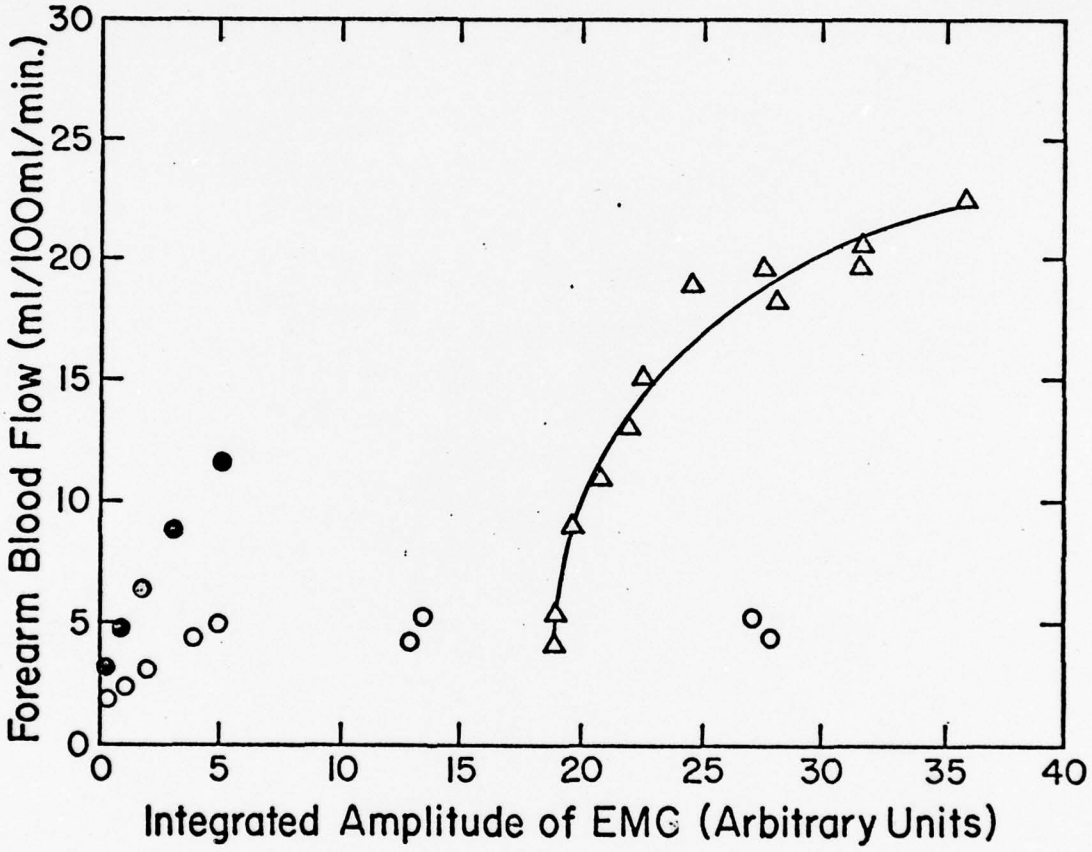

Forearm Blood Flow (ml/100ml/min.)
30
25
20
15
10
5
0
0
5
10
15
20
25
30
35
40
Integrated Amplitude of EMG (Arbitrary Units)

FIGURE 4

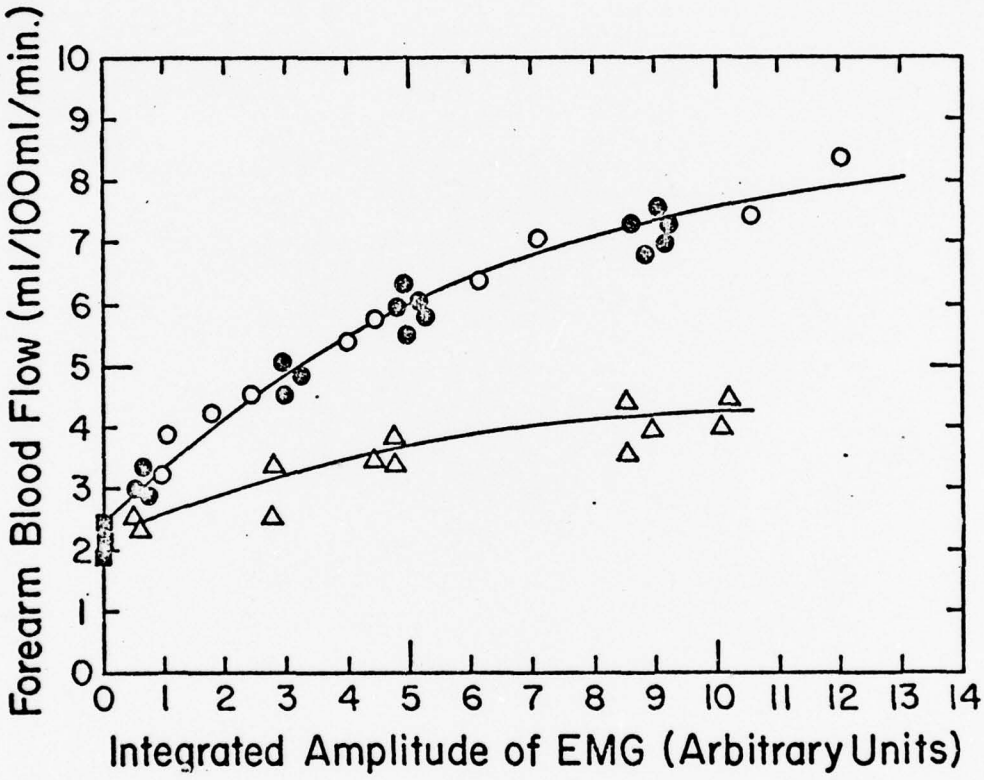

Forearm Blood Flow (ml/100ml/min.)
0
1
2
3
4
5
6
7
8
9
10
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Integrated Amplitude of EMG (Arbitrary Units)

FIGURE 5

INVESTIGATION 5

THE DEVELOPMENT OF ISOMETRIC TENSION DURING ASYNCHRONOUS STIMULATION OF FAST AND SLOW MUSCLES IN THE CAT.

INTRODUCTION

When muscles are stimulated experimentally by synchronous impulses along the motor nerve or a mixed nerve, frequencies far higher than are physiological, as high as 100-300 Hz,are necessary to elicit a smooth tetanic contraction (6). Also, during tetanic stimulation of mixed muscle, the tension decays to less than 10% of the origi al strength in 1 min (2), much more rapidly than in voluntary maximal effort in which the tension decays only to 50% of its original value in 1 min (13, 18). In short, synchronous stimulation of muscles commonly used in experiments bears no relationship to voluntary contractions , and, in consequence, studies concerned with the problems of muscular function or fatigue when such stimulation is used must be regarded with serious reservations.

During voluntary muscular activity, the tension generated by active muscle is a function of both the number of motor units recruited and their frequency of firing (1, 14). From studies on reflex activation of motor units in the cat (14) and brief voluntary isometric contractions in man (4, 14, 15, 17), it seems clear that, once recruited, the frequency of firing of a motor unit varies between 5 and 20 Hz during weak isometric contractions and may be as high as 40-80 Hz during strong isometric contractions. But even during sustained maximal isometric contractions, the frequency of firing of motor units exceeds 80 Hz only in unusual circumstances (12).

It is generally recognized that the activation of motor units during voluntary activity is asynchronous. Surprisingly, however, experimental stimulation of motor nerves has rarely used anything but synchronous impulses The only studies in which the stimulation has been other than synchronous

are those from the laboratory of Rack and Westbury (10, 16) who divided the ventral roots of the spinal cord (L_6, L_7, and S_1) of the cat into 5 electrically isolated bundles so that stimulation of each bundle elicited the same isometric tension in the soleus muscle. Stimulation of each bundle in rotation at frequencies as low as 10-15 Hz elicited smooth contractions of soleus. The tension developed during rotary stimulation was not only smoother but was also greater than the tension developed during synchronous stimulation of all the ventral roots at those frequencies. Rack and Westbury were able to elicit nearly maximal tetanic contractions of soleus during rotary stimulation at 35-50 Hz, depending on the length of the muscle (see their Fig. 9).

In the present series of experiments, we have examined the interdependence of muscle fibers in developing tension in 3 different muscles with widely varying populations of fiber types, using the method of rotary stimulation. In a companion investigation (11) we have examined isometric endurance in fast- and slow-twitch muscles using the method of rotary stimulation along with a logical sequence of recruitment and rate coding.

METHODS

The experiments were performed on 16 female cats whose weight averaged 2.6 kg. They were anesthetized with ∝-chloralose given intraperitoneally (75 mg/kg) and subsequently maintained with supplementary intravenous doses. Body (rectal) temperature was maintained at 37 to 39° C.

Preparation of muscles

Following cannulation of the left carotid artery and the jugular vein and a tracheotomy, the cat was placed in a prone position with one hind limb fixed rigidly by steel pins through the knee and ankle.

Two muscles of mixed-fiber populations, the plantaris and the medial gastrocnemius and a slow-twitch muscle, soleus, were exposed for study. All fat and fascia were removed to expose the muscles, their motor nerves, and the sciatic nerve. Plantaris and soleus were dissected free, but the medial and lateral heads of *gastrocnemius* were left attached, freed only from the surrounding musculature. Only one muscle was examined on each leg. The nerves and blood supply to all other muscles in the leg were ligated and cut.

The tendon of the muscle under study was attached to a stainless steel bar and the muscle's length adjusted to produce its greatest active isometric tension when stimulated. In addition, the angle and height of the bar was set so that the muscle contracted as nearly as possible in the same planes of motion as in the intact leg. The tension generated by the contracting muscle was measured as the deformation of the stainless steel bar by 4 strain gauges arranged as a Wheatstone bridge. The resultant electrical output was then displayed on a Western Model 1971 0-1ma panel meter and recorded on a Hewlett Packard model 770 B data recorder and/or Sangamo-Tandberg series 100 FM tape recorder for subsequent analysis. The temperature of

the muscles was controlled at 37 $\pm$ 0.5° C. All exposed tissues were covered with liquid paraffin.

Stimulation

The muscle was stimulated 1) directly or 2) indirectly through either the sciatic nerve or the appropriate ventral roots. The stimulus was a square wave of 0.2 ms duration, applied through platinum electrodes. To avoid a back-response during synchronous stimulation of the motor nerve (3), a second stimulus was applied synchronously with a pair of platinum electrodes placed 2 cm proximal to the main stimulation site. In experiments where ventral root bundles were stimulated, a dorsal laminectomy was performed to expose L_4 to S_3. The ventral roots from L_6, L_7, and S_1 were then carefully dissected free. These ventral root segments were then divided into either 2, 3, 5, or 10 sub-bundles so that stimulation with a supramaximal pulse to each of the bundles in a set would produce approximately the same tension. The stimuli were applied either as single impulses or in 3-sec trains. For examination of twitches, the pooled ventral roots were divided into 2 sub-bundles and stimulated under paraffin with single, paired impulses delivered from a Grass model S8 two-channel stimulator; the interval between the impulse to each set of motor units was adjusted between 10 and 500 msec. For sustained (3-sec) rotary stimulation, the bundles (of 2 to 10 groups of rootlets) were stimulated under paraffin oil from a digital ring-counter and pulse-shaping network which produced stimulation of each of the nerve bundles in rotation, through platinum electrodes (Fig 1). To ensure electrical isolation of the ventral root bundles, each electrode pair on a ventral root was RF isolated. Frequent checks of the nerve bundles for cross stimulation were made by alternately recording from one nerve bundle while

stimulating the remaining ones; if an electrical cross-stimulation occurred, an action potential developed in the non-stimulated bundle and the appropriate steps could then be taken to ensure isolation. To check for nerve damage during surgery, a 3 sec contraction was delivered synchronously to all bundles. The resultant tension developed in the muscle was then compared to that developed during direct stimulation. This procedure showed nerve damage to be less than 5% during the laminectomy and nerve division.

In a similar manner, the sciatic nerve or the motor nerve to either soleus, medial gastrocnemius, or plantaris was surgically subdivided into bundles and then stimulated asynchronously. Here, however, due to the high investment of connective tissue in the peripheral nerves, there was a significant loss of strength in subsequent indirect stimulation due to surgical damage during nerve division. In an effort to minimize this damage, the peripheral nerves were only divided into 3 bundles. However, even with this maneuver, the strength was still 10-20% lower in response to indirect stimulation. Therefore, for stimulation of the sciatic and muscle motor nerve, a rotary sleeve electrode was developed as shown in Figure 2. The electrode consisted of a silicon rubber sheath which housed 3 floating electrodes. Cathodal stimulation was applied in turn to each electrode through the ring-counter and pulse-shaping network during which time the other 2 electrodes acted as anodes. As will be shown in the Results section, this arrangement resulted in the stimulation of 3 roughly equivalent and isolated bundles of motor nerves. To avoid antidromic stimulation of the motor neurons, the nerve under study was cut just proximal to the sleeve electrode. The nerve and electrode were then lifted away from the surrounding tissue and flushed continuously with mammalian Ringer equilibrated with a gas mixture of 95% O_2 and 5% CO_2 and kept at 37° C.

RESULTS

The Interactions Between Motor Units During an Asynchronous Twitch

To study the interaction between motor units during twitches induced by sequential stimulation, the motor unit population in the ventral roots emanating from L_6, L_7, and S_1 were subdivided into 2 discrete populations as described above. A single stimulus was applied to one set of motor units followed by a second stimulus at intervals as long as 500 msec apart. A typical set of results from these experiments is shown in Fig. 3, which shows the twitches recorded from plantaris, medical gastrocnemius and soleus muscles in these circumstances. The pattern of response was similar for all three muscles studied. As the interval between the twitches was decreased, the tension generated by the second population of motor units gradually became fused and enhanced until, at short stimulation intervals, a single twitch was recorded with a greater tension than could be observed for either twitch alone. The major difference among the 3 muscles was the frequency at which this enhancement occurred. Soleus motor units showed this effect at pulse intervals of 100 msec while medial gastrocnemius and plantaris did not show enhancement of the second twitch until the intervals were reduced to 75 and 50 msec respectively. The enhancement of tension was greatest in plantaris and least in soleus.

Recovery of Maximum Tension Following Tetanic Contractions

Synchronous or sequential trains of impulses were delivered through the sleeve electrode on the sciatic nerve at frequencies between 10-200 Hz for a period of 3 sec. The maximum strength the muscle could develop at any frequency was then recorded as the greatest tension developed during this period. To ensure that the muscles retained this full capacity in later experiments,

a test series of contractions were performed to determine how long the interval should be between them. Here, we stimulated the muscle either sequentially or synchronously for 3 sec at a frequency of 100 Hz. In any one experiment, 5 serial contractions (C_1-C_5) were performed with the interval between the successive contractions set at 0.5, 1, 2, 3, or 5 min. From these experiments we found that for short intervals between the contractions, the strength did not fully recover, but reached a steady state between the 2nd and 5th contraction in the series. The average tension of C_2 through C_5 was plotted as a percentage of the initial strength (C_1) for each recovery interval. Figure 4 shows the recovery in strength for each of the 3 types of muscle studied during sequential stimulation. Each point in the figure represents the mean of the steady state tension (C_2-C_5) for 4 plantaris, 4 medial gastrocnemius and 4 soleus muscles. Even with intervals as short as 30 sec between the contractions the steady state strength in soleus still averaged 98% of the initial contraction and strength recovered fully with a rest interval of only 1 min. In contrast, the strength recovered more slowly in medial gastrocnemius and plantaris; after 0.5 min recovery, the average steady state strength was 84 and 65% of C_1, respectively. Nevertheless, in both these muscles, the strength had fully recovered with an interval of 3 min between the serial contractions. This pattern of recovery of strength during serial contractions was identical with both synchronous and sequential stimulation. We therefore set the interval between the contractions at 3 min for all muscles studied in the experiments reported below.

The Development of Tension During Sequential Stimulation

If, instead of single twitches, the muscle was stimulated for 3 sec, the change from synchronous to sequential stimulation at the same frequency

of stimulation was reflected as a smoother contraction, a greater tension, and a faster rate of rise of tension. For example, Fig. 5 shows traced individual records of tension from plantaris during synchronous (1 bundle) and sequential stimulation (3, 5, or 10 ventral-root bundles) at a frequency of 10 Hz. The greatest enhancement in tension occurred between synchronous and sequential stimulation where the motor-neuron pool innervating plantaris was divided into 3 bundles. Although the tension generated with further division of the ventral roots showed further increases, the main effect of increasing the number of bundles stimulated in a sequential manner was to make the contractions smoother. This was true at all low frequencies, as illustrated in Fig. 6 which shows the average maximum tensions recorded during synchronous (0) and sequential (□, ●, Δ) stimulation of ventral roots serving plantaris, medial gastrocnemius, and soleus at frequencies between 10 Hz and 200 Hz. Each point in the figure represents the mean of experiments on 4 animals for each muscle described. Isometric strength was greatest in medial gastrocnemius, less in plantaris and least in soleus; the respective strengths averaged 7.4, 5.10 and 2.52 kg. For ease of comparison, the strength of each muscle was normalized in terms of the maximum strength recorded during sequential stimulation at a frequency of 100 Hz (which produced a tetanic contraction at maximal strength). At low frequencies, the tension developed by any of the 3 muscles examined was greater with sequential than with synchronous stimulation. This effect was most pronounced with plantaris and gastrocnemius and disappeared by the time the stimulation frequency reached 100 Hz for plantaris, 75 Hz for medial gastrocnemius and 50 Hz for soleus, frequencies that resulted in smooth tetanic contractions for synchronous stimulation. In contrast, the tension developed by the muscle during sequential stimulation was maximal when stimulation frequencies were near 50 Hz for plantaris and gastrocnemius and 30 Hz for

soleus. Increased "desynchronization" of stimulation by dividing the ventral roots into 3 (□), 5 (●) or 10 (△) bundles resulted in only small further increases in the tension generated.

The Use of a Sleeve Electrode on the Sciatic Nerve to Produce Sequential Stimuli

From a geometrical consideration, assuming the sciatic nerve to be a perfect cylinder, the current fields applied through 3 electrodes placed in equi-distant fashion around a nerve should be able to recruit all underlying motor units within the nerve with minimal overlap of the electrical field. If we assume, first, that, as in Fig. 7, the invasion of stimuli follows an even pattern of distribution and, second, that motor and sensory fibers are randomly distributed in the sciatic nerve, then approximately 17% of the motor units would be involved in overlap firing. A rotary electrode was applied to the sciatic nerve and the electrodes were excited for 3 sec either synchronously or in rotation at frequencies between 10 and 200 Hz. This procedure was repeated at voltages that were 1) of sufficient intensity to recruit ½ of the motor units in the nerve and at twice and 4 times that intensity. The premise was that sequential excitation of the electrodes in the sleeve electrode would lead to the firing of those motor units resident in the shaded portions of Fig. 7 at double or triple the intended frequency. For example, if the frequency of stimulation were 20 Hz at supramaximal voltage, then motor units found in areas of geometric overlap would be stimulated at 40 or 60 Hz. If that happened, it would result in a change in the shape of the tension-frequency diagram obtained when separate bundles of ventral roots were sequentially stimulated (See Fig. 6). It was expected that the multiple firing of those motor units affected by overlap would take the form of an enhancement of tension at low frequencies and a decrease in tension at higher frequencies because of high-frequency block or partial block in some motor units. Further, since muscles fatigue very rapidly at

high frequencies of stimulation, the influence of the overlap of units stimulated by the rotary sleeve electrode ought to be detectable as a reduction of the strength generated by the muscle after only a short period of stimulation.

Figure 8 illustrates the results of a typical set of experiments performed on soleus. The ordinate shows the normalized tension generated by the muscle during synchronous (open symbols) and rotary (closed symbols) stimulation of the sciatic nerve (B, D) and the ventral roots of the spinal cord (A, C). The pattern of response relating the frequency of stimulation to tension during stimulation of either ½ or all motor units was similar whether the excitation was applied to the ventral roots or through the rotary sleeve electrode on the sciatic nerve. Thus, at threshold voltages, if double or triple firing of motor units occurred, the effect was sufficiently small as to be undetectable. Thus figures A and B illustrate the average results of the ½ threshold and threshold stimulation. When the threshold voltage was doubled, there was no change in the tension developed by rotary stimulation of the ventral root bundles. But doubling the threshold voltage of the sleeve electrode on the sciatic nerve shifted the frequency tension curve as predicted, presumably due to repetitive firing in some motor units (panels C and D). Furthermore, there was a rapid fall in tension within the 3-sec stimulation at frequencies above 100 Hz. In some cats, overlap was occasionally seen even at threshold voltages. This was always remedied when the sleeve electrode was removed, cleaned, and the platinum wires realigned. The procedures described formed a test for proper electrode placement and for the presence of electrical cross-firing. At the beginning of any experiment with the sleeve electrode, the frequency-tension curve from synchronous and sequential stimulation was compared through threshold voltages to ensure that

electrical cross firing was not present.

The Influence of Conduction Velocity on Desynchronization of Stimuli

Due to the different conduction velocities of motor neurons, even a synchronous stimulus applied to the ventral roots of the spinal cord should become, to some extent, desynchronized by the time the impulse reaches the target muscle. We explored this matter by comparing the tension generated by muscles during stimulation in the frequency range of 10 to 200 Hz with 1) electrodes placed directly on the muscle, 2) sequential and synchronous stimulation through electrodes placed a) on the motor nerve close to the muscle, b) on the sciatic nerve about half-way along the thigh and c) on the ventral roots. To stimulate the motor nerve and the sciatic nerve sequentially, a 3-channel sleeve electrode was employed as described in Methods. The results of these experiments are shown in Fig. 9. Clearly, at low frequencies, there was an enhanced tension with both synchronous as well as sequential stimulation the further the distance was between the site of stimulation and the muscle. We believe this fact demonstrates that even a synchronous stimulus applied at the spinal cord becomes, to some extent, desynchronized by the time it reaches the muscle.

DISCUSSION

Rack and Westbury (16) showed that when stimuli were applied in rotation to sub-divisions of the appropriate ventral roots, the resulting contractions of the cats' soleus muscle were both stronger and smoother than with synchronous stimulation. We have confirmed and extended those findings to gastrocnemius and plantaris muscles and have inquired further into the interaction of motor units in response to a single stimulus and to 3-sec trains.

In interpreting their findings, Rack and Westbury suggested that internal movement in the muscle in an unfused tetanus "reduces the tension below that developed in a truly isometric state." It is difficult to know precisely what they meant by that. For our part, we believe that the benefits obtained by firing groups of muscle units in rotation are largely attributable to the engagement of the series elastic element. Thereby, when we twitched each half of the population of a muscle's motor units in sequence, reduction of the interval between those stimuli led to fusion with a resultant tension greater than the sum of the tensions produced by each group of motor units. The obvious explanation is that, in partial or total fusion, the series elastic elements had not returned to their resting state when the second group of units contracted. The same explanation can be invoked to explain the continued increase in tension and the markedly smoother contractions seen, for example, in Fig. 3, when the number of bundles of motor units were increased up to 10. Even at such a low frequency (10 Hz) it is not hard to imagine that sequential firing of a sufficiently large number of ventral root bundles would result in as smooth a contraction as we find in voluntary contractions. It is quite possible that a further contributory factor involved in the tension generated in these fused or partially-fused contractions may be the positive feed-back system described by Hill (9) between tension and muscular activity.

In each of the 3 muscles we examined, the difference in the tension developed between sequential and synchronous stimulation diminished as the frequency increased. However, maximal tetanic tension was always reached at a lower frequency with sequential than with synchronous stimulation. The frequencies at which tetanic tensions were developed, as would be expected,

were lowest for soleus and highest for plantaris, with an intermediate value for gastrocnemius which has a mixed population of fibers.

The singularly rapid fall in tension during supramaximal synchronous stimulation is not surprising in the light of these observations. Yet such frequencies have commonly been used in investigations into the characteristics of isometric function and fatigue (2). In those conditions, fatigue usually manifests itself as failure of transmission across the neuromuscular junction or the muscle membrane. A feature of our results is that sequential stimulation of motor units in a whole muscle allows the generation of a smooth tetanic tension at frequencies that are within the range found in voluntary contractions in man (1, 14). The consequences of that finding are: 1) that isometric contractions induced by indirect stimulation of motor nerves more nearly imitate voluntary contractions if the stimulus is applied to excite groups of motor units in a sequential manner and 2) that all the results of investigations into sustained isometric function and fatigue resulting from synchronous stimulation must be regarded with serious reservations. Our present results support the need to hold such reservations and show that even though some degree of desynchronization of synchronous stimulation occurs as a result of different conduction velocities in motor neurons of different size, a much more effective method of inducing smooth muscular contractions is to rotate the firing of groups of motor units. In a following study (11) we have shown how important these factors are in permitting the development of isometric contractions at any required tension and maintaining those contractions to fatigue.

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FIGURE LEGENDS

Figure 1: A schematic diagram of the stimulator used in these experiments.

Figure 2: A schematic diagram of the rotary sleeve electrode which was placed around the sciatic or muscle motor nerve. The electrode employed 3 floating electrodes enclosed in a silicon rubber sheath.

Figure 3: The twitch tension developed by 2 discrete motor unit populations during paired asynchronous stimulation. The interval between the twitches was set at 500, 300, 100, 75, 50, 25, 15 or 0 ms.

Figure 4: The recovery in strength during serial tetanic isometric contractions lasting 3 sec in duration in plantaris (△), medial gastrocnemius (□) and soleus (0) in the cat.

Figure 5: The tension recordings from the plantaris muscle of the cat during indirect synchronous (1 bundle) and (3, 5, and 10 bundles) sequential stimulations of the ventral roots of the spinal cord in the cat.

Figure 6: Illustrated here is the maximum isometric strength developed by plantaris, medial gastrocnemius and soleus during a 3 sec isometric contraction at stimulation frequencies between 10 and 200 Hertz during synchronous (0) and asynchronous stimulation. During this latter form of stimulation, the ventral roots were subdivided into either 3 (□), 5 (●) or 10 (△) bundles.

Figure 7: A cross sectional representation of the rotary electrode in place on the sciatic nerve at rest (A) and during stimulation with sufficient voltage to recruit 40% (B), 75% (C) and 100% (D) of all motor units.

Figure 8: The relationship between isometric tension measured after a stimulation period of 1 sec applied to the L_6, L_7 and S_1 ventral roots with just maximal (A) and twice maximal (C) stimulation is contrasted with stimulation applied to the sciatic nerve with a sleeve electrode at maximal (B) and supermaximal (D) intensity. Both synchronous (open symbols) and asynchronous (closed symbols) stimulation were used.

Figure 9: The relationship between the tension developed and the frequency of stimulation of plantaris, medial gastrocnemius and soleus during both synchronous and sequential stimulation applied to the ventral roots of the spinal cord (△), the sciatic nerve (0), motor nerve (●), and to the muscle (□). All tensions have been normalized in terms of the tension generated during asynchronous stimulation at a frequency of 100 Hertz.

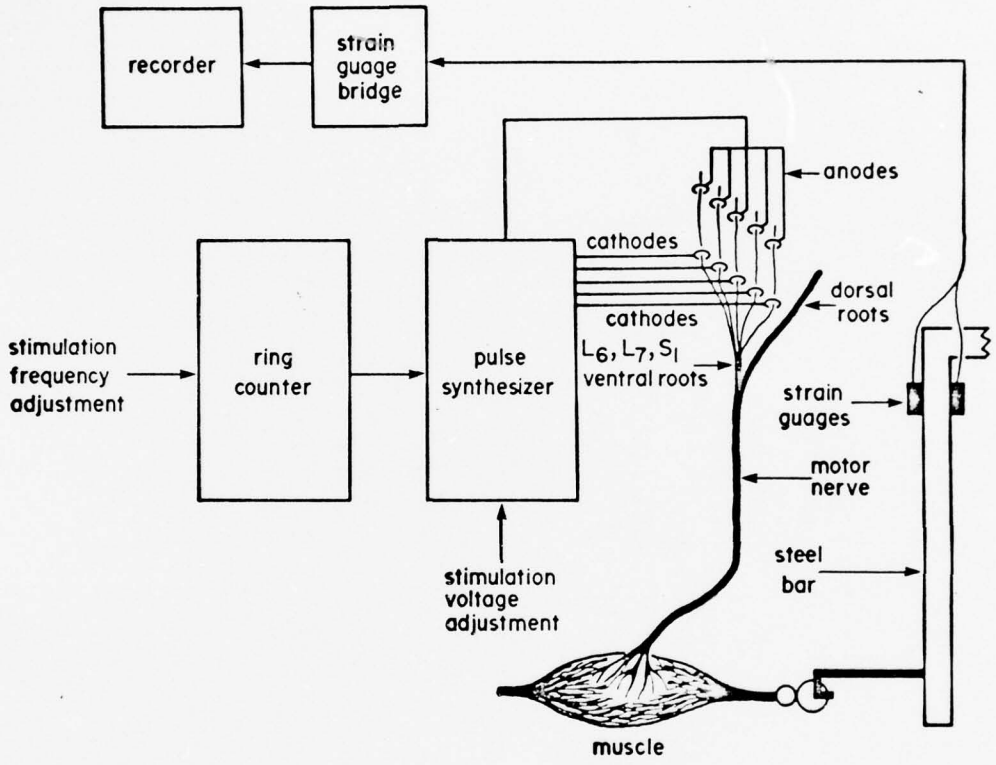

recorder
strain guage bridge
anodes
cathodes
dorsal roots
cathodes
L_6, L_7, S_1 ventral roots
stimulation frequency adjustment
ring counter
pulse synthesizer
strain guages
motor nerve
steel bar
stimulation voltage adjustment
muscle

Figure 1

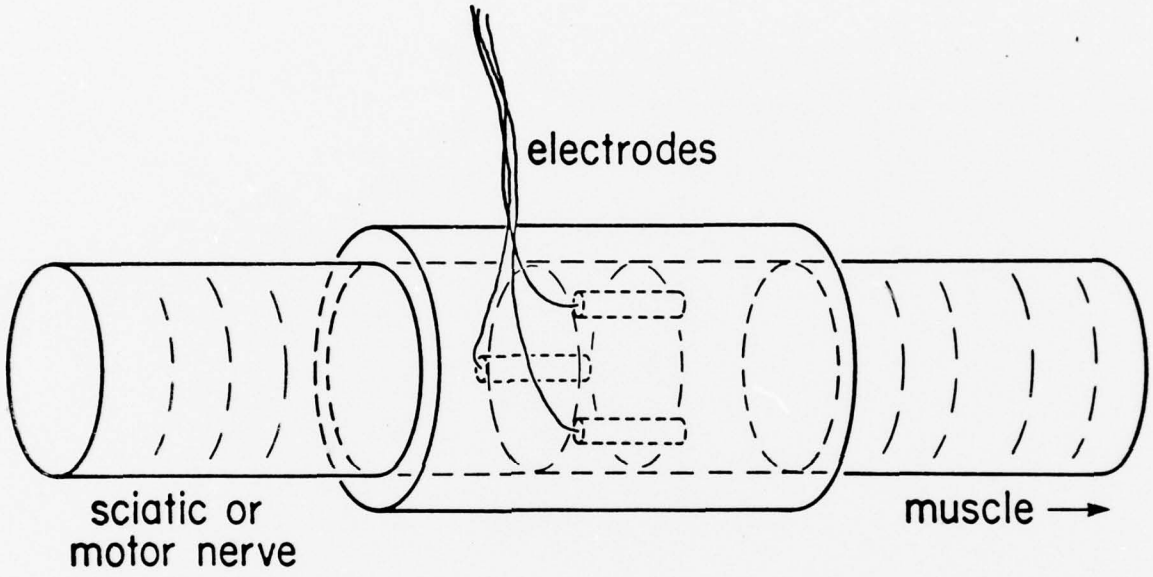


Figure 2


Plantaris
500 g
Medial gastrocnemius
1000 g
Soleus
300 g
Twitch Interval (ms)
500
300
100
75
50
25
15
0

Figure 3

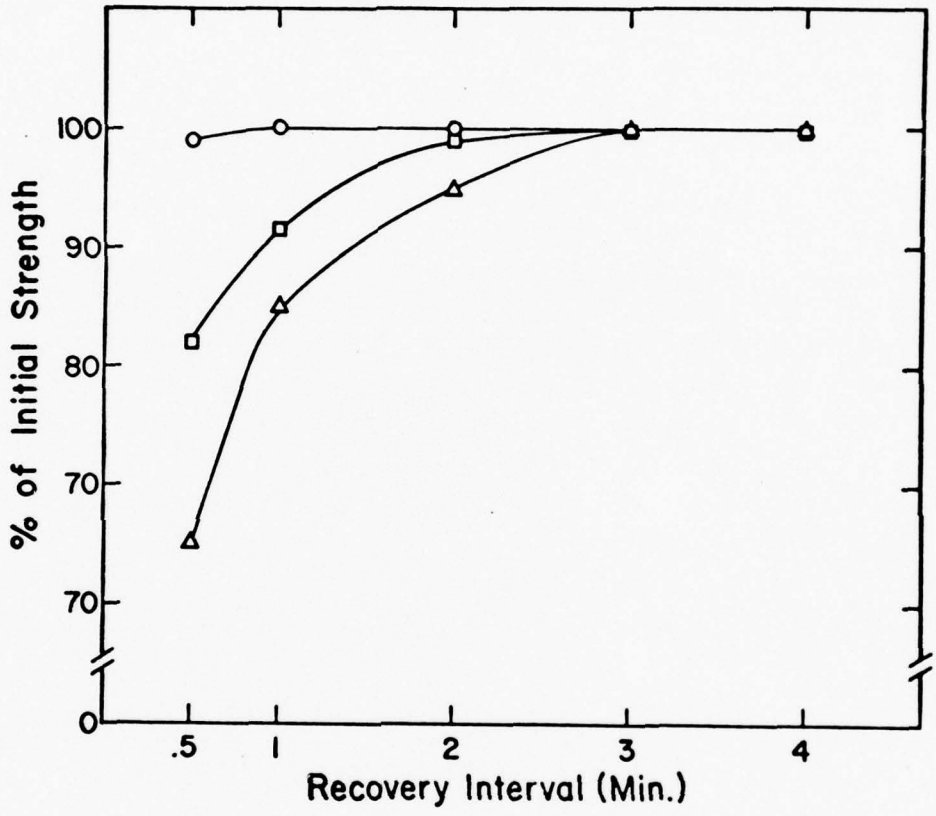

% of Initial Strength
100
90
80
70
70
0
.5
1
2
3
4
Recovery Interval (Min.)

Figure 4

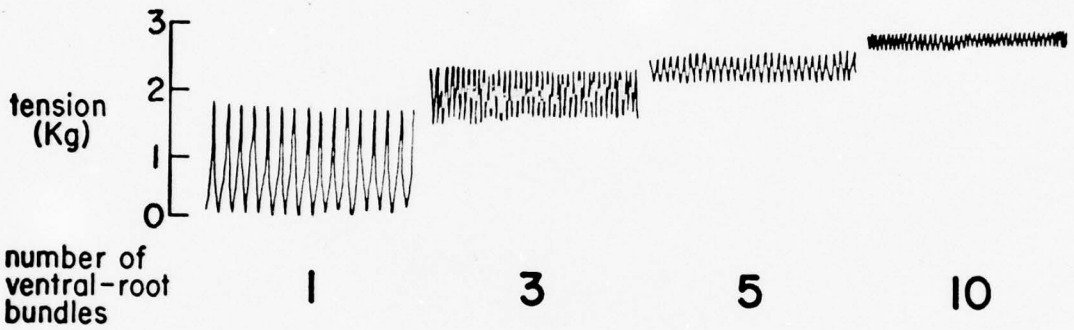


Figure 5

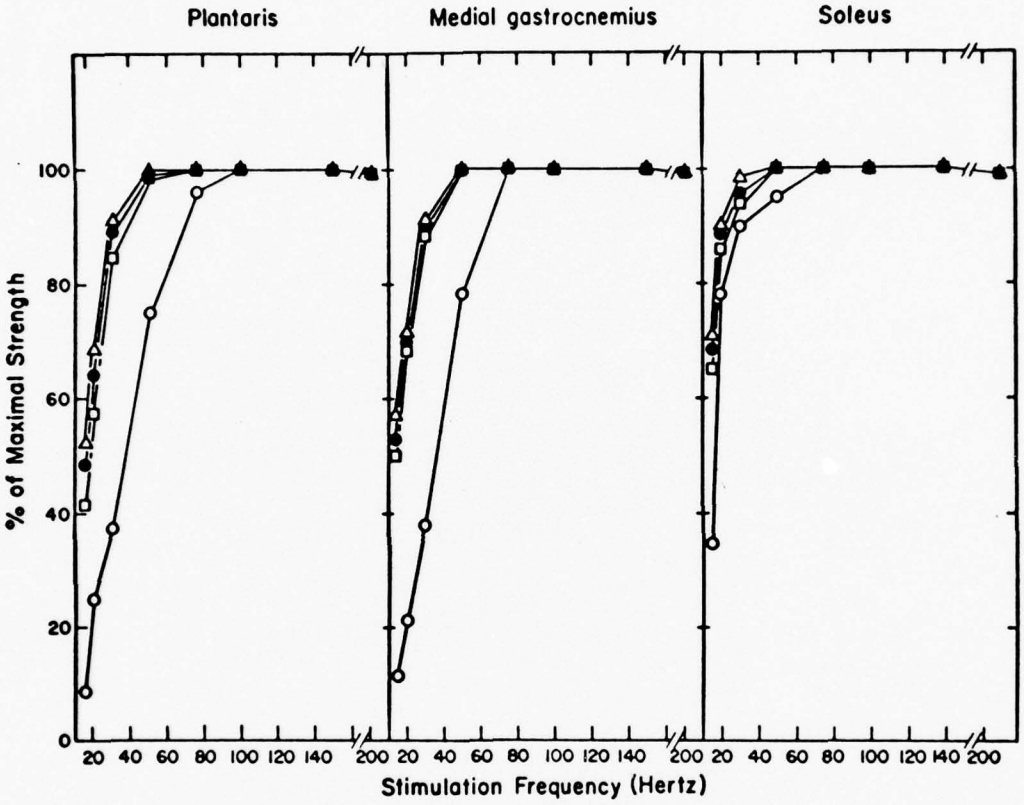

Plantaris
Medial gastrocnemius
Soleus
% of Maximal Strength
0
20
40
60
80
100
20 40 60 80 100 120 140 200
Stimulation Frequency (Hertz)

Figure 6

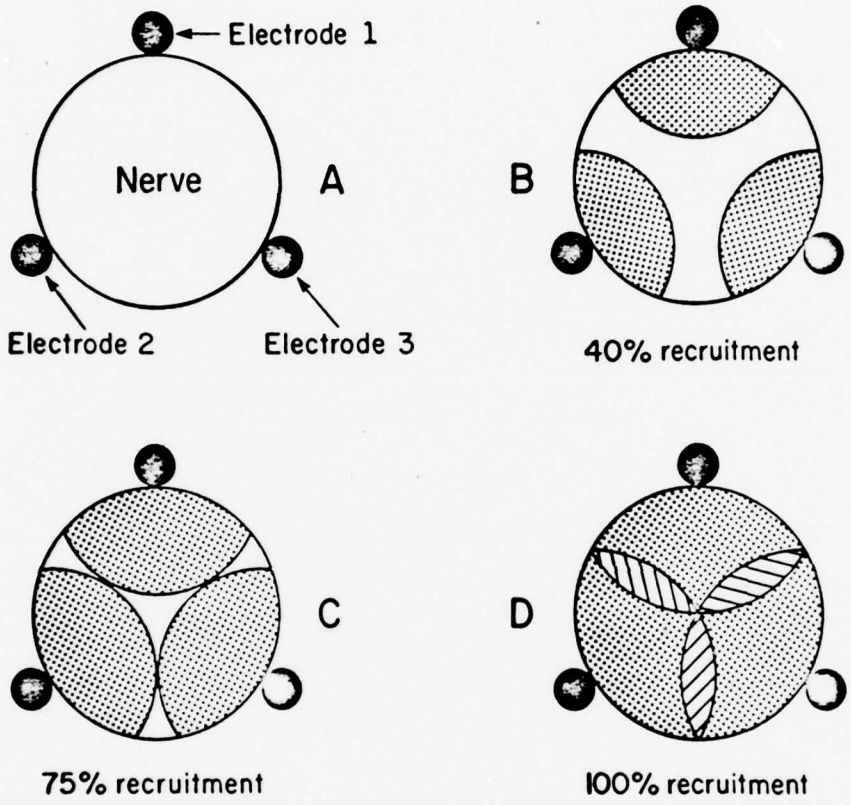

Electrode 1
Nerve
A
Electrode 2
Electrode 3
B
40% recruitment
C
75% recruitment
D
100% recruitment

Figure 7

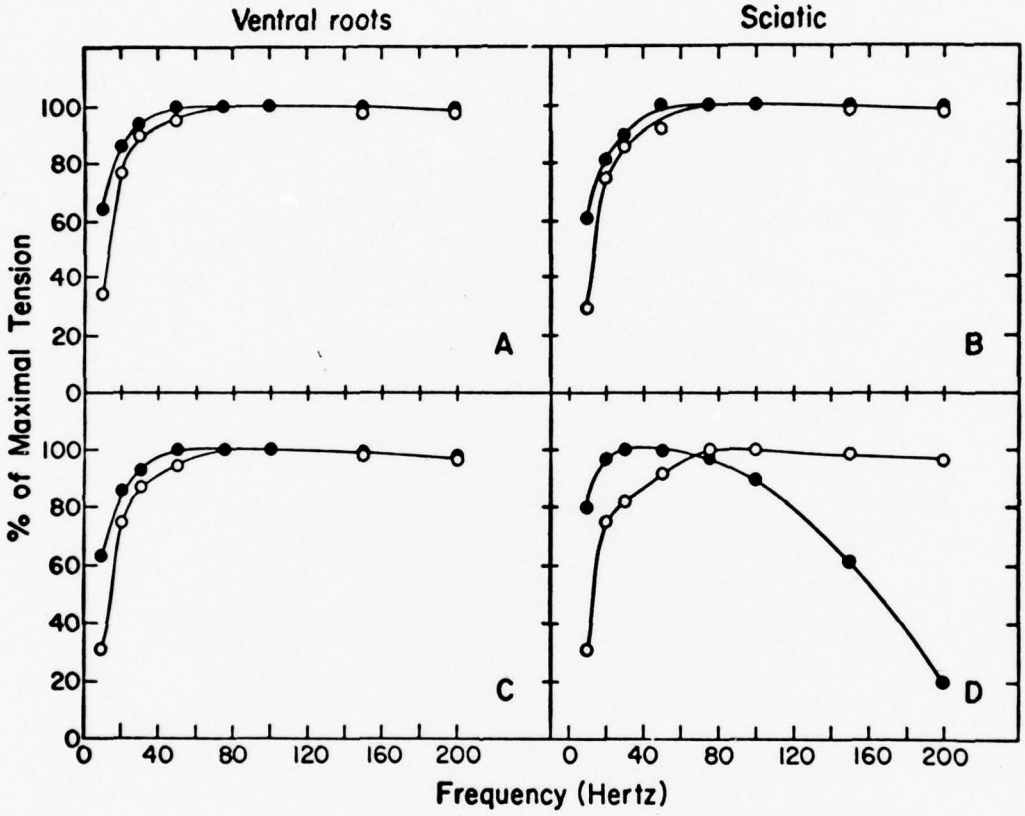

Ventral roots
Sciatic
% of Maximal Tension
100
80
60
40
20
0
A
B
C
D
0
40
80
120
160
200
Frequency (Hertz)

Figure 8

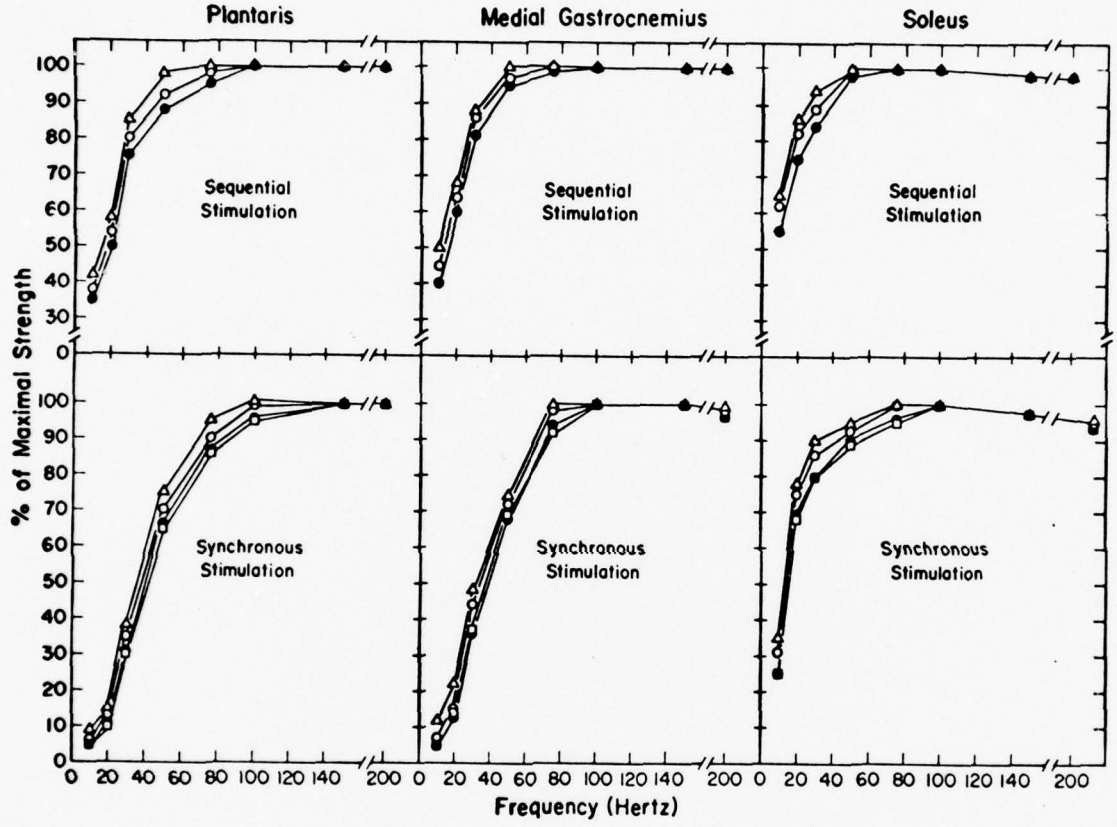

Plantaris
Medial Gastrocnemius
Soleus
Sequential Stimulation
Synchronous Stimulation
% of Maximal Strength
Frequency (Hertz)

Figure 9

INVESTIGATION 6

ISOMETRIC ENDURANCE IN FAST AND SLOW TWITCH MUSCLES IN THE CAT.

INTRODUCTION

In another investigation (12) we confirmed and extended Rack and Westbury's (13) findings that when the motor units of a muscle are fired in rotation, smooth contractions are achieved at low frequencies of stimulation. Further, even for fast-twitch muscles we were able to produce a complete, fused tetanus at frequencies within the physiological range for voluntary contractions. Most other studies of isometric function and fatigue have involved synchronous stimulation of motor nerves at frequencies much higher than those found in voluntary contractions and conclusions as to the cause of fatigue from the results of such studies must be regarded with reservation.

Until now, it has not been possible to induce, and maintain to fatigue, isometric contractions at any required sub-maximum tension. The investigation reported here describes a method by which this can be achieved and describes some of the factors which affect the development of muscular fatigue in muscles with widely different compositions of types of muscle fiber. The method used was based on 1) the stimulation of groups of motor units in rotation, first described by Rack and Westbury (13) and confirmed and extended by ourselves (12), and 2) the logical application of that stimulation in a manner imitative of our present understanding of the pattern of recruitment and rate-coding of motor units to develop isometric tension. That understanding emerges from evidence from voluntary contractions in man (e.g. 1, 8) and from reflex muscular activity in animals (9). While there is still room for doubt concerning the proportions of recruitment and rate coding in the development of isometric tension, the general principles are agreed upon. In consequence, we selected the model put forward by Milner-Brown and Stein (8)

(see their Fig. 9) in designing our method of stimulation. While Milner-Brown and Stein (8) were describing the development of tension in brief contractions, there is some evidence (1) to suggest that recruitment and rate coding follow a similar pattern of development in longer contractions at sub-maximum tensions.

METHODS

Forty-two female cats weighing an average of 2.9 $\pm$ 0.6 kg were used in these experiments. The animals were anesthetized with α chloralose (75 mg/kg body weight) injected intraperitoneally, and maintained with intravenous booster doses as needed.

A heating pad, placed under the cat, maintained the rectal temperature within the range of 37 to 39° C. Blood pressure and heart rate were monitored through an arterial cannula inserted into the left carotid artery.

Surgery

The surgical procedures have been described elsewhere (12). Briefly, after one back leg was fixed rigidly at the knee and ankle, soleus, plantaris or the medial gastrocnemius was isolated and its tendon attached to the dynamometer. The nerves and blood supply to all other muscles were ligated and cut. The muscles were kept at 37 $\pm$ 0.5^{o} C under paraffin. For most experiments, a special sleeve electrode (12) was placed around the sciatic nerve, which was cut proximally; the distal portion of the nerve was drawn out of the bath and perfused with oxygenated Ringer's solution at 37° C. In some experiments the muscle was stimulated sequentially through bundles of the ventral roots from L_6, L_7 and S_1.

Stimulation

Two types of stimulation were used in this study. Most often, the stimulation was through the sleeve electrode on the sciatic nerve resulting in rotary stimulation through 3 sets of electrodes. However, in some experiments we compared the results from the sleeve electrode with either direct or indirect synchronous stimulation, applied through platinum electrodes with a square wave stimulus of 0.2 msec at threshold intensity.

Pulses were delivered to a rotary electrode through a digital-analog hybrid computer, the details of which are described elsewhere (12). Briefly, the system consisted of a strain gauge bridge and amplifiers to measure tension, a central data processing unit and a pulse-synthesizer and ring-counter as shown previously (12, Fig. 1). The central data processor provided control voltages for the pulse-synthesizer and ring-counter, permitting adjustment of the stimulation voltage to vary recruitment, and of the frequency of rotation of the ring-counter between 10 and 200 Hz. In operation, the maximum isometric tension of the muscle was first determined by stimulating the sciatic nerve at a supramaximal voltage and at frequency of 100 Hz for 3 sec. After a 10 min interval, a target tension was set manually for the fatiguing isometric contraction. On command, the central processor initiated a program to set and maintain the target tension by first locking the stimulation frequency at 15 Hz and using recruitment to maintain and hold the target and then, once all the units were recruited , by increasing the rate coding.

In one series of experiments we examined the relation of frequency of stimulation to endurance time. Here, recruitment alone was used to sustain the target tension with the frequency locked throughout the contraction at frequencies from 50 to 200 Hz.

Experimental Procedures

Recovery of isometric endurance. First, it was necessary to measure the recovery of isometric endurance following sustained contractions in order to set the remaining protocols. This was accomplished by examining the endurance of the three muscles under study during a series of 5 serial fatiguing contractions at either 40 or 70% of the muscle's maximum tension. The interval between the contractions was 3, 10 or 30 min. On any one of the 5 cats, only one series of 5 contractions were performed on each leg. Assessment of the results led us to set the interval between the test contractions in subsequent experiments at 30 min.

Relationship of tension and endurance. In experiments on 6 cats we examined the relationship between endurance and strength in isometric contractions held to fatigue at tensions between 3 and 100% of the muscle's maximum strength, depending on the muscle examined. Experiments were completed on 4 soleus, 5 plantaris and 4 medial gastrocnemius muscles. We also examined the effect of arterial occlusion on isometric endurance in the same 3 muscles. Occlusion was produced by a pneumatic cuff placed around the cat's upper leg and inflated to 300 mm Hg for the duration of the contraction. In addition, on 6 muscles (2 each of plantaris, medial gastrocnemius and soleus) 16 serial contractions were performed, half with and half without occlusion.

Influence of sustained sub-maximum tension on muscular strength. On 6 cats we examined the decrease in the maximum strength during, and the recovery of maximum strength following a fatiguing isometric contraction at tensions of 40 and 70% of the muscle's maximum strength. First, during the fatiguing contraction we interrupted the rotary stimulation from time to time with a 1-sec train of direct stimulation at 100 Hz. Similarly, the

strength was assessed during recovery by 3-sec trains of synchronous or rotary stimulation 1, 3, 7, 10, 20 and 30 min after fatigue.

Site of muscular fatigue. Finally, we tried to differentiate between muscular and neuromuscular failure as the cause of fatigue during isometric exercise. First, fatiguing isometric contractions were induced at tensions of either 40 or 70% of the muscle's maximum strength in plantaris, soleus, or medial gastrocnemius. By definition, the maximum strength during indirect sequential stimulation had been reduced at the point of fatigue to that of the target, i.e. either 40 or 70% of the muscle's maximum strength. At that time, a direct synchronous stimulus was applied to the fatigued muscle. The direct stimulation lasted 1 sec at a frequency of 100 Hz. On any one muscle, one contraction at 40% and one at 70% of the muscle's strength was performed with a 30 min rest interval between them; the order in which the two tensions were applied was selected at random. This procedure was repeated on each of 4 different muscles for soleus, plantaris and medial gastrocnemius.

From the results of these experiments, we concluded that fatigue was not the result of transmission failure. This finding was contradictory to that of Brown and Burns (2) who found neuromuscular failure to be present during isometric contractions in soleus. But these investigations used synchronous stimulation frequencies up to 250 Hz while our frequency of stimulation did not exceed 60 Hz. Therefore, in further experiments, we locked the stimulation frequency at 50, 75, 100, 150 or 200 Hz and used recruitment alone to maintain, to fatigue, a tension of 40% of maximum strength. At the end of the contraction, the muscle was stimulated directly at a frequency of 100 Hz at a supramaximal voltage. On any one cat leg, only one muscle was examined. Four muscles of each type were examined.

RESULTS

Endurance of and recovery from sustained sub-maximum tensions

In these experiments, the endurance times of 5 successive fatiguing isometric contractions were measured at 40% or 70% of the maximum strength in plantaris, medial gastrocnemius and soleus muscles. The interval between the contractions was constant at 3, 10 or 30 minutes. A clear pattern emerged between the first and subsequent contractions for all 3 muscles as illustrated in Fig 1 where the interval was 3 min. At either tension, in any of the three muscles, the endurance of the second (C_2) through the fifth contractions (C_5) reached a steady state, shorter than the endurance for the first contraction; this is a pattern reminiscent of voluntary contractions in man (6, 11). The reduction in endurance was most pronounced in plantaris where the second and subsequent contractions lasted for only about 1/3 of the time of C_1. The soleus, a slow twitch muscle, was still able to contract with about 3/4 of the endurance of C_1 while the results for gastrocnemius, a mixed-fiber muscle, fell between soleus and plantaris. Because the endurance for C_2-C_5 always reached a steady state, the average endurance times of those contractions are shown for each muscle and for each recovery period in Fig. 2. For soleus, both tensions, the recovery was almost complete within 10 min and complete within 30 min. Recovery was slower for the other two muscles. After 30 min, medial gastrocnemius had only about 93% of the endurance of the first contraction, and plantaris could only maintain the target tension for about 85% of the endurance time of the first contraction. Additional experiments showed that full recovery required an interval of about 1.5 hr for medial gastrocnemius while plantaris required more than 2 hr for complete recovery. In the following series of

experiments, it was impractical to wait in excess of 2 hr between contractions. In consequence, since a steady state endurance was reached after 30 min rest, the time between serial contractions was set at this interval. To avoid the difference in endurance between the first and subsequent contractions, the first contraction in any experiment was discarded from the results unless otherwise stated.

Figure 3 shows the isometric endurance measured between 5 and 100% of the muscle's maximum strength in plantaris, medial gastrocnemius and soleus without circulatory occlusion. Each point represents the mean endurance of 4 different muscles of each type $\pm$ the standard deviations. Clearly, there was a striking difference in the endurance times of the different muscles. With its normal circulation plantaris fatigued rapidly at all tensions examined; even at a tension of only 5% of the muscle's strength the average endurance was 302 sec. In two cats, the tension was reduced to 3% of the muscle's strength and fatigue still occurred. In sharp contrast, the endurance in soleus was substantially greater while the results for gastrocnemius fell between those for soleus and plantaris. At all tensions below 30% of the maximum strength of soleus, the contraction was maintained indefinitely (i.e. more than 4 hr); the exact tension below which fatigue did not occur was variable. This is reflected in the large standard deviation for the endurance of soleus when contraction at a tension of 30% of its maximum strength; the individual endurance times for the 4 muscles contracting at this tension were 1201, 1086, 1860 and 1215 sec. Further, for soleus, the difference between a non-fatiguing (25% of the maximum strength) and a fatiguing (30% of the maximum strength) contraction was only in the number of fibers recruited, since either tension was achieved by rotary stimulation at a frequency of 15 Hz with recruitment alone. Since the additional motor

unit recruitment caused fatigue it seems reasonable to suppose that the additional recruitment of motor units increased the intramuscular pressure, thereby restricing the muscle's own blood supply to a level incompatible with continued contraction. This possibility may well have received support from the results obtained on one cat, which was hypertensive (resting blood pressure = 280/210 mm Hg). The results from that cat are not included in this study; the soleus did not fatigue until the tension was greater than 35% of its strength. Since the hypertensive cat had a high mean blood pressure, it is possible that the perfusion pressure might have offset the mechanical compression of the local blood vessels, thereby allowing the muscle to tolerate higher tensions without fatigue. The maximum strength of soleus, medial gastrocnemius and plantaris muscles were 2.5, 5.1 and 7.5 kg respectively. Thereby at all tensions below 1.5 kg, the endurance of soleus was much larger than for the other 2 muscles.

Fig. 4 shows the endurance time for each muscle after the circulation had been occluded compared to that with the circulation free (open symbols). Arterial occlusion (closed symbols) had no influence on the endurance time for plantaris at tensions above 40% of the muscle's strength. At tensions progressively below 40% of the muscle's strength circulatory occlusion resulted in a steadily reduced endurance. However, even at 10% of the muscle's maximum tension, endurance was only reduced by about a quarter by circulatory occlusion. In the gastrocnemius muscle occlusion reduced endurance at tensions below 70% of the muscle's maximum strength. In addition, the endurance during arterial occlusion for contractions exerted at lower tensions was reduced by a greater proportion than in the plantaris. For example, the endurance for an isometric contraction at a tension of 10% of the muscle's maximum strength in medial gastrocnemius was reduced by at

least two thirds during circulatory occlusion. The greatest proportional reduction in endurance during circulatory occlusion was found in the soleus. Here, isometric endurance was markedly reduced at all tensions.

Decrease in strength during, and recovery of strength following fatiguing isometric exercise.

By interrupting the normal pattern of stimulation during a sustained fatiguing contraction at sub-maximum tensions with a direct or indirect train of impulses lasting 1 sec at a frequency of 100 Hz, we were able to measure the decrease in the maximum isometric strength during a fatiguing isometric contraction (Fig. 5). Two tensions were examined, 40 or 70% of the muscle's maximum strength. Because of the differences in the endurance time and strength between the plantaris (Δ) medial gastrocnemius (□) and the soleus (0), the data have been normalized. Thereby, the ordinate represents the percentage of the initial strength generated by any of the three muscles while the abscissa represents the percentage of endurance time. Since the decrease in strength during the fatiguing contractions was the same for interposed direct and indirect 1-sec trains, those points represent the average of the results from 8 experiments with both types of stimulation. For all three muscles examined, there was a linear decrease in strength during the fatiguing isometric contractions at either 40% or 70% of the maximum strength, as has been reported in voluntary contractions in man (12).

However, while the decrease in strength was the same during the fatiguing isometric contractions for any of the three muscles, this was not the case for the recovery of strength following these contractions. Figure 6 shows the strength developed by 3-sec stimulation of plantaris (Δ), medial gastrocnemius (□) and soleus (0) at 1, 3, 10, 20, and 30 minutes following

fatiguing isometric contractions at either 40 or 70% of the muscle's strength. Recovery of strength after fatiguing contractions at either tension was fastest for soleus, in which the strength returned to its original value in 10 min. In contrast, the strength in gastrocnemius and plantaris took 30 min for full recovery.

Isometric endurance during direct and indirect stimulation at set frequencies

In this final series of experiments, the frequency of stimulation was locked at 50, 75, 100, 150 or 200 Hz for the duration of a fatiguing contraction. Recruitment alone was used to maintain the target at either 40% or 70% of the muscle's maximum strength carried to fatigue. To assess neuromuscular failure, a direct stimulus at a frequency of 100 Hz was applied at the point of fatigue. For comparison, a direct stimulus was also applied following fatiguing contractions performed as described in previous series of experiments, i.e. with the frequency of asynchronous stimulation set at 15 Hz at the beginning of the contraction and allowed to rise after all muscle fibers were recruited. The results are shown in Figure 7. For ease of comparison, both the endurance (———) and the direct isometric tension (----) have been normalized. When any of the three muscles were brought to fatigue at either 40% (lower panels) or 70% (upper panels) of their maximum strength at stimulation frequencies starting at 15 Hz and allowed to vary (shown here as a point at 15 Hz), the strength from both the indirect and direct stimulation at the point of fatigue were equal. Although the endurance was slightly shorter when stimulation was locked at 50 or 75 Hz, the strength from direct and indirect stimuli was exactly equal to that of the target tension for all three muscles. However, above a frequency of 75 Hz, the endurance rapidly decreased and this decrease was greatest in soleus and

least in plantaris. Along with the decrease in endurance, there was a progressive increase in the tension derived from direct stimulation at the point of fatigue. Thus, for example, after stimulation at a frequency of 200 Hz, the endurance for plantaris, medial gastrocnemius and soleus at a tension of 40% of their maximum strength had been reduced to 49, 46 and 39% of the control value. At fatigue, the strength in the respective muscles in response to the direct stimulus averaged 55, 57 and 72% of the original maximum tension.

DISCUSSION

When groups of motor units are stimulated in rotation through the motor nerves, sub-maximal isometric tensions can be selected and maintained to fatigue if the pattern of recruitment and rate coding follows currently established principles for the development of strength. The relationship between tension and endurance is quite different for the 3 muscles examined and follows a pattern to be expected from their fiber-composition. The soleus, comprised of slow-twitch fibers served with a rich supply of blood vessels, showed fatigue only when the tension exceeded 30% of the maximal strength. Plantaris, comprised solely or mainly of fast-twitch fibers, developed fatigue at tensions as low as 3% of maximal strength. The medial gastrocnemius, with a population of both fast and slow-twitch fibers, showed a tension-endurance curve between that for the other two muscles. In fact, the gastrocnemius muscle has a population of fibers that is not dissimilar to that of most human muscles and has an isometric endurance quite similar to that seen in man when the cat gastrocnemius is stimulated by our technique (10). We do not believe that our method of artificial stimulation is the

same as in voluntary contractions. Nevertheless, the method more closely approximates voluntary contractions than methods employed hitherto and certainly results in similar patterns of fatigue and recovery as are found in voluntary contractions. We found little difference in endurance times whether recruitment or rate coding provided the main part of the stimulation, at least until the frequency increases above the levels found in voluntary contractions.

The occlusion of the circulation to the 3 muscles may mean different things. In the case of the soleus muscle, in which by far the bulk of the motor units are slow-twitch in nature, it is reasonable to assume that circulatory occlusion affects all motor units in a similar manner. But in both the gastrocnemius and the plantaris muscles, where the motor units are of a mixed fiber-population, it is not clear how important circulatory occlusion is to one or other of at least 3 main types of fiber. What is clear is that the plantaris muscle is proportionately less affected by arterial occlusion than are, respectively, the gastrocnemius and soleus muscles. Our interpretation of these results is that fast-twitch fibers are less affected by arterial occlusion than slow-twitch fibers, partly because of their biochemical make-up and partly because of their paucity of blood supply. It is possible that in the 3 muscles examined, the progressively lower relative tensions at which circulatory occlusion affects the maintenance of sub-maximal tensions may reflect the effect of progressively increasing intramuscular hydrostatic pressures when the circulation is not artificially occluded. It is equally possible that fast-twitch fibers which are vulnerable to fatigue normally operate without the benefits of a local blood supply (5). However, our results incline to support the view that even these units with a relatively poor blood supply operate more

effectively if that supply is not occluded. That view is by no means conclusive and is probably invalid if the proportion of motor units in a mixed muscle is heavily weighted by slow-twitch fibers. However, the available evidence (e.g. 3) shows that the proportion of slow-twitch fibers in the gastrocnemius of the cat is small. We found it noteworthy that in the soleus muscle, comprised of at least 95% slow-twitch fibers, and in which a rich blood supply is considered to be crucial to its continued function, arterial occlusion affected continued isometric contraction less than anticipated. The dependence of the function of the soleus muscle on its rich blood supply has long been postulated, and a recent study purports to support that view (4). It is of interest to find that in the absence of its blood supply the soleus appears to be surprisingly well-equipped to maintain sub-maximum tensions.

The strength of all 3 muscles declined linearly during sustained sub-maximum tensions. Similar results have been obtained during voluntary contractions in man over a wide range of sub-maximum tensions (12). The recovery of the strength of the different muscles followed a predictable pattern, with recovery occurring most quickly in the soleus muscle and least quickly in the plantaris muscle. At this time we have no explanation as to why the strength of a muscle declines linearly at all sustained sub-maximal tensions in all muscles, irrespective of their population of fiber-types.

In these experiments, in which fatigue was induced in muscles at stimulation frequencies within the normal physiological range, it appears that the fatigue occurred in the contractile elements of the muscle fibers. This does not exclude the occurrence of a simultaneous failure of transmission at the myoneural junction or at the muscle's membrane. But at the variety

of tensions examined, simultaneous failure of more than one part of the system would have to be construed as fortuitous. When the experimental conditions were adjusted so that the stimulation of motor units was above the normal physiological range, fatigue resided, at least in part, in neuromuscular transmission. It seems that at frequencies below 80-100 Hz, fatigue occurs in the contractile mechanism, while at higher frequencies, a block or partial block of transmission develops. These results are consistent with previous results (2) but cast real doubts on the concept that fatigue of electrical transmission occurs in voluntary contractions, except possibly in the sustained maximal effort in some muscles in some individuals (7) and in other selected circumstances. In another investigation concerned with voluntary isometric contractions at varying tensions in man (12), we have reason to believe that fatigue may be due to failure of either the contractile elements in muscles or of electrical transmission, depending on the tensions exerted; but in the present investigation there is no evidence to believe that electrical transmission is the vulnerable site of fatigue, whatever the tension exerted. It may be that in sub-maximum, sustained contractions in man, the frequencies of firing motor units do indeed become high enough to induce transmission fatigue; there is no direct evidence presently available.

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FIGURE LEGENDS

Figure 1: This figure shows the isometric endurance (expressed as a % of the initial endurance) recorded during a series of 5 fatiguing contractions whose tension was set at 40 or 70% of the maximum strength in plantaris (△), medial gastrocnemius (□) and soleus (○).

Figure 2: This figure illustrates the average steady state endurance (C_2-C_5) recorded for contractions at tensions of 40 and 70% MVC in plantaris (△), gastrocnemius (□) and soleus (○). The interval between contractions was set at 3, 10, and 30 minutes.

Figure 3: This figure illustrates the average isometric endurance recorded for plantaris (△), gastrocnemius (□) and soleus (○) in the cat. each point shows the mean endurance of 4 muscles studied ± the respective standard deviations.

Figure 4: This figure illustrates the average endurance during sustained isometric contrations in plantaris (△), medial gastrocnemius (□) and soleus (○) with the circulation free (open symbols) and occluded (closed symbols).

Figure 5: This figure illustrates the maximum isometric strength measured by direct stimulation of plantaris (△), medial gastrocnemius (□) and soleus (○) during fatiguing isometric contractions at either 40 or 70% of the muscle's initial maximum strength.

Figure 6: This figure shows the recovery in maximum strength following contractions of either 40 or 70% of the initial maximum strength determined for plantaris (△), medial gastrocnemius (□) and soleus (○) in the cat. Recovery of strength was assessed at 1, 3, 10, 20 and 30 min following the fatiguing contraction.

Figure 7: This figure shows the isometric endurance during fatiguing isometric contractions performed at either 40 or 70% of the maximum strength of plantaris (△), medial gastrocnemius (□) and soleus (○) for stimulation at frequencies to 200 Hz. At the point of fatigue, isometric strength was assessed by direct stimulation (----). Endurance and strength have been normalized in terms of the endurance and strength measured as in Fig. 3.

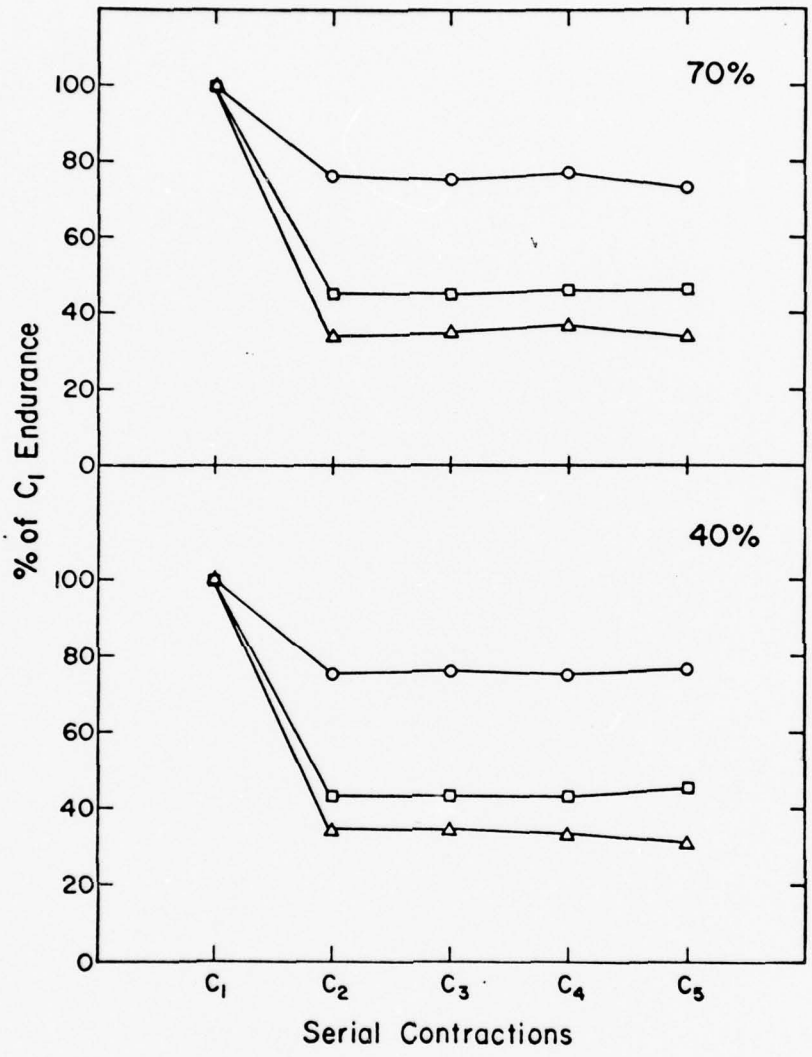

70%
40%
% of C_1 Endurance
100
80
60
40
20
0
C_1
C_2
C_3
C_4
C_5
Serial Contractions

Figure 1

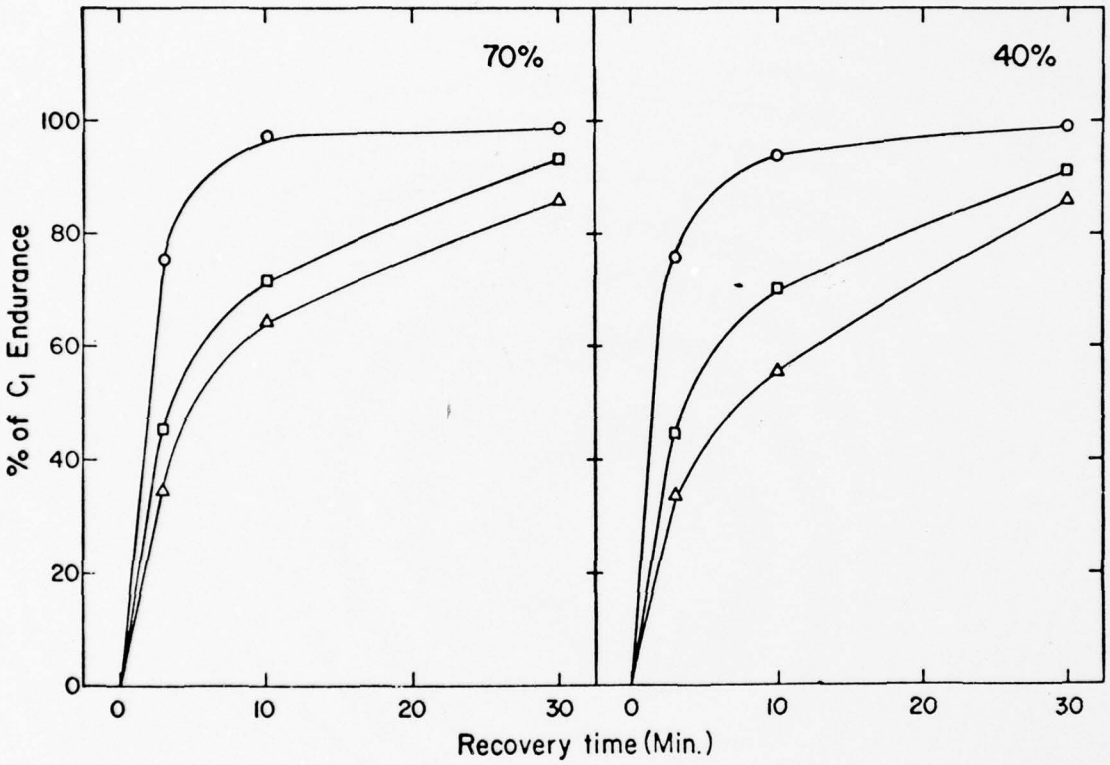

70%
40%
% of C_1 Endurance
100
80
60
40
20
0
0
10
20
30
Recovery time (Min.)

Figure 2

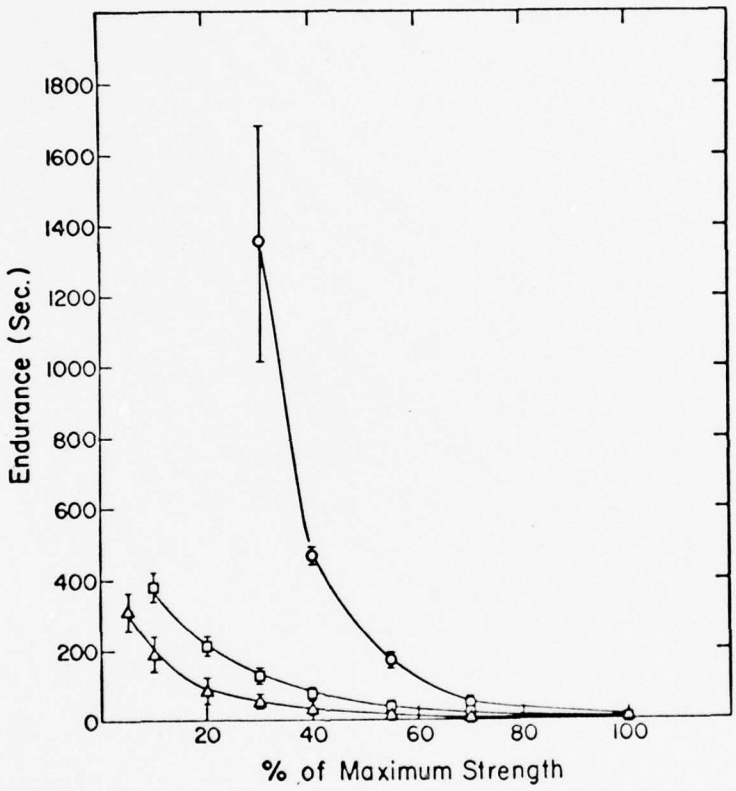

Endurance (Sec.)
1800
1600
1400
1200
1000
800
600
400
200
0
20
40
60
80
100
% of Maximum Strength

Figure 3

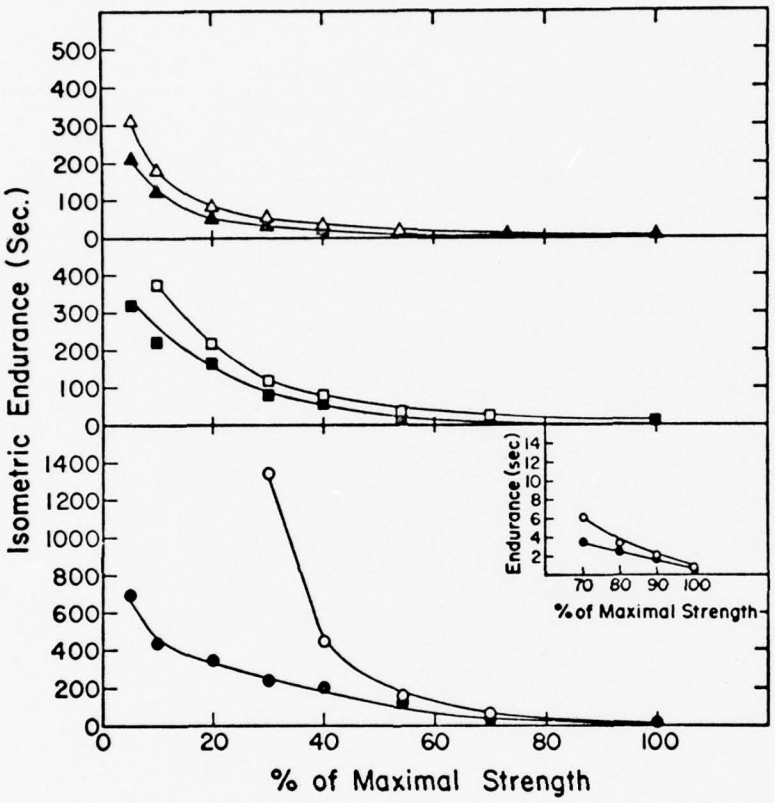

Isometric Endurance (Sec.)
500
400
300
200
100
0
400
300
200
100
0
1400
1200
1000
800
600
400
200
0
0
20
40
60
80
100
% of Maximal Strength
Endurance (sec)
14
12
10
8
6
4
2
70
80
90
100
% of Maximal Strength

Figure 4

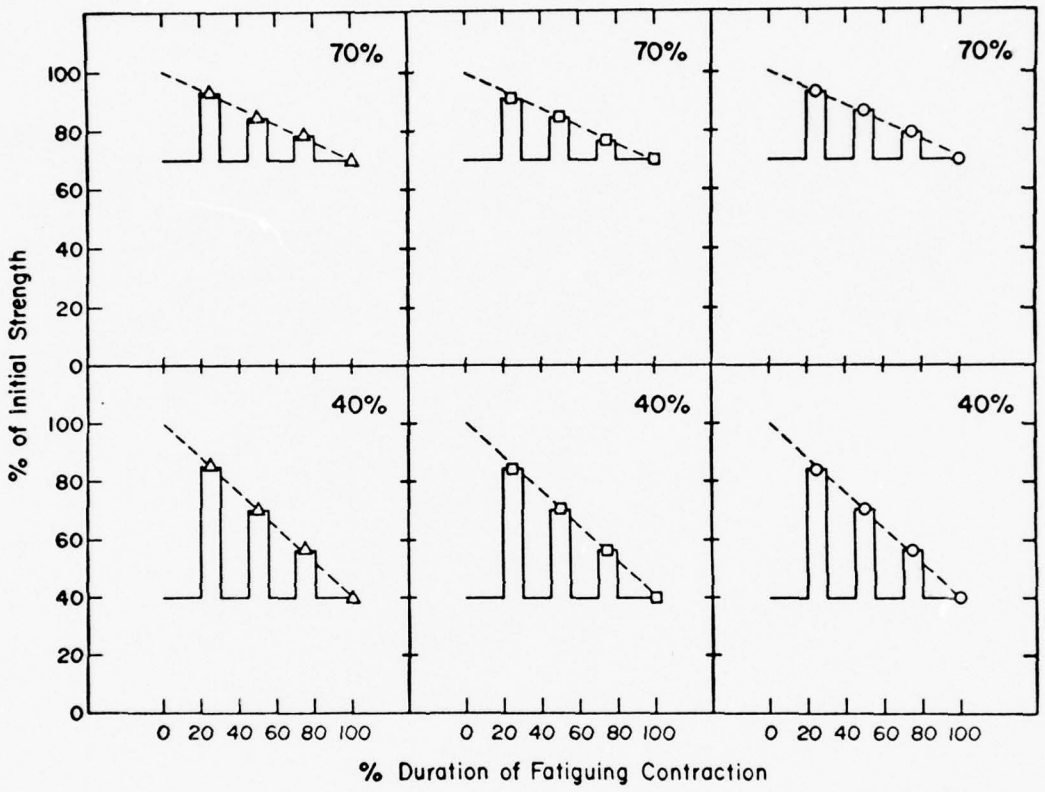

70%
70%
70%
40%
40%
40%
100
80
60
40
20
0
0 20 40 60 80 100
% of Initial Strength
% Duration of Fatiguing Contraction

Figure 5

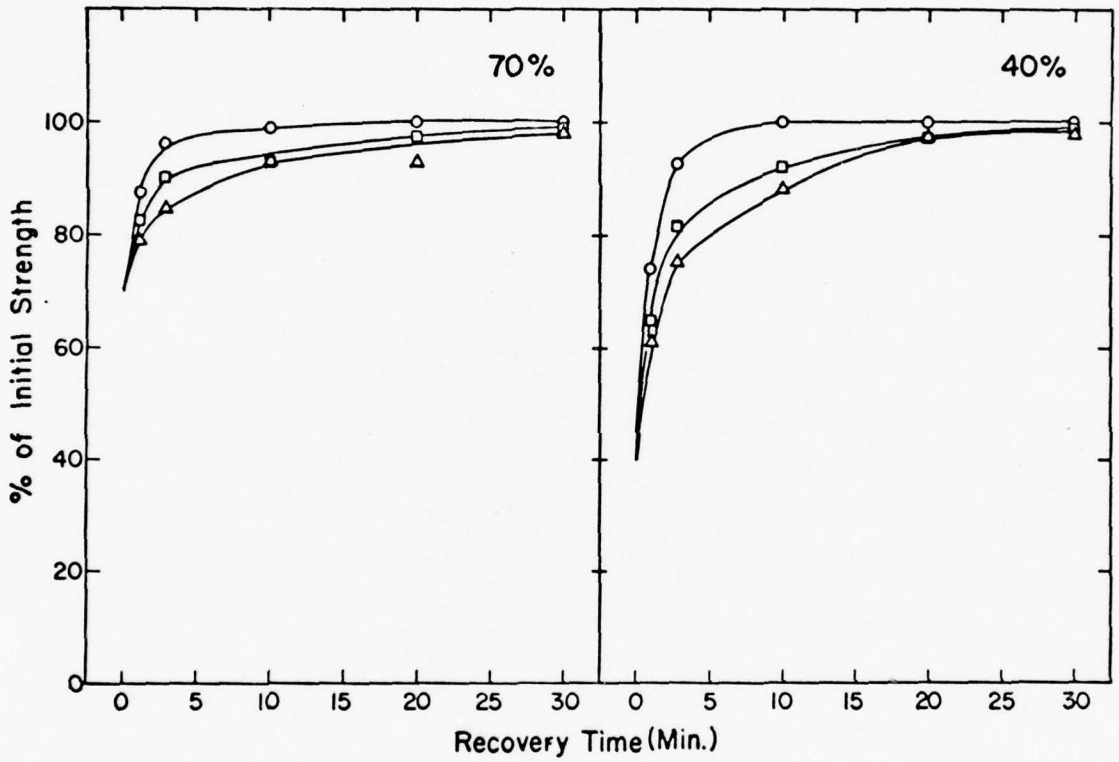

70%
40%
% of Initial Strength
100
80
60
40
20
0
0
5
10
15
20
25
30
Recovery Time (Min.)

Figure 6

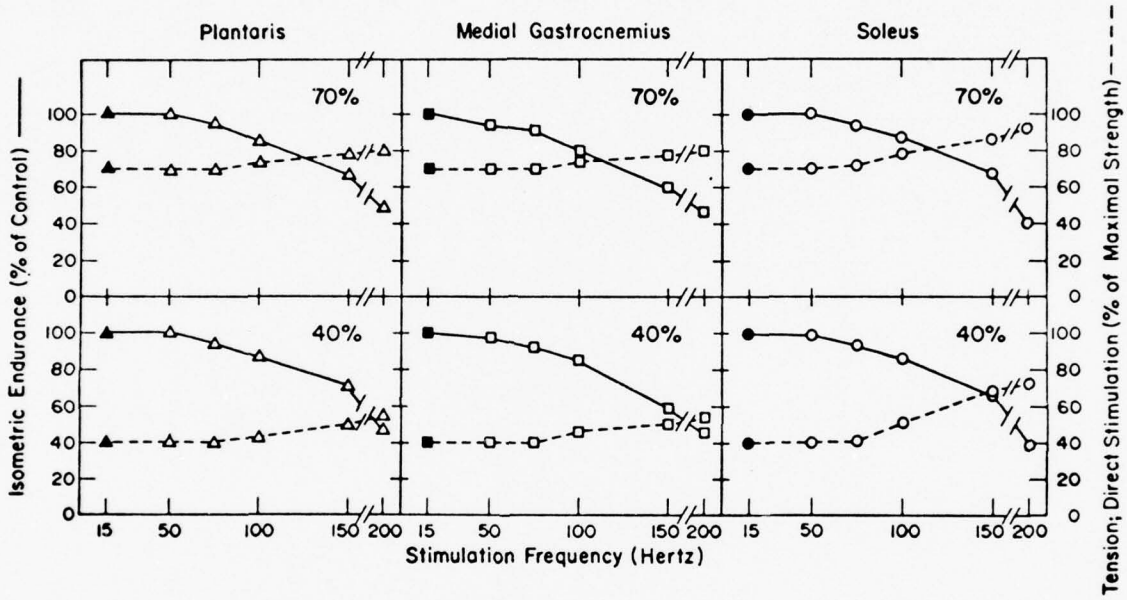

Plantaris
Medial Gastrocnemius
Soleus
70%
40%
Isometric Endurance (% of Control) ——
Tension; Direct Stimulation (% of Maximal Strength) - - - -
Stimulation Frequency (Hertz)
0
20
40
60
80
100
15
50
100
150
200

Figure 7

INVESTIGATION 7

A COMPUTERIZED METHOD FOR THE STIMULATION OF MAMMALIAN MUSCLE.

INTRODUCTION

When a muscle contracts isometrically, tension is produced by the combination of the recruitment of motor units and an adjustment of their frequency of firing of those motor units, a process termed rate coding (7). For weak isometric contractions recruitment alone seems to be the predominant method of generating tension with the frequency of firing of a given motor unit being constant at between 5 and 20 Hz. However, at these low motor unit firing frequencies, the tension that could be developed by all the motor units is only about 50% of the muscle's maximum strength. For strong isometric contractions, rate coding is the method by which tension is adjusted, the frequency of firing of motor units increasing generally to 40 or 50 Hz during maximal efforts, (1, 7). But most studies on muscular function stimulate the muscle, either directly or indirectly,at frequencies most often in the range of 100-300 Hz, much higher than the normal physiological range. The tension generated in this way decays rapidly due, in part, to neuromuscular block (2). In investigations where the muscle is stimulated at low frequencies (usually 10 Hz or less) the contractions are weak and unfused, a condition not normally seen during voluntary activation. Thus, until now, there has been no method of stimulation whereby the muscle can produce smooth graded contractions and maintain tension for any length of time.

In the present investigation this problem has been resolved by the combination of two techniques. First, to produce smooth contractions at low frequencies, a method of sequential activation of the motor units has been employed, as first described by Rack and Westbury (12). Second, to

set the pattern of recruitment and rate coding in a manner analogous to that found during voluntary activity, a computer was used to control the stimulator. The muscle examined here was medial gastrocnemius in the cat since this muscle has approximately the same fiber composition as found in most muscles in man (4, 5).

METHODS

Twelve female cats weighing an average of 2.6 $\pm$ 0.4 kg were used in these experiments. The animals were anesthetized with an intraperitoneal injection of α-chloralose (75 mg/kg body weight) and maintained with booster doses given intravenously through a jugular cannula During the experiments, the cats' rectal temperature was maintained within the range of 37-39° C. Blood pressure and heart rate were monitored through an arterial cannula inserted into the left carotid artery.

Surgery

All experiments were conducted with the cat placed prone on a steel table with one of its back legs fixed rigidly by 2 steel pins driven through the knee and ankle joints. The dorsal aspect of the leg was then exposed from the sacral spinal cord to the calcaneus and freed from the underlying fascia. Medial and lateral gastrocnemius were freed from the surrounding muscles with only their respective tendons being separated from each other. A brass hook tied to the tendon of the muscle was connected to a stainless steel bar. The bar was adjusted so that the muscle was prestretched to

its optimal length and contracted in, as nearly as possible, the same planes of motion as in the intact leg. Four strain gauges on the steel bar transduced the isometric tension of the muscle into an electrical output which was a part of the feedback stimulator described below. The sciatic nerve was exposed and cut just distal to the spinal cord. The distal section of the nerve was stimulated with a rotary sleeve electrode (11) placed approximately 10 mm from the cut end; the nerve was continuously perfused with Ringer's solution at 37° C. All exposed muscles were bathed in liquid paraffin warmed to 37° C.

Asynchronous stimulation

Impulses were delivered sequentially to parts of the sciatic nerve through the sleeve electrode. This device consisted of 3 floating platinum electrodes encased in silicon rubber and in spatial equidistance around the long axis of the sciatic nerve. Stimulation of the cathodes was applied through each electrode in turn, during which time the other two electrodes acted as anodes. From a geometric consideration, assuming the sciatic to be a perfect cylinder, such an arrangement allows for the electrical subdivision of the sciatic into 3 populations of motor fibers. Although some repetitive firing of some part of these populations must occur on theoretical grounds, in practical terms, no difference in maximum tension or endurance is detectable (9). By varying the stimulating voltage delivered through the rotary electrode, the recruitment of motor units can be controlled. Fig. 1 shows the tension developed by medial gastrocnemius during brief (3 sec) isometric contractions where the frequency of stimulation was held constant at 100 Hz (panel A). No tension was developed by the muscle until

the stimulation voltage exceeded 50 mv. Above this voltage, the tensions rose slowly at first but then almost linearly as the voltage increased to a value of about 300 mv, above which the tension reached a plateau; presumably, all motor units were recruited. Rate coding was adjusted by changing the frequency of stimulation through the rotary electrode. For example, when the stimulating voltage was set at 400 mv and the frequency of stimulation was varied between 10 and 100 Hz, a frequency-tension diagram was established as shown on Fig. 1 (panel B). Although the muscle could only develop 44.3% of its maximum strength when stimulated at 10 Hz, the tension developed by the muscle rose rapidly when the frequency of stimulation was increased. The muscle's maximum strength was developed when the stimulation frequency exceeded 75 Hz.

In the experiments described below, both the voltage and the frequency of stimulation were applied in a manner imitative of our present understanding of voluntary contractions. The voltage and frequency were controlled by a hybrid digital-analog computer system as shown in Fig. 2. The system consisted of a strain gauge bridge and amplifiers, a central data processing unit (CP) and a pulse synthesizer and ring counter. The central data processor provided control voltages for the pulse synthesizer and ring counter, adjusting the stimulation voltage between zero and threshold voltages to vary recruitment, and was capable of adjusting the frequency of rotation of the ring counter between 10 and 200 Hz. Thus, with each rotation of the ring counter a 0.2 ms square wave pulse was delivered to each of the three electrodes on the sciatic nerve. The active tension developed by the muscle was transformed into an electrical output through the strain gauge bridge amplifier which provided a feedback of muscle tension to the central processor. At the start of an experiment, the maximum isometric tension of the muscle was determined by stimulating the sciatic nerve

asynchronously at a supramaximal voltage at 100 Hz for 3 sec. The maximum strength was assessed as the peak tension recorded during that time. Ten min later, the required sub-maximal tension was set for the fatiguing isometric contraction. On command, the central processor then initiated a program to set and maintain the target tension. This program was based on our current knowledge of the patterns of recruitment and rate coding during brief and sustained isometric contractions (1, 7), employing first recruitment and then rate coding to achieve and maintain a given target tension. Since recruitment alone can develop about ½ of the maximum voluntary strength in man (7), a frequency from Fig. 1B was chosen which was expected to elicit a similar tension in the cat. This frequency, 15 Hz, was well within the frequency range (5-20 Hz) reported for voluntarily activated motor units in man during recruitment (1, 7, 8). A typical example of such a program is shown in Fig. 3. The illustration shows the tension generated by the muscle (———), the proportion of the fibers recruited (— — — —) estimated from Fig. 1, and the change in stimulation frequency allowed by the CP(--------) during a fatiguing contraction of the medial gastrocnemius muscle in the cat to produce and maintain a tension of 40% of its maximum strength. Initially, the processor locked the stimulation frequency at 15 Hz with the stimulation voltage set at zero. The target was then compared to the tension the muscle was generating and, since the target was greater than the tension, the system controller allowed the stimulation voltage to increase at an initial rate of 200 mv/sec. As the target was approached, this rate decreased asymptotically to a rate as low as 20 mv/sec. If the target was exceeded, the stimulation voltage was decreased by the error detector circuit. The frequency of oscillation of this circuit was damped to 8-10 Hz, a frequency similar to that seen for normal tremor during muscular contraction in man. In medial gastrocnemius, to reach the target tension of 40% of maximal tension about 3/4 of

the fibers were recruited. During the first 5 sec of the contraction, tension was maintained while recruitment decreased by 3% to finally plateau at 72% of the total fiber population. At first, the stimulation voltage at this time was usually about 250 mv. However, as the muscle fatigued, it was necessary to increase the stimulation voltage to maintain the target tension by the further recruitment of motor units. At 90% of the duration of the contraction, an increase in the stimulating voltage could no longer elicit the maintenance of tension (i.e. all motor units were recruited). This was sensed by the CP which then locked the stimulation voltage at that level (about 350 mv) for the remainder of the contraction. This was necessary since any further increase in the stimulation-voltage above this level would lead to electrical overlap and double firing of some motor units in the asynchronous sleeve electrode (9). At this point, the CP began to increase the frequency of firing of motor units to maintain the required tension. Eventually, further increases in the frequency of stimulation could no longer maintain the target and the contraction ended. The maximum frequency of stimulation at fatigue was 40 Hz. The pattern of stimulation was the same for fatiguing isometric contractions performed at any tension. However, recruitment alone at a frequency of 15 Hz could only generate a limited proportion of any muscle's maximum strength (Fig. 1B). Therefore, to reach target tensions at or above this level, the CP recruited all fibers at the onset of the contraction and maintained the target by "rate coding" alone.

Experimental Procedures

Two series of experiments were performed. First, isometric endurance was measured for sustained contractions where the tension was set between 5 and 100% of the muscle's maximum strength. Eight tensions were examined

on each of 4 different cats; the order of the contractions were selected at random. Since the steady state endurance in the 2nd and subsequent of a series of contractions has been shown to be 7% less than that of the first when 30 minutes were allowed between contractions (9), only the second and subsequent contractions of any series have been reported. For a basis of comparison, the isometric endurance of 3 human subjects was used; 2 male and 1 female volunteers (age range 22-29 years) were asked to immerse their arms in a 37° C water bath for 30 minutes prior to a fatiguing contraction at either 20, 30, 40,55, 70 or 100% of their maximum voluntary strength. From previous work (10) it has been shown that such a period of immersion will raise the temperature of the forearm musculature to 37° C. Isometric endurance was measured for the handgrip muscles with a portable handgrip dynamometer similar to one described previously (3). Endurance for only one tension was examined on any experimental day.

Finally, a second series of experiments assessed the relationship between frequency of stimulation and tensions before, during, and after a fatiguing isometric contraction at a tension of 40% MVC. Following a series of 3 sec isometric contractions at frequencies between 10 and 100 Hz, a series of 12 contractions were sustained either half way or to fatigue. Immediately after, a 3 sec contraction was exerted at any of six frequencies between 10 and 100 Hz, the order of presentation being selected at random.

RESULTS

Isometric Endurance

The isometric endurance in the medial gastrocnemius muscle of the cat for tensions between 5 and 100% of the cat's maximum strength is shown in Fig. 4 (□). For tensions greater than about 10% of the maximum strength, the muscle fatigued rapidly. For example, although the endurance for a contraction sustained at 10% of the muscle's strength lasted an average of 382 seconds for the 4 muscles examined, contractions sustained at 40% of the muscle's strength lasted only 75 seconds while contractions sustained at a tension of 70% of the muscle's strength lasted 17 seconds. The implication from the graph was that there was a tension below which the muscle would not fatigue. Therefore, in 2 cats, a tension of 5% of the muscle's maximum strength was set and maintained. After a period of 40 minutes, the muscle showed no sign of fatigue so the contraction was terminated. Thus, a tension equal to 5% of the maximum strength was found to be non-fatiguing. To find out how the endurance times during artificial sequential stimulation compared to that recorded during voluntary muscle contraction, we measured isometric endurance in 3 human subjects at tensions between 10 and 100% of their maximum voluntary strength. These results are also plotted in this figure as the average endurance for these individuals (●). There was a striking similarity of the endurance measured in man and in the cat. Although the endurance in the cat was somewhat lower for most tensions examined, this difference may be due to differences in experimental procedure, since, in the cat, endurance was measured during serial contractions. In the human subjects, however, endurance was only measured at one tension on a given experimental day. The only major difference in endurance between

man and cat was that tensions below about 15% of the maximum strength appeared to be nonfatiguing in man while 10% of the maximum strength was limiting in the cat.

Isometric tensions

The average isometric tension generated from all motor units during 3 sec isometric contractions at various frequencies between 10 and 100 Hz before (O), half way through (▲) and after (●) a fatiguing isometric contraction at 40% of the muscle'smaximum strength is shown in Figure 5. Each point in this figure illustrates the mean tension of contractions exerted in 4 muscles. As the muscle fatigued and reduced its maximum tension it was able to generate higher tensions at progressively lower frequencies. At fatigue, any stimulation frequency above 80 Hz was able to develop the same tension in the muscle.

DISCUSSION

During voluntary activity, skeletal muscle can exert smooth isometric contractions when the asynchronous frequency of firing of its motor units is as low as 5-20 Hz (1, 7, 8). During strong isometric contractions, or during fatiguing isometric contractions, the frequency may reach as high as 50 Hz (1, 7) but rarely exceeds 80 Hz (6). All studies on muscular performance with artificial stimulation to date have failed to take these physiological constraints into account. Previous investigations have enquired into the performance of muscle during either synchronous low frequency activation where the tension exerted by the muscle is weak and unfused, or have sti-

mulated the muscle synchronously at frequencies above 100 Hz or as high as 500 Hz to produce smooth tetanic contractions resulting in a rapid neuromuscular block (2).

In the present investigation, the muscle was stimulated sequentially, a form of activation which more nearly approximated the normal asynchronous activation of muscle during voluntary activity in that smooth and powerful contractions can be developed at low stimulation frequencies. Further, the tetanic tension of medial gastrocnemius was developed at a stimulation frequency of 75 Hz, a frequency again within the reported physiological range. Using the pattern of recruitment and rate coding reported by others during brief (7) and sustained isometric contractions (1), the computer described here was able to set and sustain fatiguing isometric contractions in the cat. The results of these experiments showed a striking similarity in endurance between contractions exerted artificially in the cat and voluntarily in man. It was surprising, however, that the frequency of stimulation at fatigue for any tension examined was usually about 40 Hz, a frequency well below that necessary to develop the optimal tension of the pre-fatigued muscle. Further investigation of this anomaly showed that as the muscle fatigued, the tension-frequency curve (Fig. 1B) shifted to the left such that the fatigued motor units were able to develop their optimum strength at progressively lower frequencies (Fig. 5). The tension frequency curve, at fatigue, closely resembles the tension-frequency curve for soleus (11), a muscle composed almost entirely of slow-twitch fibers (4). Because of the greater fatiguability of the fast twitch units within medial gastrocnemius, it seems likely that the slow twitch units assume a progressively greater role in developing the tension generated by the muscle as it fatigues. Thus, it is not surprising that the tension frequency curve for gastrocnemius should take on the appearance of that for soleus during these contractions.

in strength associated with aging, an increase in body weight factor increased

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Heart Rates

As has been reported previously(15, 17) there was an approximately linear

FIGURE LEGENDS

Figure 1: Figure 1 shows the relationship between tension and stimulation voltage and frequency of a rotary sleeve electrode placed around the sciatic nerve during stimulation of the medial gastrocnemius in the cat.

Figure 2: This figure illustrates diagramatically the computer system used to stimulate muscle.

Figure 3: This figure illustrates the changes in recruitment (— —) and stimulation frequency (- - - -) imposed by the central processor during a fatiguing contraction whose tension (——) was set at 40% of the muscle's maximum strength. The % of the total fibers recruited was estimated from recordings of the stimulation voltage and tension generated during brief isometric contractions from a voltage of 0 to just superthreshold in intensity (Figure 1A).

Figure 4: Illustrated here is the average isometric endurance determined for the medial gastrocnemius muscles of 4 cats (□) during artificial stimulation compared to that recorded from 3 human subjects during voluntary contractions (●).

Figure 5: This figure shows the maximum tension generated by medial gastrocnemius during 3 sec bouts of stimulation at various frequencies before (○), halfway through (▲) and after (●) a fatiguing isometric contraction at a tension of 40% MVC.

blood pressure in either sex.

Resting diastolic blood pressure was significantly increased with weight factor only in women ($p < 0.01$). Systolic blood pressure at rest,

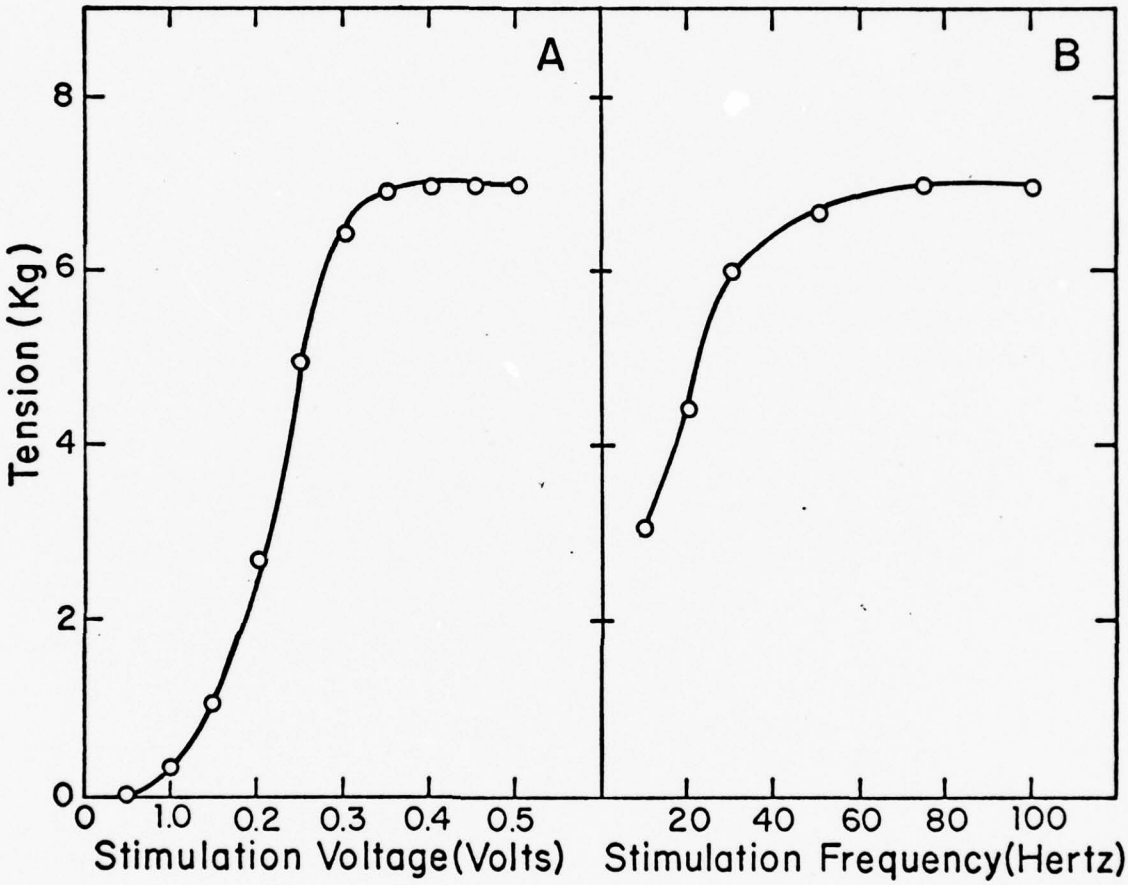


FIGURE 1

associated with an increase in blood pressure at the end of the 40% MVC as illustrated by the family of curves at varying ages. Also, at any given age,

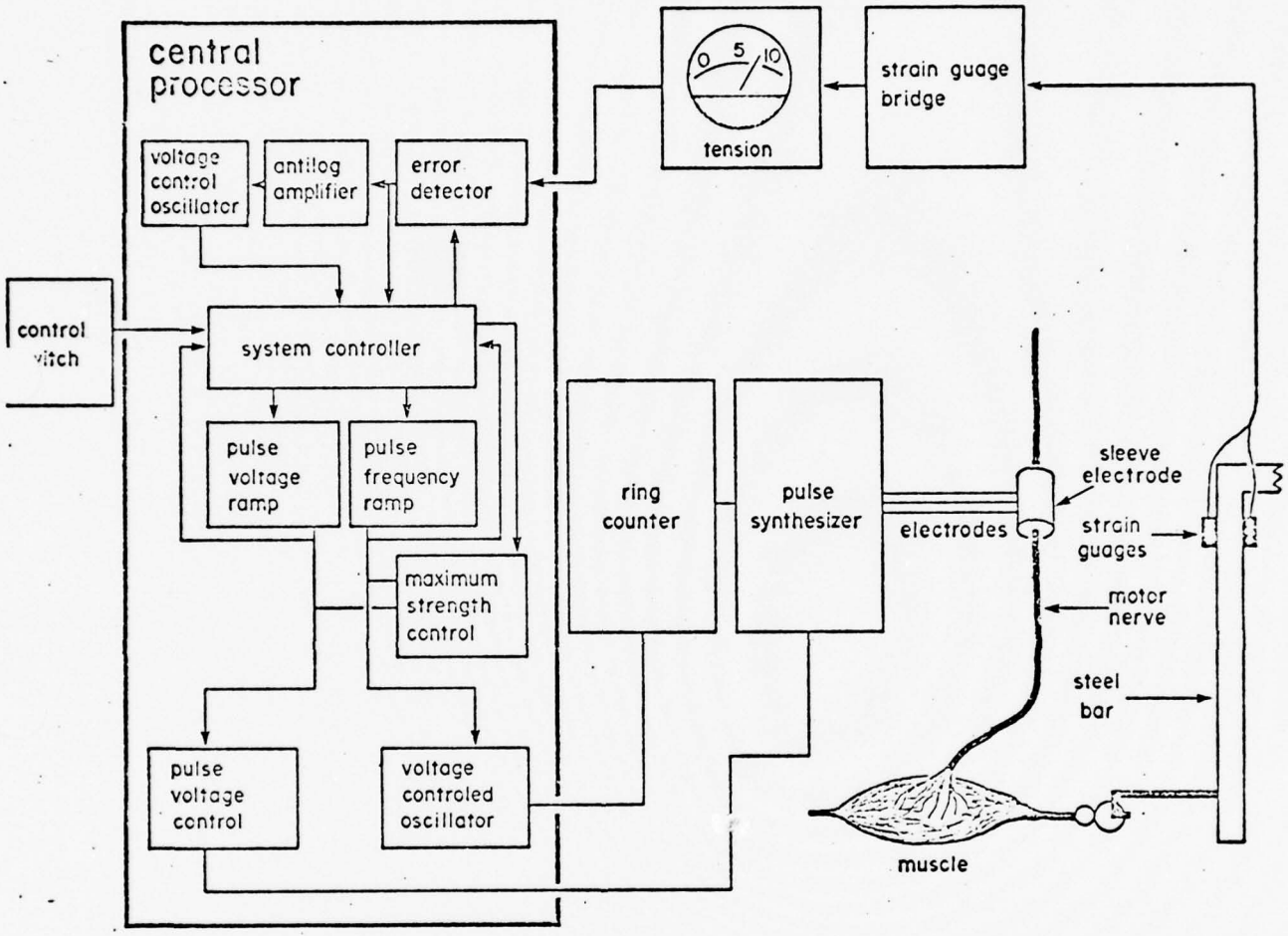

central processor
voltage control oscillator
antilog amplifier
error detector
0 5 10
tension
strain guage bridge
control vitch
system controller
pulse voltage ramp
pulse frequency ramp
maximum strength control
pulse voltage control
voltage controled oscillator
ring counter
pulse synthesizer
electrodes
sleeve electrode
strain guages
motor nerve
steel bar
muscle

FIGURE 2

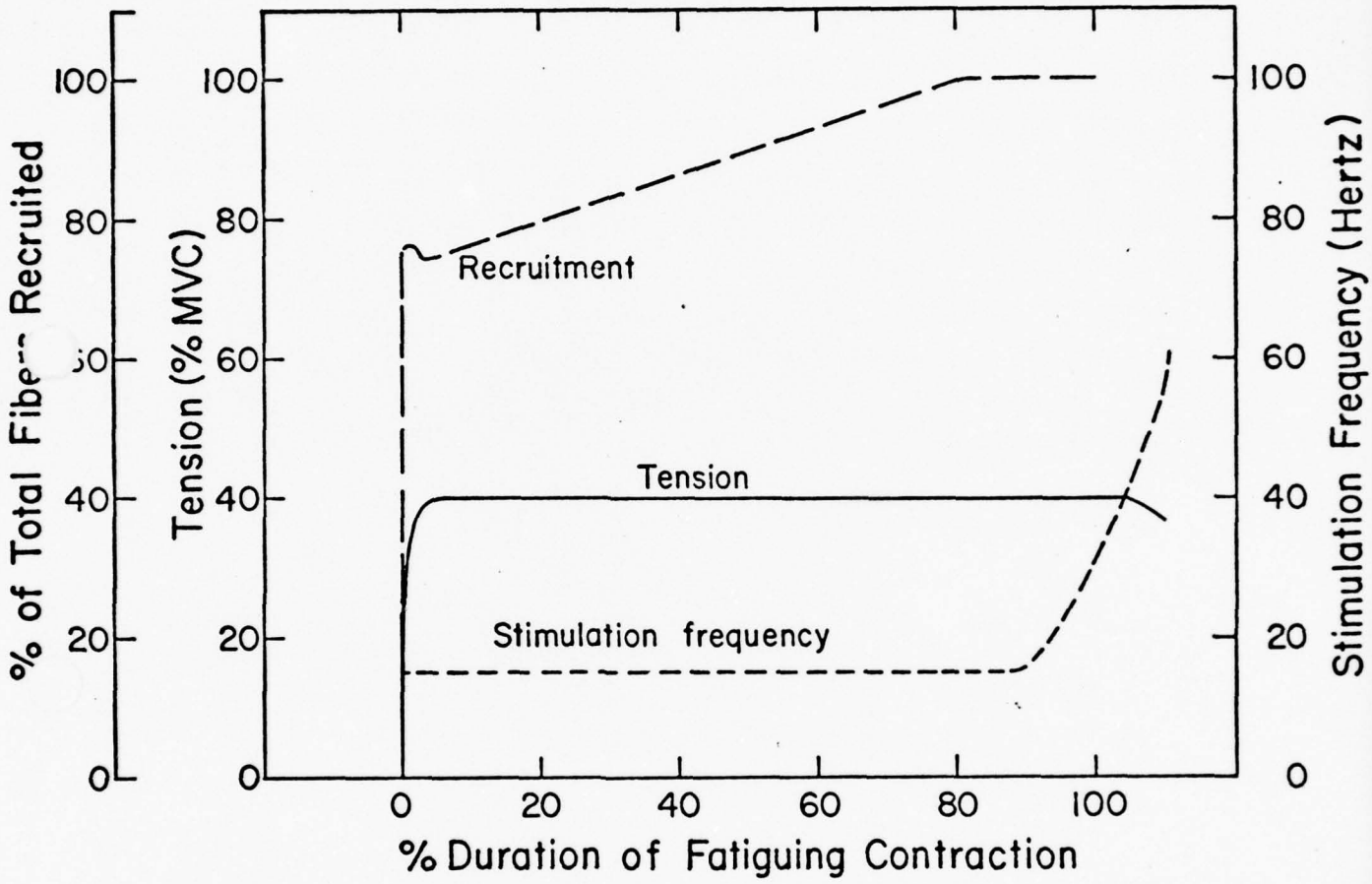

% of Total Fibers Recruited
Tension (% MVC)
Stimulation Frequency (Hertz)
Recruitment
Tension
Stimulation frequency
% Duration of Fatiguing Contraction
0
20
40
60
80
100

FIGURE 3

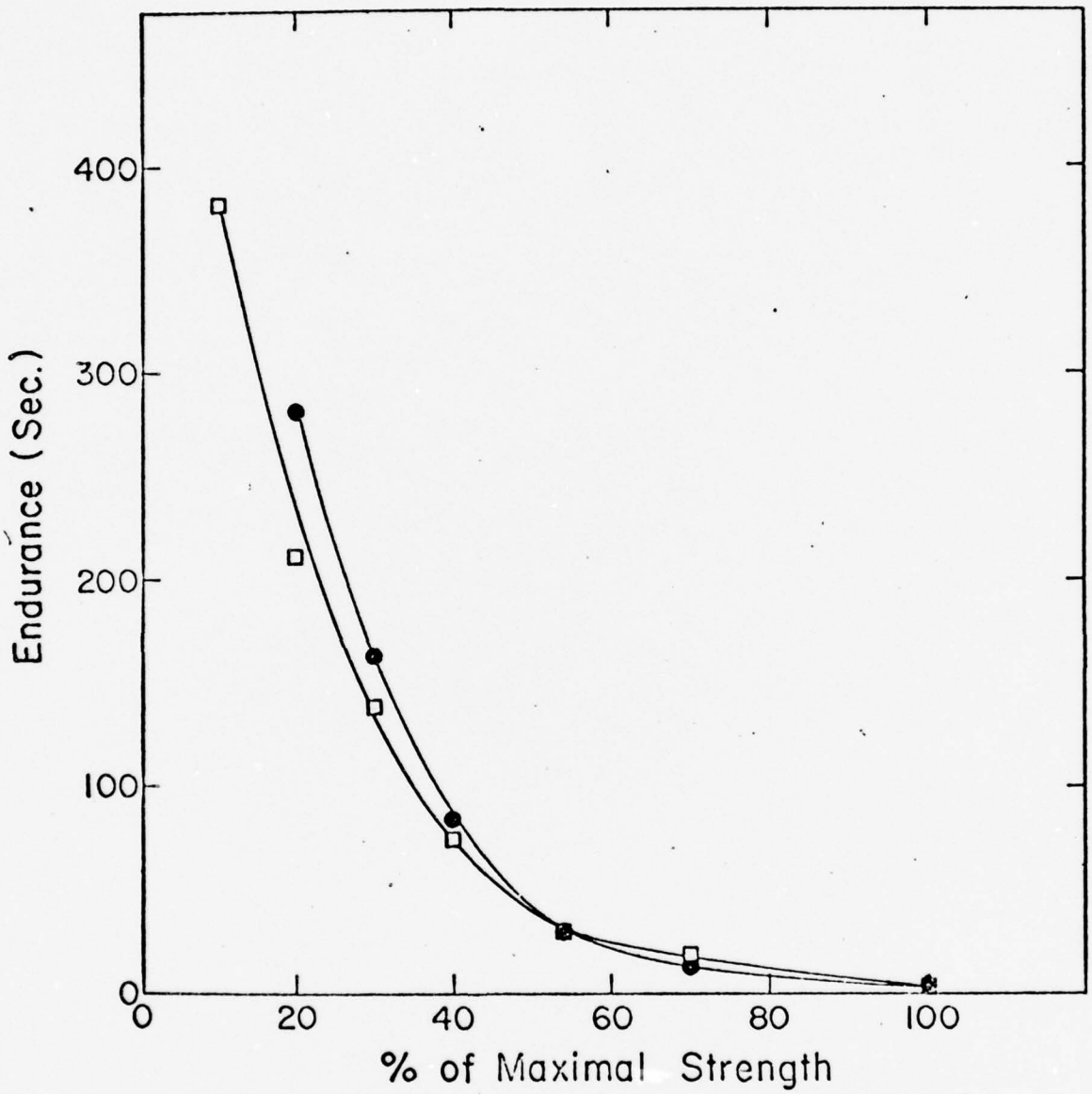

400
300
200
100
0
Endurance (Sec.)
0
20
40
60
80
100
% of Maximal Strength

FIGURE 4

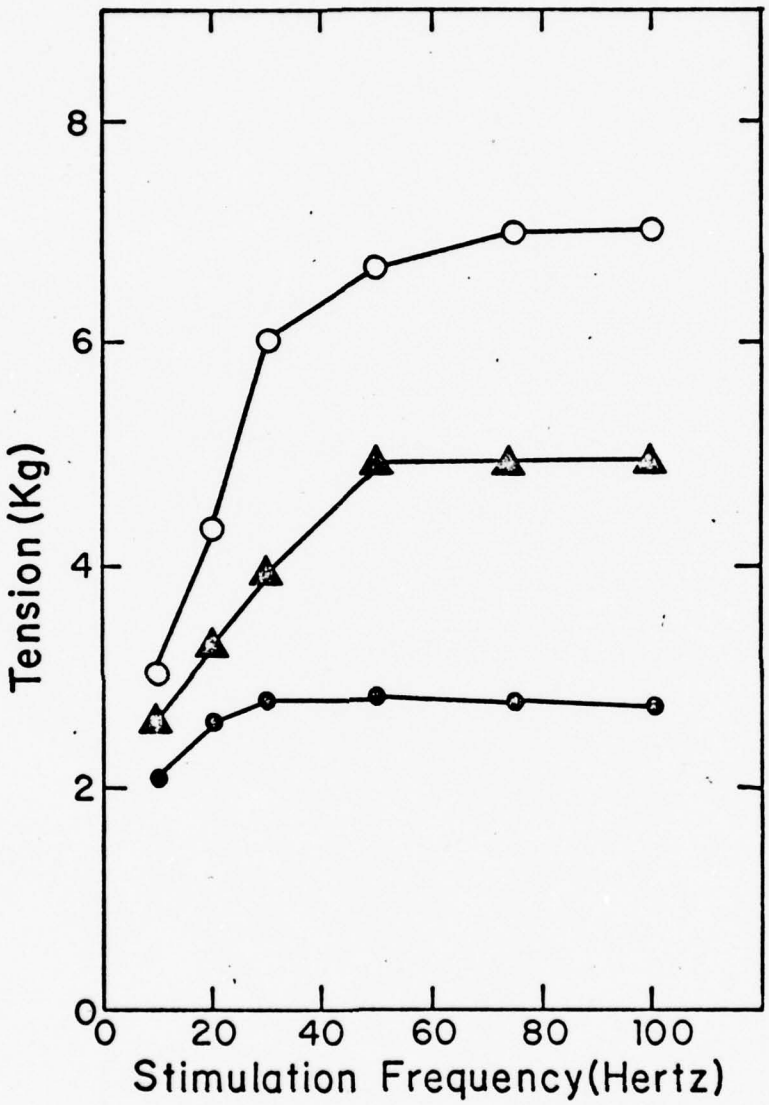

8
6
4
2
0
Tension (Kg)
0
20
40
60
80
100
Stimulation Frequency(Hertz)

FIGURE 5

INVESTIGATION 8

ISOMETRIC STRENGTH, ENDURANCE, AND THE BLOOD PRESSURE AND HEART RATE RESPONSES DURING ISOMETRIC EXERCISE IN HEALTHY MEN AND WOMEN, WITH SPECIAL REFERENCE TO AGE AND BODY FAT CONTENT.

INTRODUCTION

The endurance of fatiguing static effort has been reported to be independent of the muscle group involved, of muscle strength (11, 18), and to be unaltered by dynamic or static training (6, 10, 14).

During sustained isometric contractions held to fatigue, the cardiovascular system responds with a modest rise in heart rate, and a marked rise in both systolic and diastolic blood pressures (8). After isometric exercise, blood pressure and heart rate rapidly return to control values. While these changes have been clearly established in young men, little attention has been paid to the influence of inherent factors such as aging, sex, and body fat content which might modify these responses.

The present investigation assessed the influence of aging and body fat content on sustained isometric exercise and the associated blood pressure and heart rate responses in men and women. Since aging is reported to be commonly associated with an increase in body fat (21), these variables are confounded so that a population selected to study the effect of age on some physiological response will contain a progressively greater proportion of subjects who are overweight. Most studies on any kind of muscular performance have failed to take that interaction into consideration. We have been able to do this by re-analyzing the data from two previous studies (15, 17). This has been accomplished in two ways; first, the influences of age and overweight have been analyzed separately in terms of a population trend, and second, by multiple regression, the individual contributions of each variable has been assessed.

METHODS AND PROCEDURES

Subjects

One hundred male and 83 female volunteers acted as subjects in these experiments. Their general characteristics have been reported previously (15, 17). Each individual was first interviewed, at which time the procedures used in the experiments, as well as any possible hazards of the experiment, were explained in detail. All potential subjects were then medically examined.

Since the intention was to examine only healthy individuals, volunteers were not accepted as subjects if: (1) they had a history of any form of cardiovascular disease, (2) their resting blood pressure exceeded 155/95 mm Hg, or (3) there was any evidence of abnormality in their 12 lead resting ECG.

Strength and Endurance

Isometric strength and endurance was measured on a portable strain-gauge, hand dynamometer similar to the one described by Clarke, Hellon and Lind (1). Strength was taken to be the larger of two brief (2-3 s) maximal voluntary contractions (MVC); 2 min. were allowed between these contractions. After a rest of 5 min., isometric endurance was measured as the duration of a sustained handgrip contraction at a tension of 40% MVC; the duration was measured to the nearest second. All measurements were recorded with the subject in the seated posture with male subjects nude above the waist and female subjects wearing halter tops; environmental temperature was kept constant at $24 \pm 1^{o}C$.

Heart Rate

Heart rate measurements were obtained before, during and after each endurance contraction from a continuous recording of the ECG. Since the duration of the isometric contraction varied from person to person, the heart rates during exercise were measured on a relative time scale; measurements were

made at 20, 40, 60, 80, and 100% of the duration of the 40% MVC; they were measured 1 min. before and at 30, 60, and 90 s post-exercise.

Blood Pressures

Blood pressure was measured by ausculation on the inactive arm. Measurements were made each minute at rest, as often as possible during exercise and at 30, 60, and 90 s following the contraction. As with the measurement of the heart rates, blood pressure measurements during exercise were converted by a computer to a relative time base by interpolation of the raw data at 20, 40, 60, and 80% of the endurance time, and by extrapolation for values at the end (100%) of the endurance contraction.

Assessment of Body Fat Content

In experiments involving large numbers of subjects, it was expedient to estimate body fat content empirically. From mortality figures compiled by large insurance companies, an average weight based only on height and sex has been derived. This "ideal" weight represents the statistical assessment of the weight at which the individual will live longest (21). Coincidentally, "ideal" weight corresponds with the weight of most individuals at about the age of 20 years when the body fat content averages 10-20% for men and 15-30% for women (7, 13, 20). In studies involving large populations where the individual age varies, a simple ratio of "ideal" weight to actual weight has been demonstrated to be a satisfactory index of body fat content (19). Therefore, in this study we calculated the weight factor as follows:

$$\text{weight factor} = \left(\frac{\text{measured weight} - \text{ideal weight}}{\text{ideal weight}} \right) \times 100$$

A weight factor of 0 is therefore calculated for an individual whose weight is at the "ideal" value for his height, while a weight factor of 100, for

example, would represent an individual whose weight was twice that of the table value. The table of "ideal" weight used here is the one published by the Metropolitan Life Insurance Company (21).

Statistical Analysis of Data

In the analysis of the data the calculation of means, variances, standard deviations, correlations, unrelated t tests and regression equations by the method of least squares were performed as required on a Linc computer. Where applicable the means are reported $\pm$ the standard deviation. Regression coefficients are reported $\pm$ the standard error of the slope.

Where the data was considered to be affected by more than one independent variable, the statistical analysis was based on multiple regression. The multiple regression and corresponding standard error of the regression (reported as y $\pm$ the standard error), F tests and partial correlations will be referred to as multi-factor analysis. These calculations are part of the SPSS statistical package (12) calculated on an IBM 360 computer.

Statistical significance in all cases was chosen at p values less than 0.05.

Where regression lines are drawn in figures, the upper and lower limits of the lines are set at the corresponding upper and lower levels of the actual data. Statistical analysis showed that all data distributions were sinusoidal in form.

where the tension exerted by the muscle is weak and unfused, or have sti-

RESULTS

Weight Factor and Age

The relationship between age and weight factor is illustrated in Fig. 1. The data showed a significant increase in weight factor with increased age in both men (dotted line; $p < 0.05$) and women (solid line; $p < 0.01$). While the slopes of the regression curves were similar, at all ages women had lower weight factors than men. The mean weight factors and ages for the men were $15.2 \pm 17.2\%$ and 39.9 ± 11.9 years; those of the females were $1.0 \pm 12.4\%$ and 36.4 ± 13.8 years.

sometric Strength

Table 1 first lists the simple correlations relating the strength, age and the weight factors of male and female subjects. As men aged, their strength did not vary ($p > 0.05$) but they did show a significant increase ($p < 0.01$) in strength associated with an increase in the weight factor. In contrast, there was a significant decrease in strength in women ($p < 0.01$), but no significant influence of the weight factor on strength.

Since the age and the weight factor were interrelated (Fig. 1), multi-factor statistical analysis was used to examine the independent contribution of each variable on strength. These results are shown in the listing of "partial correlations" (Table 1) and are illustrated graphically in Fig. 2. Both age and body weight factor modified the strength of men and women ($p < 0.05$). In Fig. 2 two sets of four regression lines (calculated from multiple regression equations) represent the relationship of strength to body weight factor for men and for women; regression lines of each set were calculated for subjects of 20, 30, 40, and 50 years of age. These results indicated that while there was a decrease

in strength associated with aging, an increase in body weight factor increased strength. Thus, a decrease in strength related to age may not be evident if the subject becomes overweight.

Isometric Endurance at 40% MVC

With a correlation of only 0.11, there was no significant ($p > 0.05$) change in isometric endurance with aging in men. The average endurance time for the men was 139 ± 30.9 s. Surprisingly, the average endurance of the women was substantially longer ($p < 0.01$) at 172 ± 52 s. Further, in women the isometric endurance also increased (Table 1) significantly with age ($p > 0.01$).

In men there was a significant decrease in endurance with increased weight factor ($p < 0.01$) as shown in Table 1. While a similar trend was evident in women, due to the large spread of the data, the correlation was not significant ($p > 0.05$).

Multi-factor analysis was again used to assess the relationship of age and the body weight factor, independently, on isometric endurance. The results of this analysis are listed as partial correlations in Table 1 and graphically illustrated in Fig. 3. In all subjects, both partial correlations and multiple regression confirm that while an increase in age was associated with an increase in endurance, an increase in the body weight factor was associated with a decrease in endurance. These relationships were both statistically significant ($p < 0.05$). The family of curves in Fig. 3 reveals that at any weight factor isometric endurance increased with each age decade (illustrated as endurance at 20, 30, 40, and 50 years of age). Conversely, in any decade an increase in the weight factor resulted in a decrease in isometric endurance.

Heart Rates

As has been reported previously (15, 17) there was an approximately linear rise in the heart rate and blood pressure throughout the duration of the 40% MVC. At rest there was a lower ($p < 0.05$) heart rate with age in the women, but not in the men. At the end of the 40% MVC contraction, however, age was associated with lower heart rates in both male and female subjects ($p < 0.01$).

In both men and women there was no significant relationship between the body weight factor and the heart rate either at rest or at the end of the 40% MVC contraction (Table 1). However, another variable, resting heart rate, was significantly correlated ($p < 0.01$) with the heart rate response to isometric exercise. Figure 4 illustrates by multiple regression the relationship of age and the resting heart rate on the heart rate at the end of the 40% MVC contraction. During any age decade the heart rate, which increased in all subjects during isometric exercise, had its highest absolute magnitude in individuals with higher resting heart rates. Additionally, for any resting heart rate, the heart rate at the end of the 40% MVC was highest in the younger subjects. For example, in women, where age was associated with a decrease in resting heart rate, the overall effect of age on the heart rate at the end of a 40% MVC contraction was twofold: there was (1) a decrease associated with a decrease in resting heart rate, and (2) a decrease associated with the effect of age on the rate of rise of the heart rates.

Blood Pressures

Aging was associated with an increase in systolic blood pressure at rest in both men and women (Table 1). In contrast, only in women was the diastolic blood pressure correlated significantly with aging. During exercise, the influence of aging on systolic blood pressure was further exaggerated, whereas by the end of the 40% MVC, there was no significant influence of aging on the diastolic

blood pressure in either sex.

Resting diastolic blood pressure was significantly increased with weight factor only in women ($p < 0.01$). Systolic blood pressure at rest, however, was significantly increased ($p < 0.01$) with an increase in weight factor in both the men and the women.

There was no significant relationship ($p > 0.05$) between either systolic or diastolic blood pressures recorded during exercise and the weight factor in men (see Table 1). In women, systolic but not diastolic blood pressure was related to the weight factor throughout the exercise as demonstrated by the significant correlation between the weight factor and the blood pressure at the end of the 40% MVC (Table 1).

Multiple regression was again used to assess the true contribution of age and the weight factor in eliciting a blood pressure response. In women, resting systolic blood pressure was significantly influenced by both age and the body weight factor ($p < 0.01$), the increase in blood pressure associated with each being additive. In men, although the same trend was present, the increase in blood pressure associated with age was not significant (Table 1). Figure 5 illustrates the multi-factor analysis of the effects of the body weight factor and age on systolic blood pressure at rest in women. The family of lines represents the calculated regression for weight factor and systolic blood pressure of individuals of 20, 30, 40, and 50 years of age. At any one body weight factor, aging was associated with an increase in systolic blood pressure at rest. At any age, increasing the body weight factor was associated with an increase in systolic blood pressure.

The influence of body fat on systolic blood pressure diminished during the contraction so that systolic blood pressure at the end of the 40% MVC was correlated to resting blood pressure or age in men (left panel, Figure 6) and women (right panel, Figure 6). At any resting blood pressure, age was

associated with an increase in blood pressure at the end of the 40% MVC as illustrated by the family of curves at varying ages. Also, at any given age, an increase in the resting systolic blood pressure was associated with an increase in the blood pressure at the end of the 40% MVC contraction. Thus, any factor influencing the resting systolic blood pressure affected the blood pressure during isometric exercise. For example, the blood pressure at the end of the 40% MVC contraction in men and women was increased by all three factors studied: (1) an increase in resting blood pressure due to age; (2) an increase in resting blood pressure due to weight factor; and, (3) a further increment in systolic blood pressure during isometric exercise due to aging.

Diastolic blood pressure, which always increased at the end of the 40% MVC contraction as a result of the exercise, was further influenced by only resting diastolic blood pressure ($p < 0.01$). This relationship was true for both men and women.

DISCUSSION

Since age and body weight are known to be related, multi-factor statistical analysis was used to delineate the independent contributions of age and weight to strength and endurance. Age alone was associated with a decrease in strength and an increase in endurance in both men and women. The age-associated decrease in strength and increase in endurance was masked particularly in men by the increase in body fat content in the older decades. Associated with this increase in body fat, there was an opposing increase in strength and decrease in endurance. However, the men we examined did not show as much of a reduction in strength due to age as did the women.

Endurance in women was clearly longer than that in the men. However, the weight factor was 15% less in women than in men, while the mean ages were similar. Thus, multiple regression showed that much of the difference in endurance between sexes in this population were attributable to differences in their body fat contents.

In studies involving naval personnel (9) and Air Force personnel (4), there was a significantly greater strength of the arm and leg muscles of overweight individuals. Both those authors attributed the increase in strength to a training effect of lifting extra body weight in the subject's normal daily activities. In the case of the handgripping muscles, Josenhans speculated that merely lifting extra body weight out of a chair a few times daily could increase isometric strength. While the increase in strength may be attributable to a training effect on strength by lifting additional body weight, dynamic training does not alter isometric endurance (6). On the contrary, it has been stated (6, 10, 11, 14, 18) that when an individual performs isometric exercise at a standard fraction of his own maximum strength, the endurance time will remain

the same as that of others performing the same task. However, in those studies the subjects were, for the most part, healthy young men who cannot be regarded as representative of the population as a whole. In the present investigation, with a much larger population of subjects of highly variable ages and weights, we found that although our individuals all worked at the same relative load, endurance was a function of both of these variables.

The mechanism of the decrease in strength and increase in endurance associated with aging is open to speculation. One possibility is that this increase in endurance is merely a reflection of the lower absolute work load during the sustained isometric contraction in older people. This thesis is supported by the findings from the female subjects, who had lower isometric strength than their male counterparts, and therefore exerted less absolute tension at 40% MVC, but had a longer isometric endurance. However, our additional computer analysis revealed that once the influence of age and body fat were removed from the data, there was no significant correlation between the MVC and endurance. Further, even after correcting the differences in age and body fat, our men still displayed greater strength and less endurance than the women. But other factors might influence ne strength and endurance as well. Muscle in man is a mixture of "fast" and "slow" fiber types. The "fast" fibers, low in myoglobin, have been associated with great strength and speed but low endurance while the "slow" fibers have been associated with low strength but great endurance. The relative proportions of these fibers in any one muscle varies with age (5). At birth, all skeletal muscle fibers appear to be "slow". During the period of growth and maturation, some of these differentiate into "fast" fibers (2). However, as aging proceeds, some of these "fast" fibers de-differentiate back into "slow" fibers (3). This idence, coupled with a reduction in the number of active muscle fibers due to aging (5) might help explain the decrease in strength and increase in endurance in men and women.

The influence of body fat on isometric endurance has been recently explored in our laboratory (16). Our findings were that body fat content was directly related to deep muscle temperature in the forearm. Increases in muscle temperature result in a marked decrease in isometric endurance (1) and in our studies the changes in the temperature of muscles in the forearm were sufficient, in themselves, to explain the corresponding changes in isometric endurance (16).

While the resting systolic blood pressure of both the women and the men increased with age, the resting values for the young women were lower than those of the young men but increased faster with age than the men's, until at age 60, there was no difference due to sex. These facts are in agreement with the extensive data compiled by the Society of Actuaries. Multi-factor analysis revealed that at least part of this age-associated hypertension was due to an increase in body fat content in the older individuals. In fact, the correlation of body fat content to resting systolic blood pressure was so high that in males the contribution of aging becomes statistically insignificant.

The systolic blood pressure at the end of the 40% MVC was affected by both the resting systolic blood pressure and age. It was particularly striking that the duration of the 40% MVC had no correlation to either systolic or diastolic blood pressure when the influence of age and resting blood pressure were delineated. It is usually considered that at rest the increase in systolic blood pressure is due to a decrease in the flexibility of the arteries. The decreased aortic compliance would then be responsible for the greater blood pressures in our older men during isometrics.

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TABLE 1

TABLE OF CORRELATIONS AND PARTIAL CORRELATIONS IN MEN AND WOMEN

Category	Men				Women			
	Age	Weight Factor	Age+	Weight Factor+	Age	Weight Factor	Age+	Weight Factor+
Endurance	0.110	-0.441**	0.240*	-0.480**	0.279*	-0.176	0.359**	-0.290**
Strength	-0.118	0.419**	-0.240*	0.449**	-0.503**	0.043	-0.545**	0.247*
Resting systolic BP	0.225*	0.295**	0.169	0.264*	0.602**	0.469**	0.541**	0.367**
Resting diastolic BP	0.051	0.187	-0.094	0.205*	0.283**	0.313**	0.227*	0.246*
Resting Heart Rate	-0.043	0.110	-0.069	0.132	-0.256*	0.012	-0.274*	0.102
Systolic BP at end of 40% MVC	0.325**	0.116	0.278**	0.003	0.639**	0.281**	0.604**	0.107
Diastolic BP at end of 40% MVC	0.024	0.166	-0.040	0.200	0.168	0.153	0.127	0.106
Heart Rate at end 40% MVC	-0.273**	-0.126	-0.254	-0.067	-0.476**	-0.020	-0.495**	0.157

\+ Denotes partial correlations with other variable held constant

* $p < 0.05$

** $p < 0.01$

If neither * or ** are present, then $p > 0.05$

Figure 1: The relationship of age to the weight factor is represented here as a linear regression line for men (dotted line) and women (solid line). The regression equations are: $y = 10 + (0.13 \pm .03)x$ for males and $y = -5 + (0.17 \pm .04)x$ for females.

Figure 2: Multi-factor analysis of the relationship of strength to age and body weight factor in men (upper curves) and women (lower curves). Here, strength (ordinate) is related to the body weight factor (abscissa) with four individual lines calculated for individuals 20, 30, 40 and 50 years of age. The multiple regression equations are: $y(\pm 6.9) = 51.59 - 0.138$ age $+ 0.206$ wt. for males and $y(\pm 5.4) = 37.9 - 0.247$ age $+ 0.107$ wt. for females.

Figure 3: Multi-factor analysis by multiple regression illustrates the relationship of isometric endurance (ordinate) to the weight factor (abscissa) and age (four curves for individuals of 20, 30, 40 and 50 years of age) in males (upper panel) and females (lower panel). The multiple regression equation for males is: $y(\pm 27.3) = 131.28 - 0.874$ wt. $+ 0.534$ age and for the females is: $y(\pm 48.8) = 1.429$ age $- 1.243$ wt. $+ 121.1$.

Figure 4: Multi-factor analysis relating the heart rate at the end of the 40% MVC contraction (ordinate) to the resting heart rate (abscissa) and age (illustrated as bands for individuals of 20, 30, 40 and 50 years of age). The multiple regression for men is illustrated in the left panel and that for women in the right panel. The multiple regression equations are: $y(\pm 12.1) = 56.53 + 0.744\ HR_r - 0.294$ age for males and $y(\pm 13) = 58.75 + 0.815\ HR_r - 0.411$ age for females.

Figure 5: Multi-factor analysis showing the relationship of resting systolic blood pressure (ordinate) to the weight factor (abscissa) for women at 4 ages (20, 30, 40, and 50 years old). The regression equation is: $y(\pm 12.8) = 106.3 + 0.527 \text{ age} + 0.44 \text{ wt.}$

Figure 6: Multi-factor analysis illustrating the relationship of the systolic blood pressure at the end of the 40% MVC contraction (ordinate) to the resting systolic blood pressure (abscissa) in men (left panel) and women (right panel) at four ages. The multiple regression equations are: $y(\pm 16.5) = 42.2 + 0.96\ BP_r + 0.33$ age for men and $y(\pm 15.7) = 44.35 + 0.89\ BP_r + 0.44$ age for females.

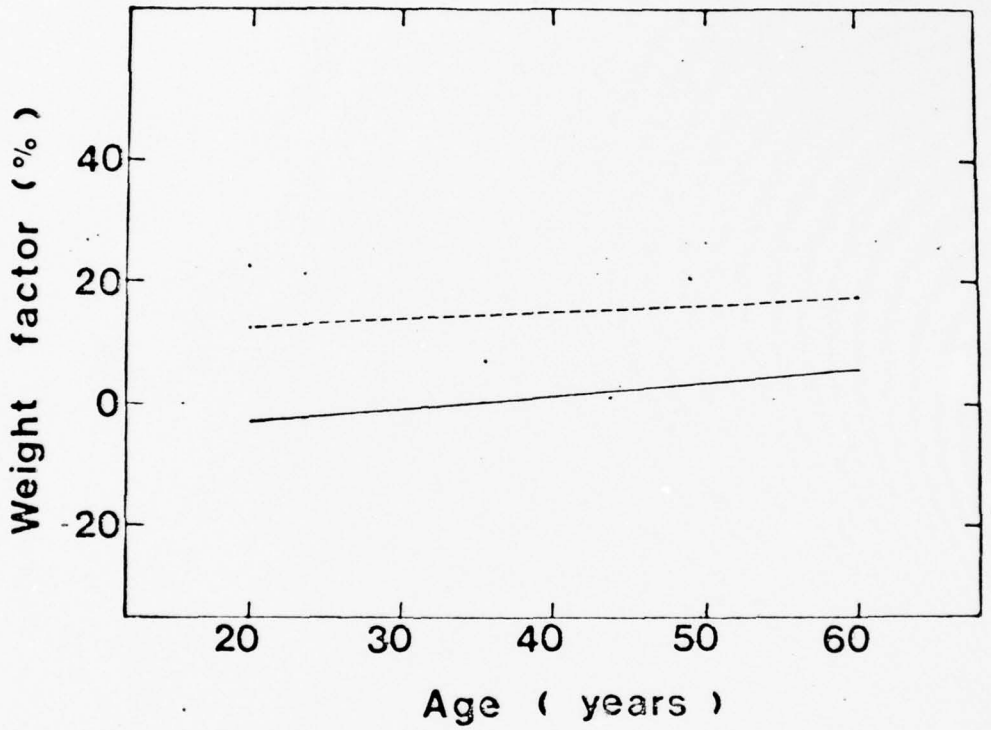
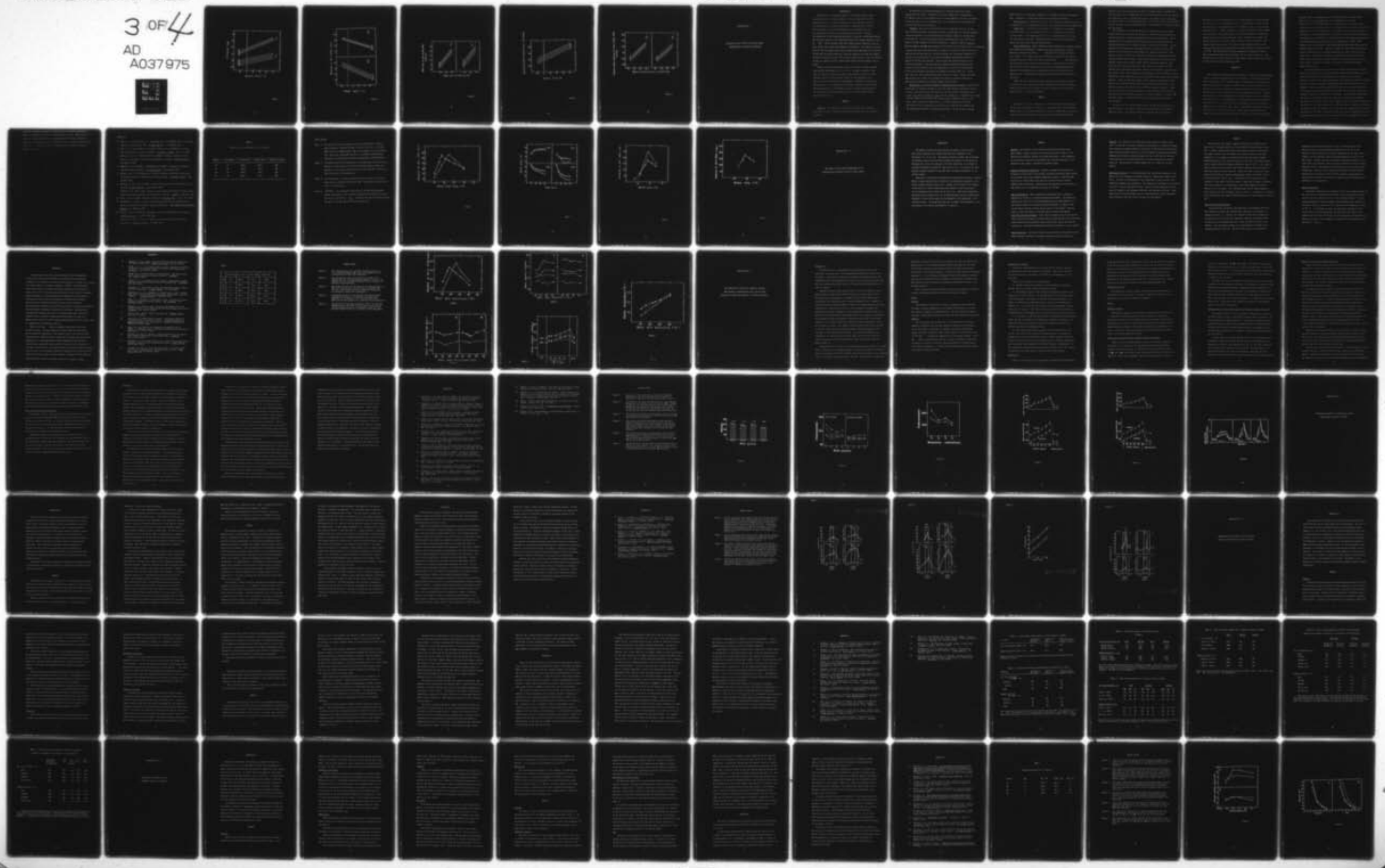


Figure 1

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THE INVESTIGATION OF METABOLIC AND CARDIOVASCULAR RESPONSES TO --ETC(U)
JUL 76 A R LIND, H BARCROFT, J S PETROFSKY AF-AFOSR-2362

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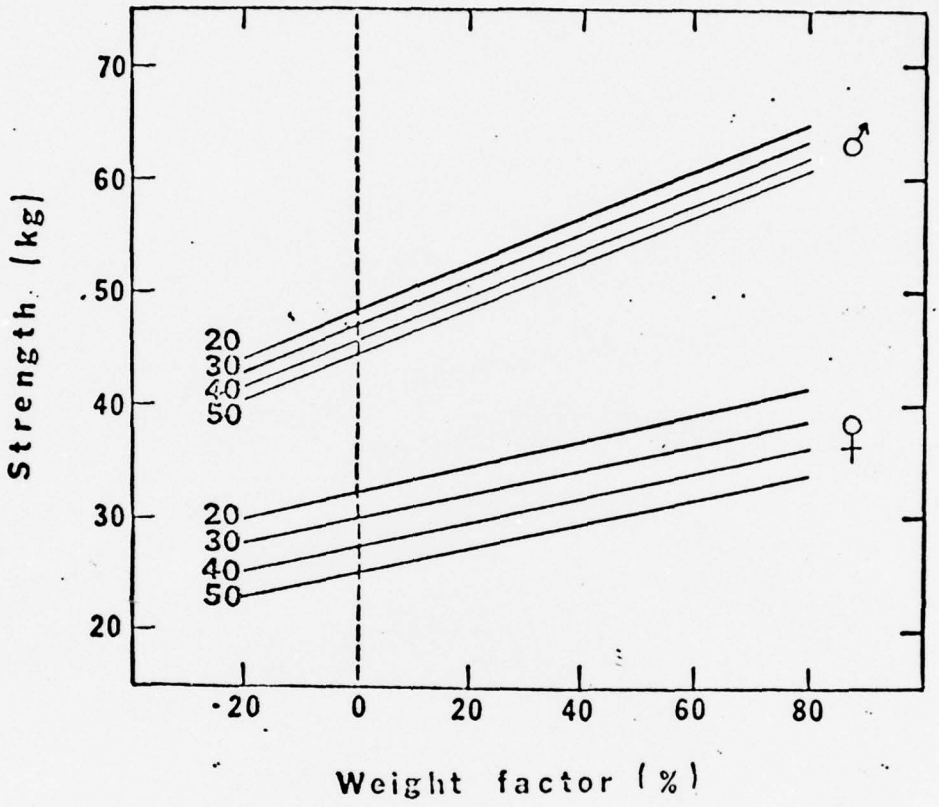

Strength (kg)
70
60
50
40
30
20
20
30
40
50
♂
20
30
40
50
♀
-20
0
20
40
60
80
Weight factor (%)

Figure 2

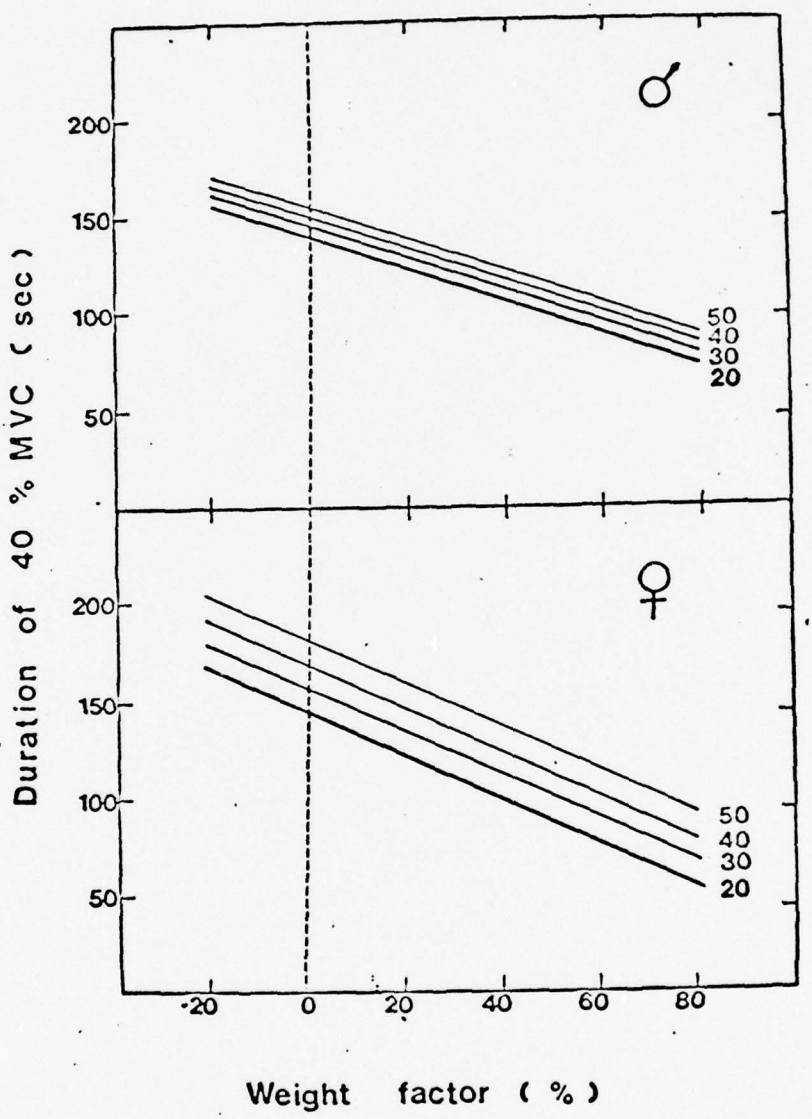

Duration of 40 % MVC (sec)
200
150
100
50
♂
50
40
30
20
♀
50
40
30
20
-20
0
20
40
60
80
Weight factor (%)

Figure 3

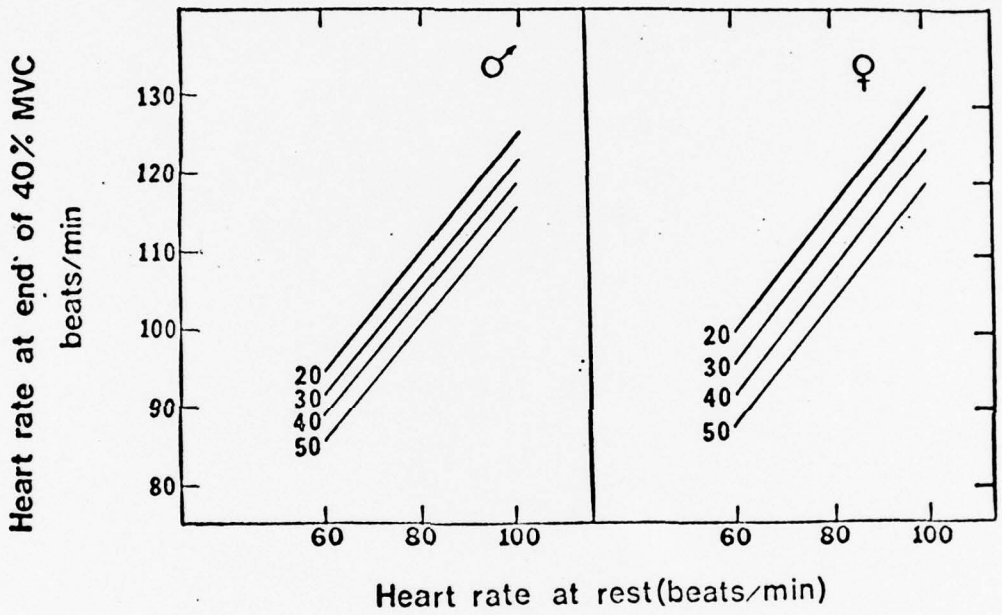

Heart rate at end of 40% MVC
beats/min
130
120
110
100
90
80
♂
♀
20
30
40
50
60
80
100
Heart rate at rest(beats/min)

Figure 4

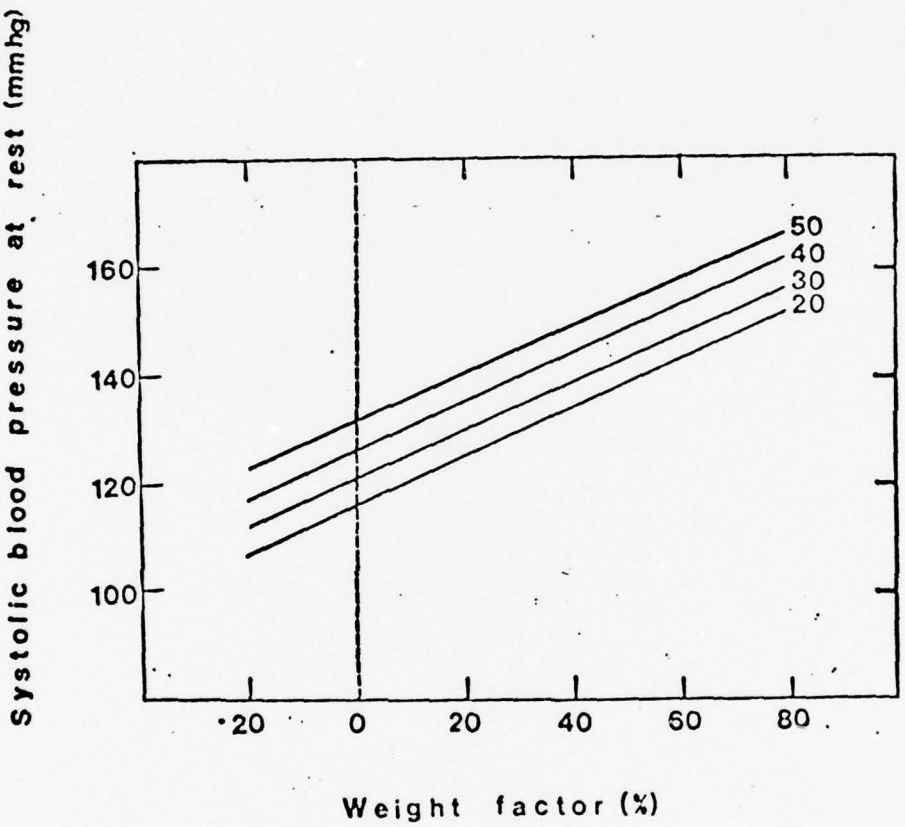

Systolic blood pressure at rest (mmhg)
160
140
120
100
50
40
30
20
-20
0
20
40
60
80
Weight factor (%)

Figure 5

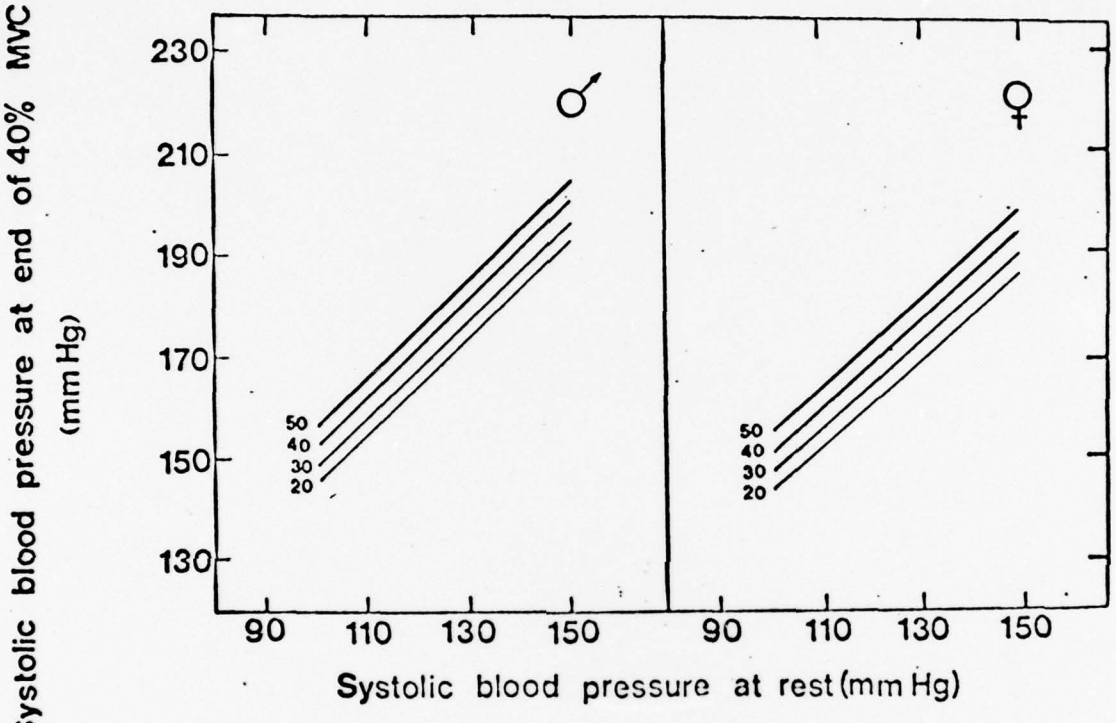

Systolic blood pressure at end of 40% MVC
(mm Hg)
230
210
190
170
150
130
♂
♀
50
40
30
20
90
110
130
150
Systolic blood pressure at rest (mm Hg)

Figure 6

INVESTIGATION 9

INSULATIVE POWER OF BODY FAT ON DEEP MUSCLE TEMPERATURES AND ISOMETRIC ENDURANCE.

INTRODUCTION

The endurance of fatiguing isometric exercise is related to the temperature of the forearm musculature. Clarke, Mellon and Lind (5) demonstrated that there was an optimum temperature of the muscles of the forearm above and below which isometric endurance fell markedly. This temperature was about 27°C measured half way between the skin and the bone in the belly of the brachioradialis muscle. However, the temperature of the resting forearm muscle of man in a comfortable environment has been reported to be considerably above this optimum temperature (2,5, 9). More recent evidence shows that forearm muscle temperature can vary quite widely under normal physiological circumstances. For example, Petrofsky and Lind (9) have demonstrated that the deep muscle temperature of the forearm of both male and female subjects is directly related to the body fat content, causing an elevation of some 1.5°C in muscle temperature for every 10% increase in body fat content over the "ideal" weight (10-15% of body weight as fat in males).

Body fat has long been known to provide a potent insulation against cold ambient environments (1, 3, 4, 6, 7). It seems reasonable, then, that the isometric endurance measured after exposure to cold or to heat should be related to the body fat content of the individual, but so far, no study has examined this relationship. Therefore, in the present investigation, muscle temperature and isometric endurance were measured following immersion of the forearm in water at various temperatures in men with different known body fat content and in one subject before and after weight loss.

METHODS

Subjects: The subjects in this study were four male volunteers whose ages, heights, weights and calculated body fat contents are listed in Table 1.

All procedures and potential hazards were carefully explained to each subject who then signed a statement of informed consent before participating. In addition, all potential subjects were medically examined, including a treadmill stress test and a pulmonary function test. All procedures were approved by the Committee on Human Experimentation.

Training: The subjects were first trained in isometric exercise. At the start of each experiment, the subject exerted two brief ($<$ 3 sec) maximum voluntary contractions (MVC) on a partable hand-grip dynamometer similar to one described previously (5). The interval between those contractions was 1 min; the MVC was taken to be the stronger of the two contractions. Isometric endurance (measured with the subject sitting) was assessed as the duration (to the nearest sec) of a sustained isometric hand-grip contraction held to fatigue at a tension of 40% MVC calculated from the MVC recorded each day. On each training day, the maximal voluntary contraction and the endurance of 5 successive fatiguing contractions exerted at a tension of 40% MVC were measured; three minutes were allowed between the successive contractions. This procedure was repeated each Monday, Wednesday and Friday of successive weeks until the coefficient of variation of the duration of the first fatiguing contraction was reduced to not more than $\pm$ 5% ; using that criterion, the training period ranged from 3 to 6 weeks. During the period when the body fat content of one subject was altered, isometric training was maintained by repeating the training regimen once per week.

Measurement of Isometric Strength and Endurance During Immersion: Following the measurement of isometric strength in air, the seated subject immersed his forearm in water. The hand-grip was also placed in the bath and after 30 minutes of immersion the subject performed a single 40% MVC contraction. A vigorous flow of water over the forearm was maintained by 2 pumps placed in opposite corners of the bath. Water temperature ranged from 7.5 to 40.0^{o}C, maintained at $\pm$ 0.1^{o}C. The series of water temperatures was presented at random for each subject and was separately randomized for replicate immersions. In any one set of experi-

ments, some or all those water temperatures were chosen to obtain the required data. A minimum of 72 hours were allowed between any 2 experiments.

Body Fat Content: The body fat content (the % of body weight which is fat) was assessed by the underwater body density method described by Keys and Brozek (8).

Weight Loss: Weight loss on one subject was achieved by a ketogenic diet (15% carbohydrates, 40% protein and 45% fat) maintained for a period of three months. The experiments on this subject occurred just before and one month after weight loss; during the month after dieting, a mixed food intake was used to keep his body weight stable.

Muscle Temperature: Muscle temperatures were measured on a separate occasion from endurance determinations. Temperatures were measured with a BC32L1 thermistor (Fenwall Instrument) implanted in a 23 gauge stainless steel needle. The resistance of the thermistor was measured with a digital ohm-meter accurate to $\pm$ 0.1 ohms (Weston Instrument). The thermistor was calibrated before and after each experiment. Fully sterile procedures were followed and the needle was inserted into the brachioradialis muscle distal to the olecranon process approximately 1/3 of the distance to the ulnar process. The puncture was protected by collodion before immersion in the water.

After the first experiment on each subject, a tattoo mark was placed at the puncture site so that the muscle temperature in repeated experiments could be assessed at the same spot; a minimum of three days was allowed between muscle temperature recordings.

RESULTS

Each point in Figure 1 represents the mean of 4 endurance contractions (2 for each subject) for two subjects who were overweight (closed circles) and two subjects of "normal" weight (open circles). Obviously, two discreet curves were obtained. While isometric endurance was similar for all the

subjects after immersion in water at 40°C the longest endurance recorded for the overweight subjects (mean body fat content, 27%) was found when the forearm was immersed in water at 17.5°C, while that of the normal subjects (mean body fat content, 17%) was found in water at 25°C. Here, as in training, for any one subject, replicate endurance determinations at any temperature differed by no more than 10 seconds.

In overweight subject JP (whose body fat content was 27%) and normal weight subject RB (whose body fat content was 18%) the muscle temperature in the brachioradialis muscle was measured under these same conditions. Muscle temperatures were recorded before immersion and every 5 min up to 30 min following immersion of the forearm in water at 10, 15, 20, and 34°C. In all experiments, the deep-muscle temperature before immersion was about 1.5°C greater in the overweight subject (Figure 2). Following immersion of the forearm in water at 34°C, this difference in deep-muscle temperature between the two subjects remained quite steady; muscle temperature increased to 34.5 and 36°C respectively for the normal and the overweight subjects. But, after immersion of the forearm in the three colder water baths, this difference in the deep-muscle temperature between these subjects was accentuated. For example, after 30 min immersion of the forearm in water at 10°C the muscle temperatures were, respectively, about 18 and 22°C for the normal and overweight subjects. Figure 3 shows the duration of the sustained contractions at 40% MVC plotted against the muscle temperatures recorded after immersion of the forearm in water at 10, 15, 20, 25, and 34°C for these two subjects. While the absolute magnitude of the endurance response differed in the 2 subjects, the longest recorded endurance occurred at a muscle temperature of about 28°C for both subjects. Above and below this temperature, muscular endurance fell markedly.

In one subject, we had the opportunity to measure the relationship of muscle temperature to isometric endurance before and after he reduced his body fat content. The subject reduced his body fat content from 39% to

27% with an associated reduction of his forearm circumference (measured over the site of the needle insertion) of 37 mm. Before weight loss his muscle temperature was measured during a 20 min immersion in water varying in temperature from 7.5 to 40°C. Isometric endurance at 40% MVC was then recorded. One month after losing weight these procedures were repeated; during that period, his body fat content remained stable. Before he lost weight, the longest endurance time for the subject occurred in water at 12.5°C. Following weight loss, however, the curve relating endurance times to water temperature shifted to the right and the longest endurance occurred in water at 17.5°C. The relationship of muscle temperature and endurance at these water temperatures before and after weight loss are shown in Figure 4. Peak endurance before (closed circles) and after (open circles) weight loss occurred at about the same muscle temperature, 28°C.

DISCUSSION

The intimate relationship between the body fat content and thermoregulation in man is abundantly demonstrated in the literature. For example, associated with an increased body fat content, there is a decrease in the metabolic and other thermoregulatory responses to cold air (1, 3, 6) or cold water (4, 7). However, most of these studies have dealt only with the core temperature and the regulation of that temperature in relation to body fat content. Although Wells and Buskirk (11) found higher subepidermal temperatures in the forearms of overweight than control subjects during dynamic exercise, no study has related the muscle temperature in a limb to the body fat content in subjects during exposure to heat and cold. This is particularly important to the study of fatigue during isometric exercise. Unlike dynamic exercise where the efficiency of muscular exercise appears to increase as the muscle temperature

increases (10). In contrast, it has been shown in earlier results (5) as well as in our present study that the peak endurance for isometric exercise occurs at a muscle temperature several degrees below the normal, resting, deep-muscle temperature of the forearm. However, even in a controlled ambient environment the temperature of the muscles of the forearm at rest is influenced by an individual's body fat content. We have recently demonstrated, for example, that a difference of 4.5°C may occur in the deep muscle temperature of the brachioradialis muscle measured at a perpendicular depth of 40% between the skin and center of the forearm between individuals whose body fat content differs by 30% (9). Further, we found that this dramatically higher muscle temperature in the overweight individual is easily reduced by simple weight loss. The higher resting muscle temperature in men who were overweight led to a reduction in their endurance for isometric exercise, a fact that could be accounted for solely on the basis of an elevated resting muscle temperature.

It is not surprising then, that in the present investigation, we found that the peak endurance for sustained effort occurred after immersion of the forearm in colder baths in the subjects with higher body fat contents. However, in terms of the muscle temperature, peak isometric performance occurred at the same muscle temperature irrespective of the body fat content of the subject. Thus, the causative agent for the difference in isometric endurance between the 2 groups of individuals (overweight and control) we studied was simply a difference in their muscle temperature. This difference illustrates the striking insulative power of the layer of fat around their forearms. For example, subject JP, before weight reduction, had a deep muscle temperature of 26°C after a 20 minute exposure in a 10°C water bath. Following a reduction of 12% of his body fat content, the muscle temperature measured under the same circumstances was 22°C, a reduction of 4°C. This loss of insulative power was associated with a decrease in forearm girth of 37 mm. Assuming the arm to be

a cylinder and that the majority of the fat in the forearm is subcutaneous, this would represent a loss of 5.8 mm of subcutaneous fat. Thus, while the elevated muscle temperature in the resting overweight subject exposed to a thermally neutral environment compromises his isometric muscular performance, a substantial advantage is achieved for the overweight subject exposed to cold environments.

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TABLE 1

The ages, heights and weights of the subjects.

Subject	Age (years)	Height (cm)	Weight (kg)	Body fat content%
JP	24	188.0	145.0	28%
CJ	26	188.0	68.2	16%
RB	38	193.0	79.5	18%
GS	25	185.4	97.0	26%

FIGURE LEGEND

Figure 1: The average duration of fatiguing isometric contractions at 40% MVC after 30 minutes immersion in water at 10, 15, 17.5, 22, 25, 30, and 40°C for two overweight subjects (●) and two subjects of normal weight (○). Each point illustrates the mean of 4 endurance determinations. Both pairs of subjects had the same mean endurance in the 22°C water.

Figure 2: Illustrating the muscle temperature at vertical depth of 2 cm into the forearm of normal subject RB (○) and overweight subject JP (●) after immersion of the forearm in water at 10, 15, 20, and 34°C. Each point shows the mean of 2 determinations.

Figure 3: The relationship of muscle temperature to the duration of a 40% MVC contraction in subjects RB (○) and JP (◐). Each point illustrates the mean of 2 measurements.

Figure 4: Duration of an isometric contraction at 40% MVC plotted against muscle temperatures after 20 minutes immersion of the forearm in water of various temperatures. Data represent the mean of 2 determinations on subject JP before (●) and after (○) weight loss.

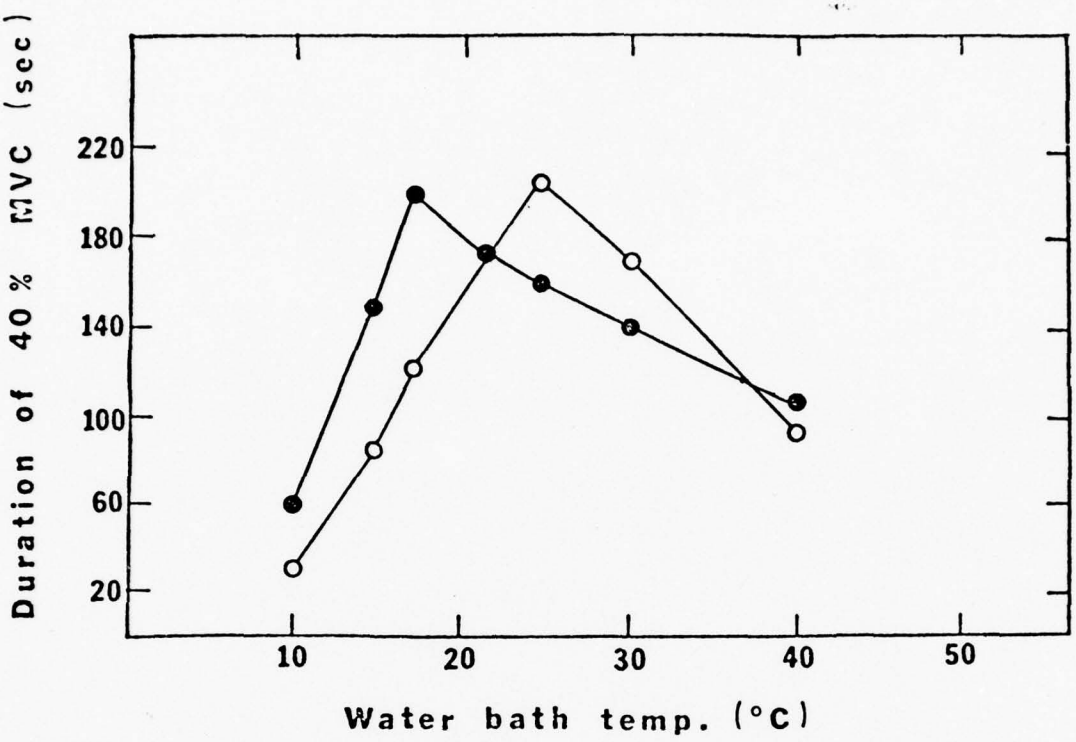

Duration of 40% MVC (sec)
220
180
140
100
60
20
10
20
30
40
50
Water bath temp. (°C)

Fig. 1

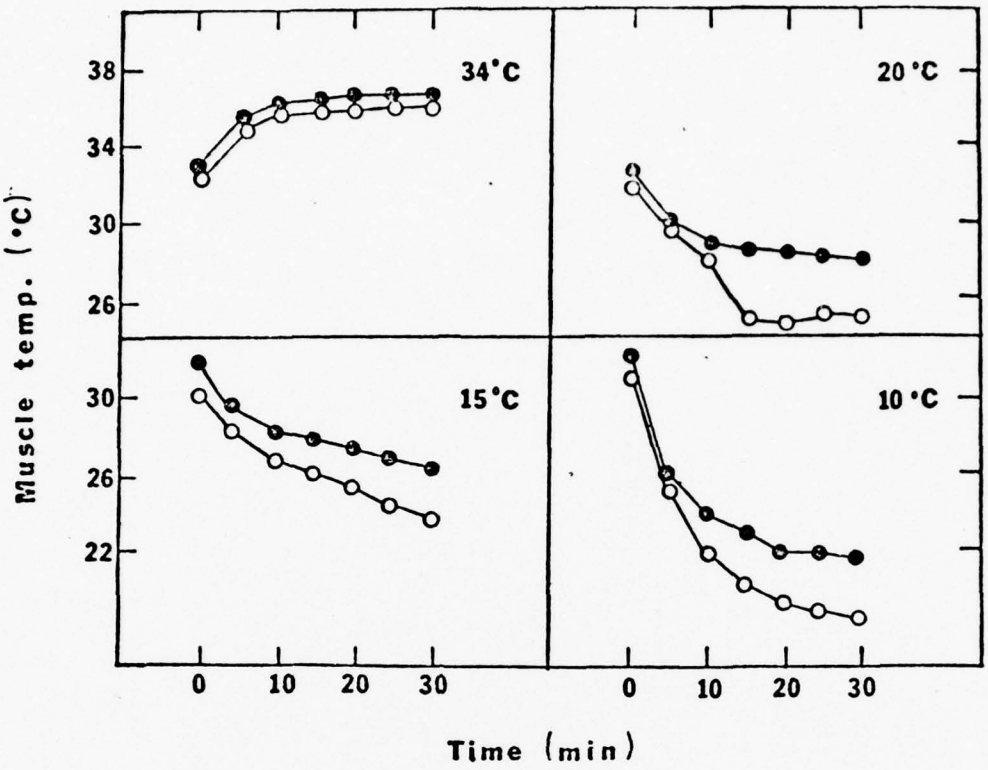

34°C
20°C
15°C
10°C
Muscle temp. (°C)
38
34
30
26
30
26
22
0
10
20
30
0
10
20
30
Time (min)

Fig. 2

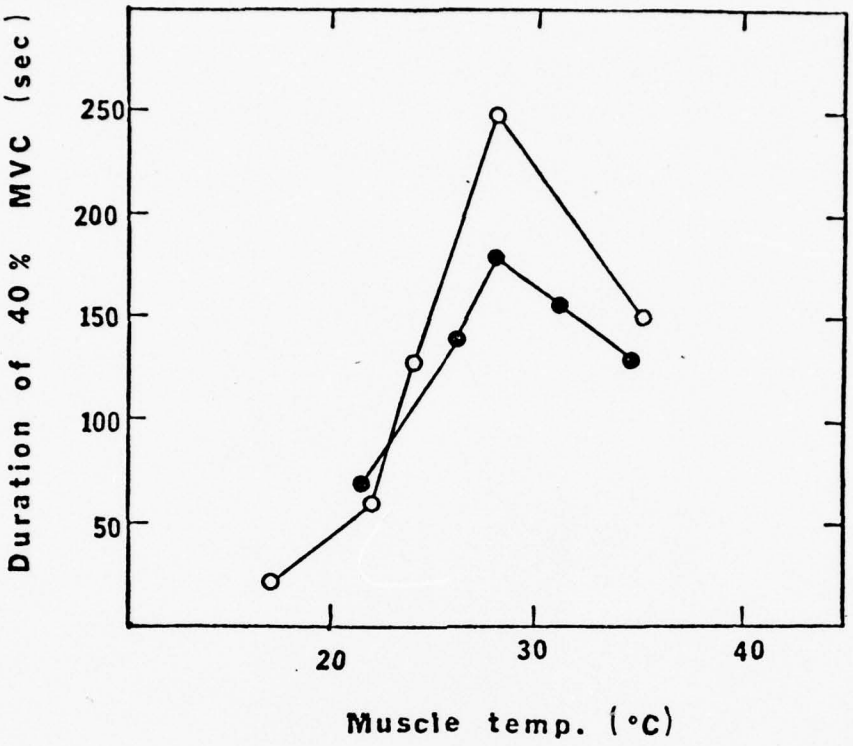


Fig. 3

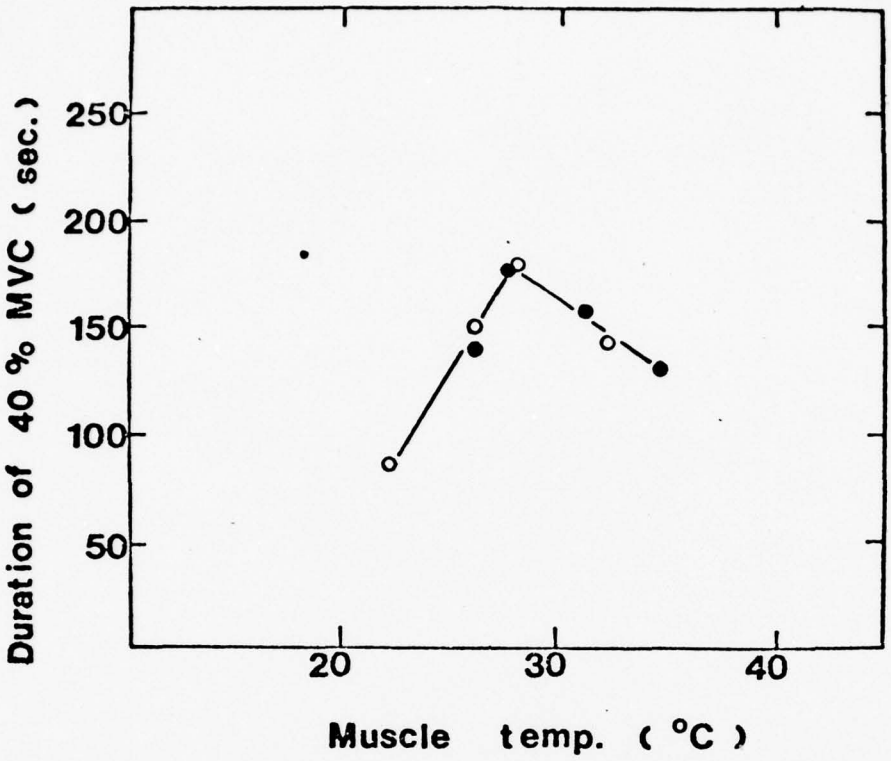


Fig. 4

INVESTIGATION 10

THE EFFECT OF DEEP MUSCLE TEMPERATURE ON THE CARDIOVASCULAR RESPONSES OF MAN TO STATIC EFFORT.

INTRODUCTION

The dramatic increase in blood pressure and modest increase in heart rate during fatiguing static exercise has been well documented in the literature (1, 6, 8, 11, 13). The absolute increase of heart rate in response to fatiguing isometric contractions increases with tension (6) and while the mechanism that drives this response is not well understood, it is thought to be mediated through the release of vagal tone (5, 11). In contrast, the blood pressure increases markedly to the same level at fatigue irrespective of the tension exerted.

Much more is known about the mechanisms controlling blood pressure response. While it remains possible that a portion of the response may originate in the central nervous system (5), there is no question that the bulk of the response is the result of a reflex originating from receptors in the active muscle (7, 10) through nerves of types III and IV (3, 12). Since muscle temperature profoundly affects endurance (2, 14) it seemed possible that the cardiovascular responses to static effort might also be dependent on the temperature of the exercising muscle. No attempt has been made to examine this possiblity; it was the purpose of the present investigation to assess it.

METHODS

Subjects: The subjects in this study were five male volunteers whose ages, heights, weights and body fat contents are listed in Table 1. All subjects were medically examined and stress-tested prior to the experiment. In a prelinimary interview all procedures were carefully explained to each subject who then signed a statement of informed consent.

Isometric Strength and Endurance: Isometric strength was assessed as the strongest of three brief (3 sec) maximal voluntary contractions (MVC) exerted on a portable strain gauge handgrip dynamometer similar to that described previously by Clarke, Hellon and Lind (2); three minutes were allowed between these contractions. Endurance was then measured as the duration, to the nearest sec, of an isometric contraction at 40% MVC.

Muscle Temperatures: Muscle temperature was measured from a thermistor implanted in the tip of a 22 gauge stainless steel needle. The needle was inserted into the belly of the bracheoradialis muscle, approximately 1/3 of the distance between the olecranon and ulnar processes to a depth of 40% of the distance between the skin and the center of the forearm. Care was taken to insert the needle in the same place on repeated experiments.

Heart Rate and Blood Pressure: Heart rate was measured over 15 sec intervals from a continuous recording of the ECG before, during and after the contractions. Blood pressures were recorded by auscultation before, during and after the contraction. One observer measured all the blood pressures on any one subject.

Body Fat Content: The body fat content of each subject was measured by underwater weighing according to the method described by Keys and Brozek (9).

Training: All subjects in this study were first trained in isometric exercise. On each day of training, following the measurement of isometric strength, five successive fatiguing isometric contractions at 40% MVC were performed with 3-min intervals between contractions. This procedure was repeated every Monday, Wednesday and Friday of successive weeks until the co-efficient of variation of the endurance of the first contraction on different days was not greater than $\pm$ 5%. The duration of training ranged from 4 to 6 weeks for any one subject.

Experimental Protocol: On each experimental day, the MVC was assessed on each subject before he immersed his forearm in water at temperatures between 10 and 40° C. The order of presentation of the temperatures for both the first and replicate experiments was randomized. The temperature of the water was controlled to $\pm$ 0.5^{o} C and was vigorously stirred. Thirty min after immersion, with the arm still immersed, one fatiguing contraction was performed at 40% MVC. Forty-eight hours were allowed between each of these experiments and all experiments were conducted at the same time of the day, for each subject.

RESULTS

On the average, the longest isometric endurance was recorded for the five subjects following immersion of their forearms in water between 22 and 25° C. However, although the overall pattern was the same for each subject, the longest endurance for each subject was recorded in water at different temperatures. For example, the thinnest subject had the longest duration following immersion of his forearm in water at 25° C while the fattest subject had the longest duration following immersion in water at 17.5° C. Our subjects could be divided into two groups, one of which comprised three thin subjects whose mean body fat content was 15.2% (range 12.3--18.2%), while the second group had mean body fat contents averaging 28.8% (range 27.6--30.0%) (Table 1). In the presentation given here, the results of the subjects have been averaged in these terms of body fat content. Each point in Figure 1 represents the average endurance for contractions at each water temperature from the subjects in the two groups. The overweight group had the longest endurance after immersion of their forearms in water at 17.5° C. In contrast, the endurance of the thin subjects was longest following immersion of their forearms in water at 25° C.

Heart rate and Blood pressure

For both groups of subjects, the heart rate at the beginning and end of the fatiguing contraction was elevated after immersion in the coldest and warmest baths (Fig. 2). However, the increase in heart rate throughout the contractions was the same for any temperature examined, averaging 25 beats per minute from the resting heart rate to that recorded at the end of the 40% MVC. This same pattern emerged for the blood pressure response of the overweight subjects (Fig. 3B). For all 3 thin subjects, blood pressure

response was reduced after immersion in the 2 coldest baths (Fig. 3A). However, the blood pressure response throughout the first 20% of the duration of the contractions at any water temperature was the same. Fig. 4 compares the blood pressure response following immersion in the 10° C and 40° C baths. Although there was an elevated resting blood pressure in the colder bath, the increase in both the systolic and diastolic blood pressures from rest to 20% of the duration of the contraction was of a similar order of magnitude. However, as the contraction continued, the blood pressures recorded from the subjects in the 10° C bath reached a plateau while the blood pressure recorded in the warm bath steadily increased throughout the durations of the contractions.

Muscle Temperatures

Deep muscle temperatures was measured at 40% of the distance between the skin and center of the forearm in the belly of the brachioradialis muscle in one of the thin subjects and one of the overweight subjects. The deep muscle temperature of the thin subject was consistantly lower than that of the fatter subject by as much as 6.5° (after the 30 min immersion in water at 10° C). In an attempt to reduce the deep muscle temperature of the fatter subject to those temperatures recorded in the thin subject after immersion in the 10 and 15° C baths, the bath temperature was reduced to 5° C. However, even after a 2 hr immersion, the deep muscle temperature was still above 20° C. (Fig. 5).

DISCUSSION

In the present study it has been demonstrated that the temperature of the muscle could be varied between 20 and 40° C with no discernible influence on the response of either the blood pressure or the heart rate in spite of a large variation in isometric endurance. However, the blood pressure in the thin subjects was found to be sharply diminished after immersion in water at 10 or 15° C. The reason that this did not occur in the 2 overweight subjects appears to be that the deep muscle temperature of these subjects was insulated from the cold by the layer of fat around their forearms. Since the heart rate during exercise was unaffected by cold water the response may originate in the CNS and hence would be virtually unaffected by the peripheral "paralysis" induced by the cold bath. This hypothesis is supported by previous data where it was demonstrated that a heart rate response could be elicited in amputees by having them try to make the amputate limb contract (5) but is absent during stimulation of the ventral roots in anesthetized or decerebrate cats (3).

However, our data point to peripheral mediation in the blood pressure response. Previous evidence has clearly shown that this reflex can be mimicked by stimulation of the ventral roots in cats (3) and occurs in patients with complete cervical lesions when the muscles are electrically stimulated (4). This hypothesis is further supported by the fact that blood pressure remains high after isometric exercise if the circulation to the limb is arrested (10). The small increase in the blood pressure throughout the early part of the fatiguing contractions reported here and which was unaffected by cold, may be due to central stimuli; Freyschuss (5) has suggested that the pressor response to isometric exercise is central in origin.

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Table 1

	Age (yrs)	Ht. (cm.)	Wt. (kg)	% Body Fat
RB	38	193.0	79.5	18.2
BH	34	162.0	51.3	12.3
CJ	26	188.0	68.2	16.1
JP	24	188.0	145.0	27.6
GS	25	185.4	97.0	30.0

FIGURE LEGENDS

Figure 1: The average duration for a 40% MVC fatiguing contraction in 2 overweight subjects (●) and 3 thin subjects (O) as a function of the water bath temperature.

Figure 2: The average heart rate at rest (O) and at 100% of the duration (●) of a 40% MVC fatiguing handgrip for the 3 thin subjects (A) and 2 overweight subjects (B) as a function of the water bath temperature.

Figure 3: The average systolic (s) and diastolic (d) blood pressures at rest (O) and at 100% of the duration of a 40% MVC (●) for the 3 thin subjects (A) and 2 overweight subjects (B) as a function of water bath temperature.

Figure 4: The average systolic (s) and diastolic (d) blood pressure throughout the duration of a 40% MVC contraction after immersion of the forearm in 10° C (o) and 40° C (●) water for the thin subjects as a function of water temperature.

Figure 5: The deep muscle temperature measured at 40% of the distance between the skin and center of the forearm in the belly of the brachioradialis muscle for overweight subject JP (●) and thin subject RB (O) as a function of water temperature.

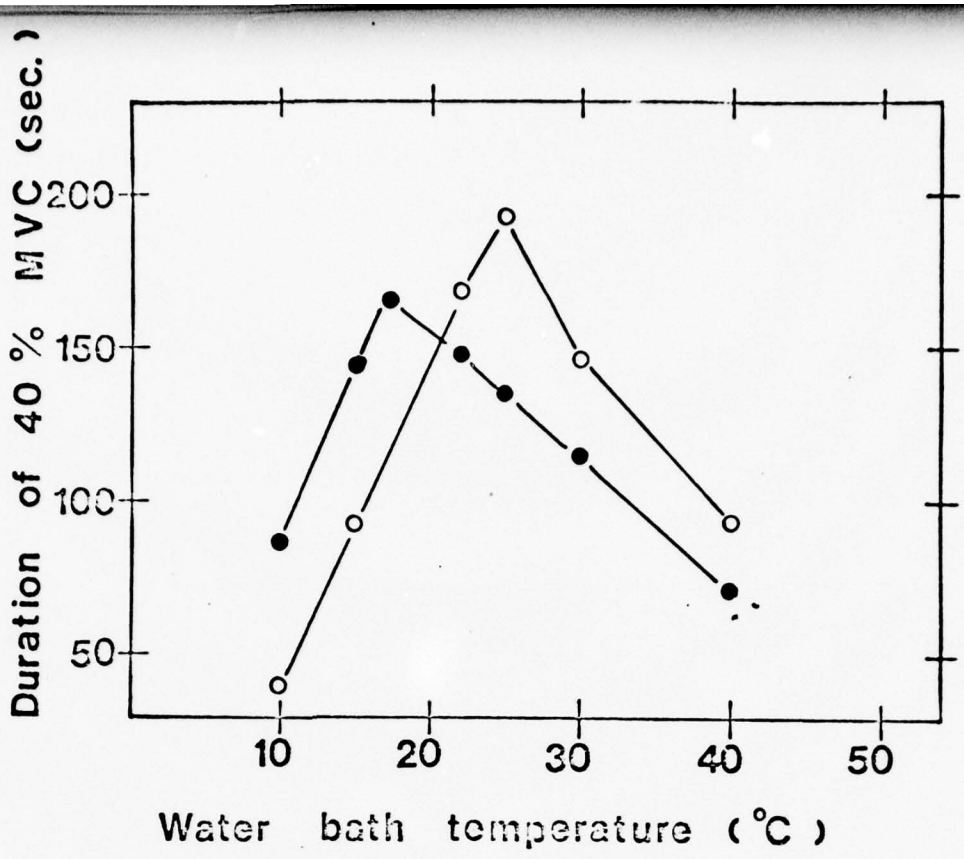


FIGURE 1

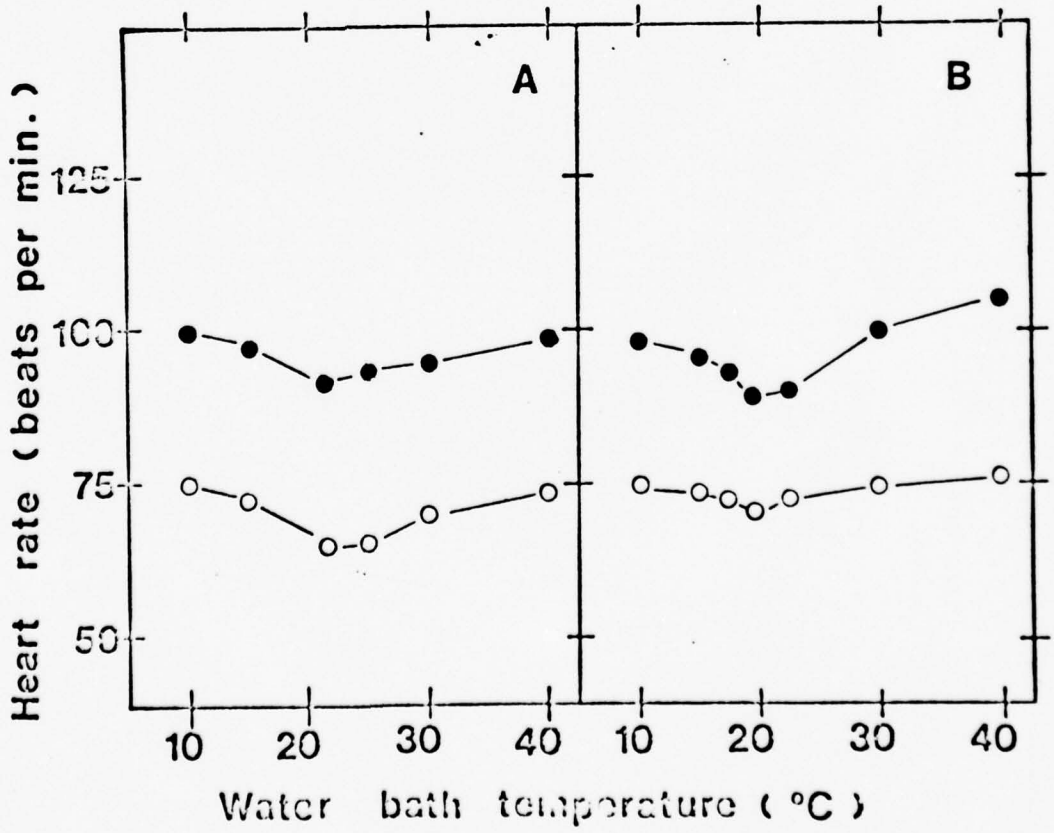


FIGURE 2

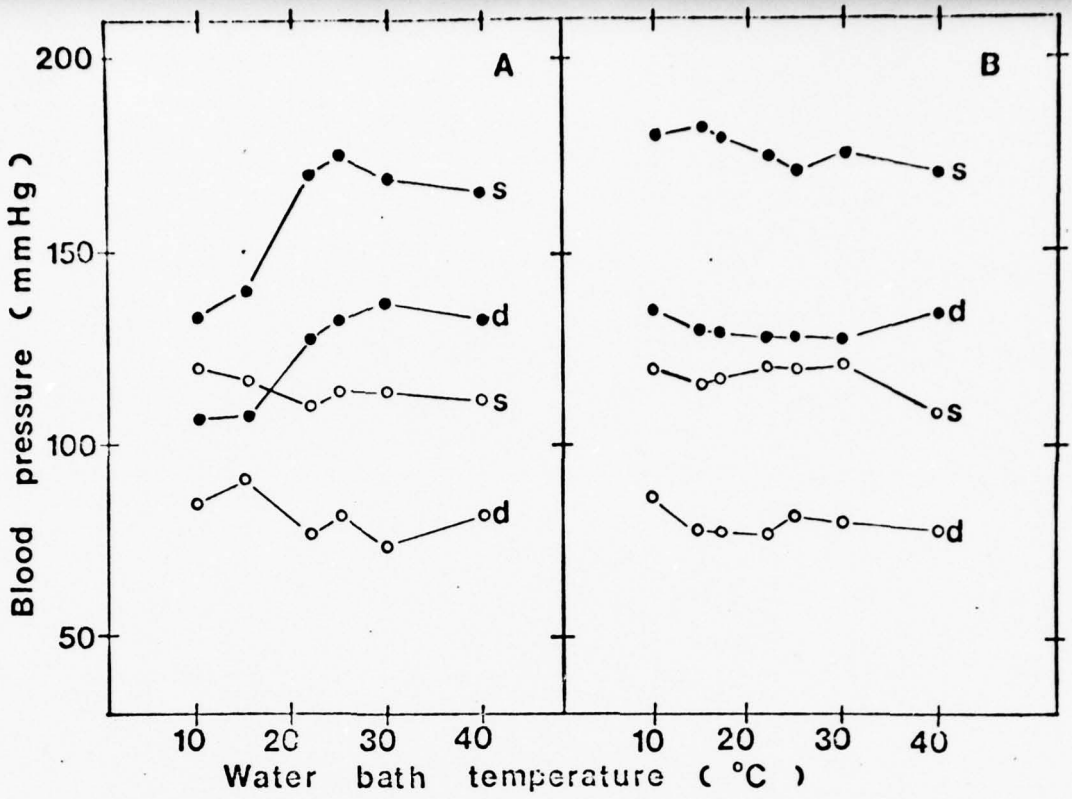


FIGURE 3

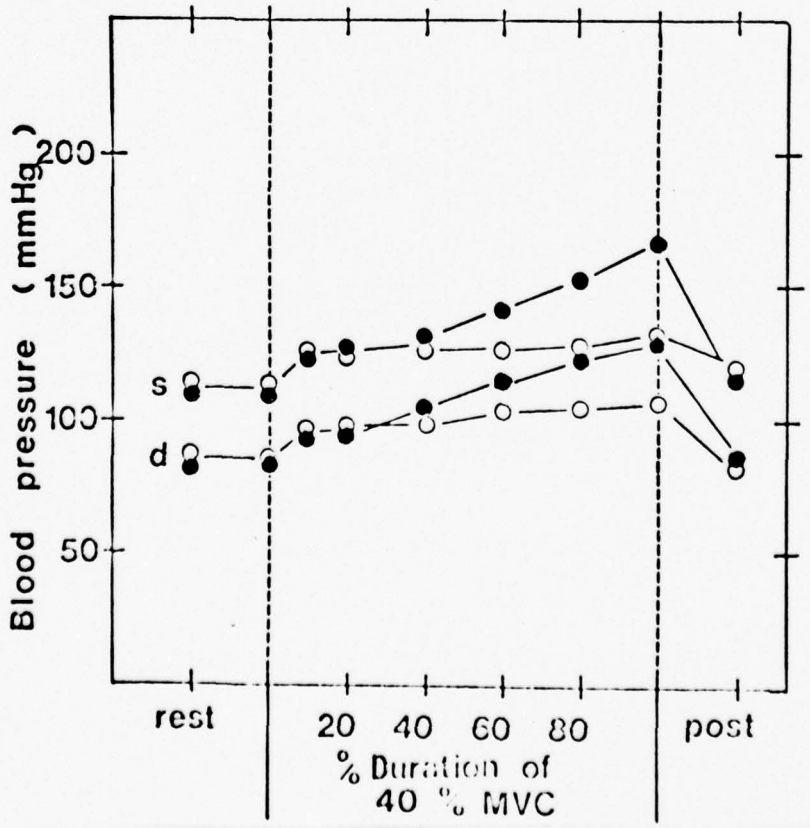


FIGURE 4

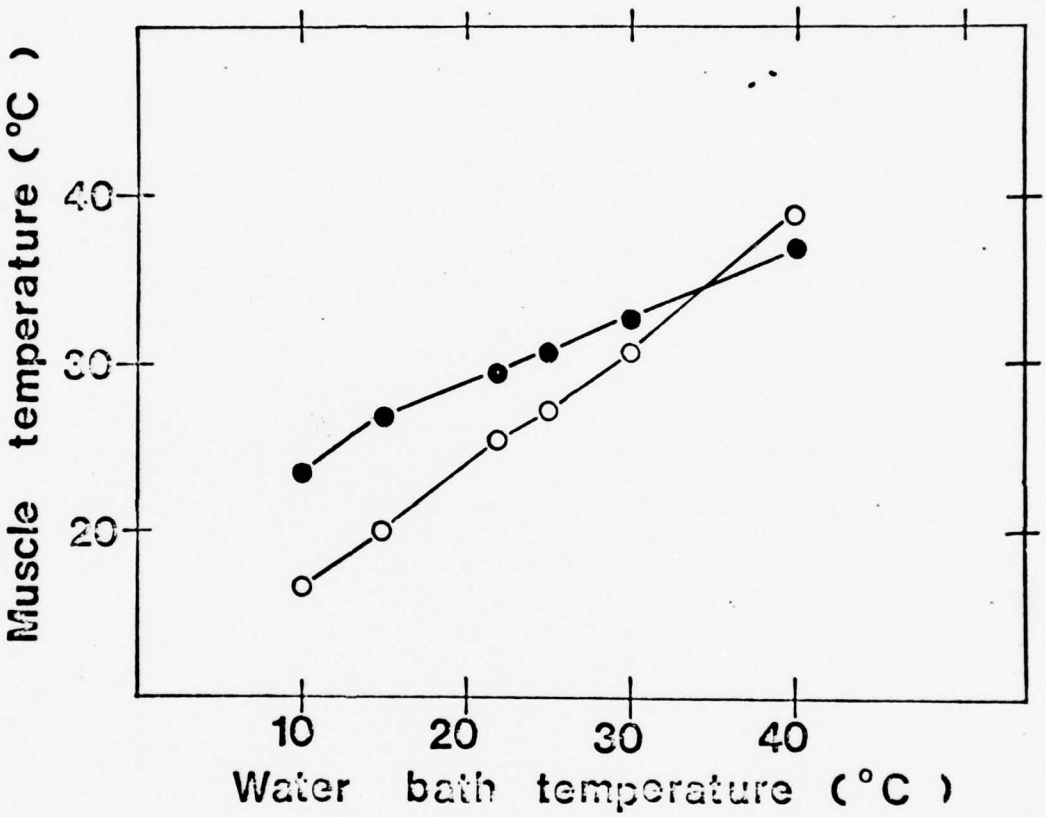

Muscle temperature (°C)
40
30
20
10
20
30
40
Water bath temperature (°C)

FIGURE 5

INVESTIGATION 11

THE INFLUENCE OF POSTURE ON ISOMETRIC STRENGTH AND ENDURANCE, FOREARM BLOOD FLOW, AND THE BLOOD PRESSURE AND HEART RATE RESPONSE TO ISOMETRIC EXERCISE.

INTRODUCTION

The development of a new generation of faster-flying aircraft will undoubtedly exaggerate some of the physiological problems that already exist for pilots. Gravitational stresses will certainly be increased and the substantially greater speed emphasizes the need for fast, accurate muscular action and fine, coordinated muscular control; both functions are threatened by the onset of fatigue.

Isometric exercise, which comprises much of the pilot's activity, notoriously induces fatigue quickly and the recovery from that fatigue is slow. The physiological consequences of isometric exercise and the development of and recovery from fatigue have been reviewed elsewhere (9, 17). Briefly the relevant features are that the amount of blood flow through muscles contracting isometrically is particularly crucial in the development of fatigue--the unremitting mechanical compression of the isometrically contracting fibers on their own blood vessels oppose the dilatation due to the release of metabolites. In consequence, fatigue can develop at tensions as low as 15% of the maximal strength of the muscles, and muscular endurance becomes progressively shorter as the tension increases. For example, fatigue develops after about 4 minutes at 30% and 1 minute at 50% of maximal strength, despite substantial reflex increases in mean arterial blood pressure to aid the local perfusion. In consequence, any factor which may further reduce the local blood flow will induce fatigue more quickly, while maneuvers which increase the local flow delay fatigue (7).

One possible aid to the pilot in combating gravitational stresses is to place him in a reclining or a recumbent posture. The evidence available on the blood flow in the resting limb clearly indicates that the flow is higher in the recumbent than in the upright, sitting posture (1, 14, 15): on that basis, it would seem

reasonable to expect the flow also to be higher in the limb of recumbent men during exercise. But recently published evidence (5) shows that the blood flow through rhythmically exercising leg muscles is higher in the upright posture than in the recumbent posture. In addition, some previously unpublished experiments in this laboratory demonstrated that during isometric hand-grip exercise, the forearm blood flow was higher in seated than in recumbent men, and furthermore, that the duration of fatiguing contractions was lower in the recumbent position.

This investigation examined further the influence of posture on muscular strength and endurance and the associated cardiovascular changes.

METHODS

Subjects

Four healthy men, aged 25 to 37 years, volunteered to act as subjects. Following a complete explanation of the methods and procedures to be used, they signed a statement of informed consent. They were medically examined, including a cardiovascular stress-test before they were permitted to take part.

Training

All the subjects were trained daily in the performance of hand-grip isometric contractions for one week, and three times per week for another two or three weeks. On each day of training, the subject exerted three maximal voluntary contractions (MVC) with an interval of 3 min between them; the strongest of these was considered to be the maximal strength. Three min later he performed the first of 4 successive isometric contractions to fatigue at a tension of 40% MVC, with an interval of 11 minutes between each fatiguing contraction. A further week of training required the subjects to perform to fatigue at 25% MVC.

Experimental Procedures

An accurate hand dynamometer (7) was used for the isometric exercise. The subjects performed the exercise in 4 postures: they were 1) seated or in three positions on a tilt-table 2) 45° head up, 3) recumbent or 4) 15° head down.

There were four stages in the investigation:

1) Maximum strength was measured in all four postures to determine whether posture, by itself, affected hand-grip strength.

2) The endurance times of four consecutive fatiguing contractions were measured at 25% and at 40% MVC. The interval between the successive contractions was constant at 11 minutes, so that the post-exercise hyperemia was wholly or substantially dissipated before the start of the following contraction (7). The tension was kept constant in any one experiment, and each experiment was repeated. Heart rates and blood pressures were recorded for 2 minutes before and throughout each contraction and for 2 minutes afterwards.

3) At a tension of 40% MVC, the protocol 2) described above was repeated, except that the circulation to the forearm was occluded by a pneumatic cuff inflated to 300 mm Hg immediately before each contraction; the cuff was deflated just after the contraction ended.

4) The forearm blood flow was measured before, during and after isometric contractions in the seated and recumbent postures. The isometric tensions were chosen at 10% MVC (which does not induce fatigue) and 20% and 40% MVC; no contraction was held to fatigue because as fatigue is approached, arm tremor makes the measurement of blood flow difficult or impossible. In some experiments venous pressures were measured, with the tip of the catheter at the back of the right atrium, to reflect right atrial pressure.

Measurements

Heart rate was measured from a continuously recorded (and monitored) ECG.

It was measured at specific fractions (20, 40, 60, 80, and 100%) of the duration of the contraction for each individual so that all the data could be compared later on a standardized scale. Blood pressure was measured by sphygmomanometry; during each contraction it was measured as often as possible and was also normalized for the duration of the contraction. Mean blood pressures were calculated as the diastolic pressure plus 1/3 of the pulse pressure. Forearm blood flow was measured by Whitney strain gauge plethysmography (18).

Statistical Analysis

The calculation of means, standard deviations and related t-tests were accomplished on a Linc computer. The level of significant difference in the assessment of the results was taken to be $p < 0.05$.

RESULTS

Hand-grip Strength

The hand-grip strength for each subject in each posture is shown in Fig. 1. Each value is the mean ($\pm$ SD) for three contractions. There was no statistical difference in the strength exerted in any posture for any subject. Furthermore, in a series of 9 consecutive contractions in the seated posture, strength remained constant. Three minutes separated each contraction in all cases. It was clear that neither posture nor repeated contractions had any effect on the maximum hand-grip strength.

Comparison of endurance times at 40% MVC in all four postures

Figure 2 shows the average endurance times of the serial contractions at 40% MVC in all 4 postures; each individual showed the same pattern of response as the group average. At 40% MVC, with a free circulation, both C_1 (■) and C_2(▲) were clearly longer in the seated than in any other posture ($p < 0.05$). There was no significant difference in the endurance times in

any of the 4 postures of C_3 (●) and C_4 (✕). Nor was there a significant difference in the endurance times of any of the 4 contractions in any other but the seated position. The first contraction was 20% shorter when recumbent than when seated, and C_2 was 17% shorter. But for C_3 and C_4 the difference in endurance time vanished.

The facts that 1) the considerably longer endurance of C_1 in the seated posture and 2) the progressive reduction in the difference in endurance times in serial contractions which leads to similar durations of endurance by C_3 and C_4, assume significance in the light of our findings on forearm blood flow during and after isometric exercise as discussed below (see Fig. 6). When the circulation to the arm was occluded, it is evident from the results shown in Fig. 2 that there was no significant difference in the endurance time of any of the 4 contractions.

Average endurance times in the seated and horizontal postures at 25% MVC

The average durations of the 4 successive contractions at a tension of 25% MVC are shown in Fig. 3; the subjects performed these contractions only in the sitting and recumbent positions. Each subject maintained the first contraction (C_1) for longer in the sitting than in the recumbent position. Although there was some individual inconsistency in the endurance of any one subsequent contraction due to posture, a similar trend was established for all subjects.

As seen in Fig. 3, the mean endurance times of all 4 contractions were consistently higher when sitting than they were in the recumbent posture, although the difference was significant only for C_1. The first contraction when recumbent was 17% shorter than when seated. This difference due to posture diminished as the series of contractions continued; the fourth contraction was only 10% shorter in the recumbent than in the sitting posture.

Changes in heart rates and blood pressures

Figure 4 shows the average systolic and diastolic pressures and the average heart rates before, during and after contractions at 40% MVC in all 4 postures. To permit a common scale for all 4 subjects, whose endurance times varied, the total endurance time for each individual has been expressed as 100%; the cardiovascular responses were then calculated at fractions of the endurance. The influence of posture on heart rates and blood pressures during isometric exercise was small.

The average increase in heart rate from rest to the end of the 40% MVC with the subject in any posture was 37.7 ± 5.2 beats/min. However, the heart rate was highest at rest and throughout most of the contraction in the 45° head-up position. In order of decreasing magnitude, heart rate was reduced in the seated, horizontal and head-down postures, respectively. The average heart rate difference at the end of the contractions in the 45° head-up and horizontal was 10.0 ± 0.8 beats/min. ($p < 0.05$). The greatest difference in the response occurred between the head-up and head-down postures. Here, on the average, the heart rate in the head-up position was 14.3 ± 3.9 beats/min higher than in the head-down position ($p < 0.05$). At 1 and 2 minutes post-exercise, the heart rate had returned to its pre-exercise values in all four postures.

There was no significant difference in the systolic or diastolic blood pressure responses in any postures before, during or after exercise at 40% MVC (Fig. 4). The increase in systolic and diastolic blood pressure from rest to the end of the contraction at 40% MVC in the sitting and recumbent positions was 64.6 and 62.0 mm Hg, respectively.

The heart rate and blood pressure responses at 25% MVC followed a similar pattern with again a slightly lower heart rate response in the horizontal posture. There was no difference in systolic pressure due to posture but the diastolic blood pressure was consistently slightly lower in the head-down

position when compared to sitting (Fig. 5). However, while the resting and exercising blood pressures were the same at 25% and 40% MVC, the heart rate response was about 10 beats per minute lower during the 25% MVC, in either the sitting or horizontal postures. The lower exercising heart rates at 25% MVC agree with the results of previous work by Funderburk et al (6) who showed that while the blood pressure response to isometric exercise is independent of the tension exerted, the heart rate response increases with the tension.

Blood Flow and right atrial pressures

The 3 panels of Fig. 6 illustrate the forearm blood flow with the subjects in the sitting (o) and horizontal (●) postures before, during and after exercise at 10, 20 and 40% MVC. At all three tensions the blood flow through the active arm in the horizontal posture was considerably lower than it was in the sitting position. In contrast, before and after the contraction, the blood flow was higher in the recumbent posture.

Venous blood pressures were measured from a venous catheter in an antecubital vein, when the tip of the catheter was aligned with the level of the right atrium. During fatiguing contractions, the venous pressures did not increase except in the last few seconds of contraction, when chest fixation occurred. Even, then, the increase in venous pressure did not exceed 2 mm Hg, similar to changes observed previously (9).

DISCUSSION

The finding that isometric muscular endurance is greater in the seated position than in the other postures examined is of functional significance. In the first of four successive contractions, the difference in endurance is about 20%. In practical terms, placing a pilot in a recumbent or semi-recumbent position, which is clearly desirable to offset disadvantageous effects from gravitational forces, may result in an increased hazard from muscular fatigue with its concomitant influence on the precision and dexterity of muscular movements. The choice of posture for pilots seems to lie in the balance between the undesirable effects of gravitational stress and those of local muscular fatigue. Our evidence makes it clear that the sitting posture was considerably the best of the four examined in terms of the ability of muscles to sustain isometric contractions.

Our results seem to point inescapably to the conclusion that the greater endurance in the sitting position is related to the local blood flow. Presumably this cannot be due to differences in the hydrostatic pressure generated by the contractions, or to differences in metabolism, since the strength of contraction was the same in both positions.

No differences were found in the blood pressure at rest or during isometric exercise in the different postures. In the sitting position, with the arm dependent and the forearm held horizontal, the hydrostatic column will be slightly greater than in the recumbent position where the arm was held by the side. That will result in an increased perfusion pressure. But the position of the forearm relative to the heart was similar in the seated and 45° head-up positions, when the endurance times were markedly longer in the sitting posture. Hence, the difference in perfusion pressure while sitting cannot be held responsible for the increased blood flow and endurance times in that posture compared to all other postures.

It seems that the influence of metabolic and purely mechanical factors can be ruled out as the cause of the increased blood flow during exercise, leading to the conclusion that the mechanism is neural. At rest the forearm blood flow is lower in the sitting than the recumbent posture, and this is considered to be due to sympathetic adrenergic constriction mediated through the low-pressure baroreceptors (14, 15). Our results fit this pattern both before and after exercise. Mosely (10) found the hyperemia following an unspecified amount of rhythmic exercise to be greater in the recumbent than in the upright posture. This difference in post-exercise hyperemia was abolished by an adrenergic blocking agent leading him to conclude that it was controlled by low-pressure baroreceptors. Folkow et al (4, 5) measured the amount of blood flow through the calf by the Xenon^{133} wash-out method during and after an undisclosed but "heavy" amount of rhythmic exercise. They found a much greater blood flow in the upright posture during the exercise and much greater post-exercise hyperemia in the recumbent posture. Those findings follow the same pattern as ours.

Folkow believes that the increased flow during the exercise depends on the mechanical increase of the "effective perfusion pressure" due to a decrease in venous pressure in the lower limb when the muscle pump becomes active. A marked decrease in venous pressure is known to occur in the foot when walking begins (13). Folkow asserts that an increase of "effective perfusion pressure" is important only when the blood vessels are fully dilated and, thereby, that this influence is important only during heavy exercise. In his view, sympathetic control is negligible both during and after work, based on results from the perfused hind limb of a cat (4), in contrast to the findings of others (3).

While those conclusions may fit the control of blood flow to the leg in heavy rhythmic exercise, they cannot explain our results, where, during

sustained contractions there is no muscle pump and where the local blood flow is higher in the sitting than in the recumbent posture even at low isometric tensions when fatigue does not occur and when the blood vessels are not fully dilated. However, during the period over which blood flow was measured there was no change in central venous pressure and, in consequence, no excitement of low pressure baroreceptors. These receptors provide the only known neural mechanism by which the blood flow to the limbs can be modified in postural changes, and are doubtless the cause of our higher resting and post-exercise blood flows in the recumbent than in the sitting position. But during exercise the influence of the low pressure baroreceptors is reversed. The cause of that reversal is unknown. It appears neither to be metabolic in nature nor to be due to differences in intra-muscular or perfusion pressures. It is possible that the low-pressure baroreceptors operate at different gains at varying absolute levels of central venous pressures but that does not permit a plausible explanation of our findings. Another possibility is that there are low pressure baroreceptors in the periphery which release vasoconstriction when the venous pressure is increased.

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FIGURE LEGENDS

Figure 1: Each set of 4 bar graphs shows the mean of 3 strength measurements from all 4 subjects in the head-up (U), sitting (S), horizontal (H) and head-down (D) position.

Figure 2: Each point in the graph represents the mean of 3 endurance measurements at a tension of 40% MVC for C_1 (▬), C_2 (▲), C_3 (●), C_4 (×) when the subjects were in the sitting (S), head-up (U), horizontal (H) and head-down (D) positions. On the left are the results with normal circulation and on the right is shown the endurance with circulatory arrest.

Figure 3: This figure illustrates the mean endurance of the 4 subjects to 4 successive contractions at 25% MVC in the sitting (●) and horizontal (○) postures.

Figure 4: This figure illustrates the mean heart rate and blood pressure responses before (0) and at 20, 40, 60, 80 and 100% of the duration, and 1 and 2 minutes after endurance contractions at 40% MVC with the subjects in the head-up (▲), sitting (■), horizontal (○) and head down (●) position.

Figure 5: This figure illustrates the average heart rate and blood pressure responses before (0) and at 20, 40, 60, 80 and 100% duration of a contraction at 25% MVC, and 1 and 2 minutes post-exercise with the subject in the sitting (■) and horzontal (●) positions.

Figure 6: The forearm blood flow recorded from the active arm before, during and after exercise. The 3 panels illustrate blood flows associated with a 10, 20 and 40% MVC with the subjects in the sitting (○) and horizontal (●) positions.

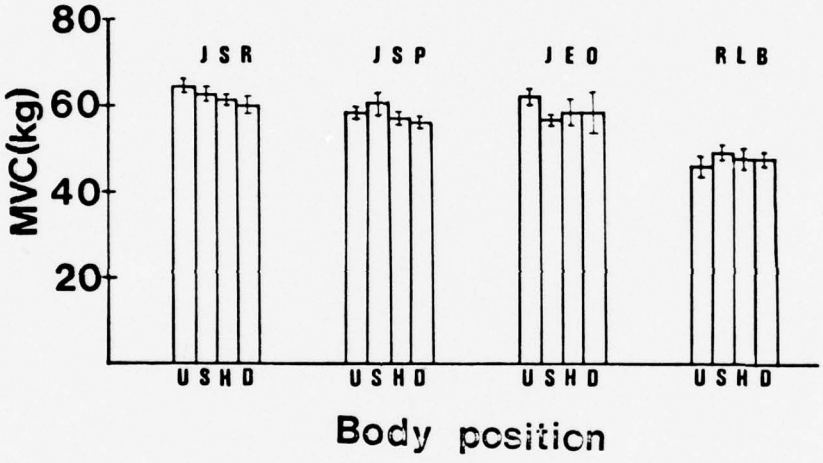

80
60
40
20
MVC(kg)
JSR
JSP
JEO
RLB
U S H D
U S H D
U S H D
U S H D
Body position

FIGURE 1

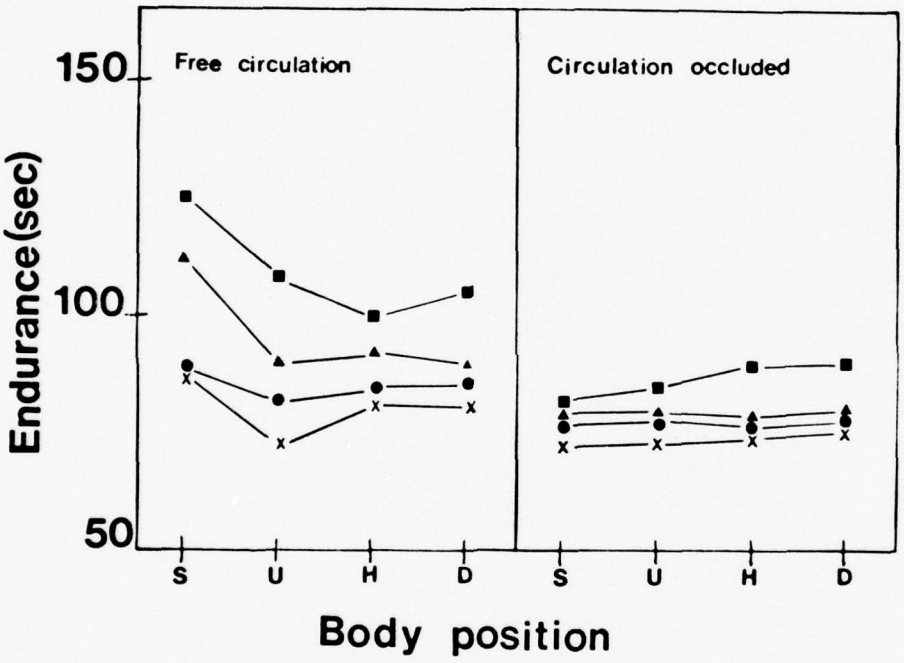

Free circulation
Circulation occluded
150
100
50
Endurance(sec)
S
U
H
D
S
U
H
D
Body position

FIGURE 2

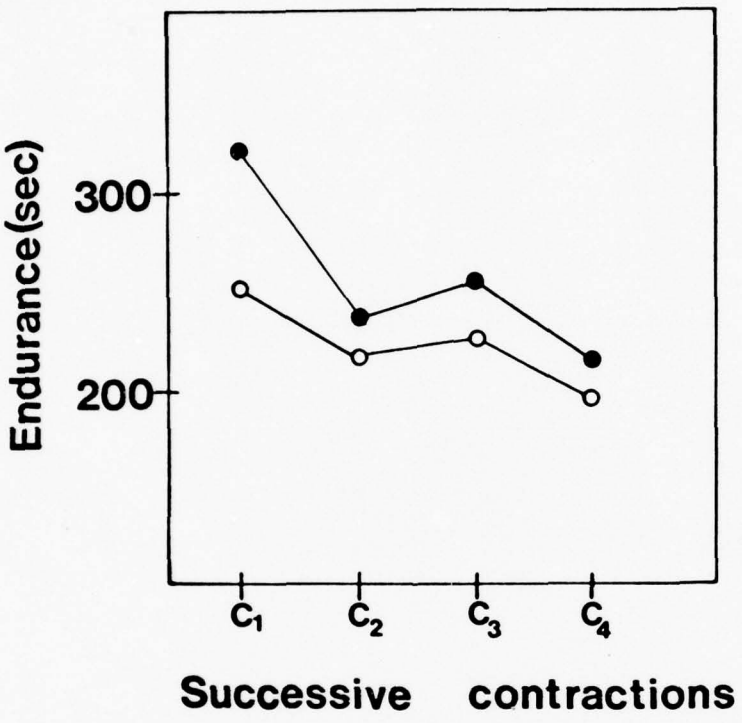


FIGURE 3

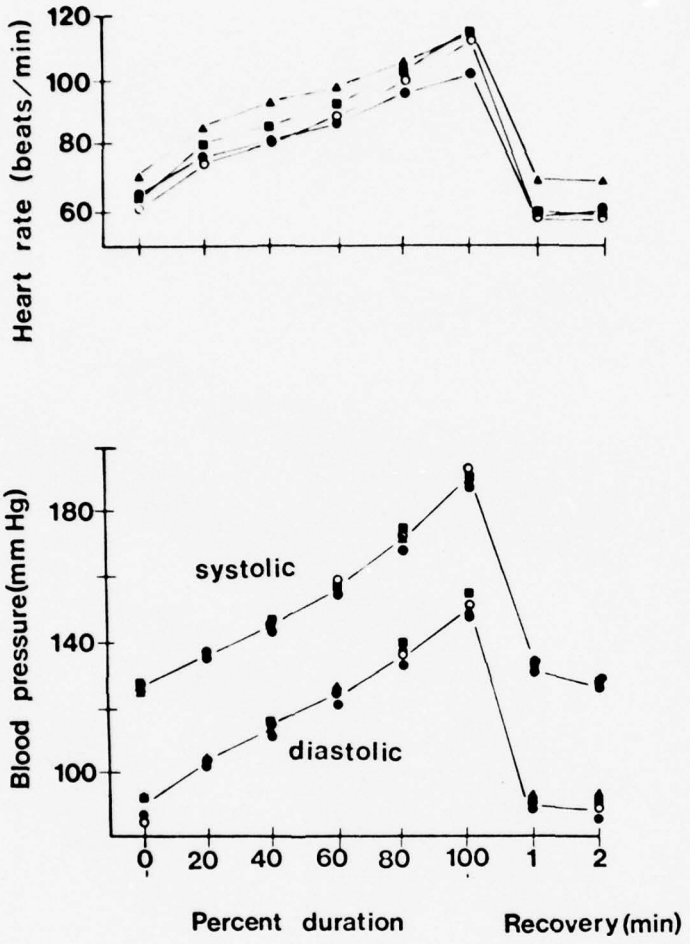

Heart rate (beats/min)
120
100
80
60
Blood pressure(mm Hg)
180
140
100
systolic
diastolic
0
20
40
60
80
100
1
2
Percent duration
Recovery (min)

FIGURE 4

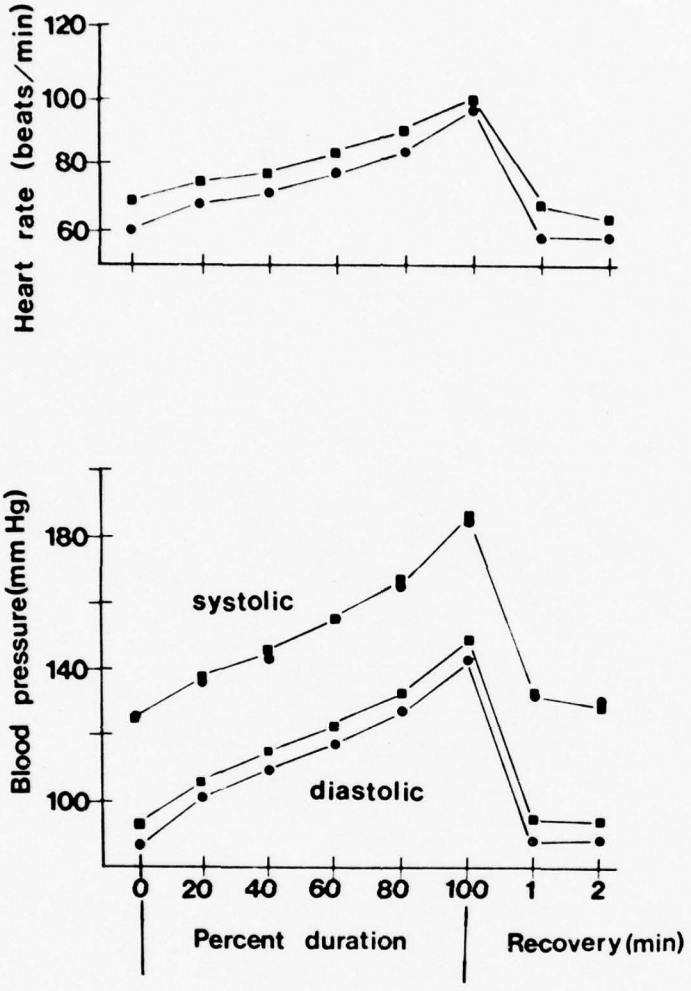

Heart rate (beats/min)
120
100
80
60
Blood pressure(mm Hg)
180
140
100
systolic
diastolic
0
20
40
60
80
100
1
2
Percent duration
Recovery (min)

FIGURE 5

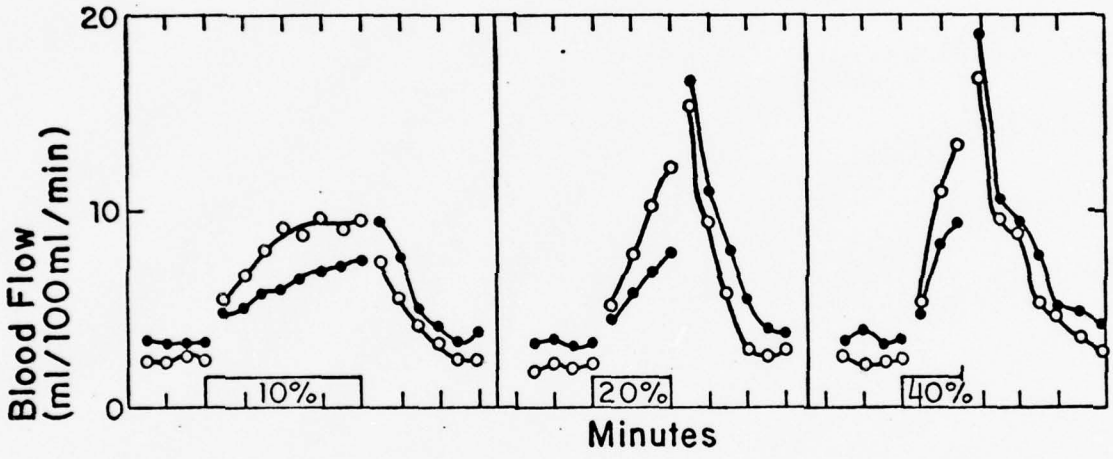


FIGURE 6

INVESTIGATION 12

RESPIRATORY RESPONSES TO SIMULTANEOUS STATIC AND RHYTHMIC EXERCISES IN HUMANS.

INTRODUCTION

We have shown (6) that sustained static muscular contraction results in hyperventilation which increases progressively throughout the course of the effort. During the isometric exercise, ventilation per litre of oxygen uptake (the ventilatory equivalent, $\dot{V}_E/l$ of oxygen) increased dramatically and the end-tidal carbon dioxide tension decreased, changes that confirm hyperventilation. In contrast, it is well known that increases in ventilation during rhythmic exercise are graded and closely match the metabolic demands of the tissues, except at extremely high work loads. Since many kinds of activity involve combinations of rhythmic and static efforts, the question arises of which type of exercise takes priority in exerting an influence or in what manner these influences on respiratory control mechanisms are integrated during such combined activity.

The purpose of the present study was to determine the relative influence of the two forms of exercise on respiratory control during combined rhythmic and static exercise.

METHODS

Six healthy male volunteers, aged from 22 to 45 years, acted as subjects. They were all medically examined and before they consented to take part they were informed in detail of the objectives of the study, the methods to be used and the potential hazards; before starting the investigation they each signed a form of voluntary consent.

Rhythmic muscular activity was performed on a Monark bicycle ergometer and static contractions on a hand-grip dynamometer. All subjects were

experienced in the use of these two devices.

At the start of each experiment, the subject exerted two brief (< 2 s) maximal voluntary contractions on the hand-grip dynamometer, with a 3 min interval between them. A rest period of 10 min then followed before the start of the experiment. Each experiment comprised a bout of cycling at 50 revolutions/min at 25, 50 or 100W for a period of about 13 min. The first 7 min of cycling was intended to permit the ventilatory responses to reach a steady state. At that point, while continuing to cycle, the subject began, and maintained, an isometric hand-grip contraction at 40% MVC until he could no longer hold that tension; the duration of that fatiguing contraction varied from subject to subject. When the subject released the hand-grip, he continued cycling for another 3 min.

For ventilatory measurements all the subjects wore a nose-clip and breathed through a rubber mouth-piece attached to a low-resistance two-way breathing valve. Tubing on the expiratory side of the valve was connected to a five-way valve to which 30 litre neoprene gas sampling bags were attached. Timed gas collections were made during each interval of rest, rhythmic exercise, static exercise and recovery. Sampling intervals in rest and late recover were 1 min in duration. In exercise and early recovery 30 s intervals were used, except for the last sample, which depended upon the cessation of the static effort. In these experienced subjects, it was evident when they were nearing the point of static exercise fatigue. Gas was collected until the instant of grip release, at which time collection was initiated in the first recovery bag by quickly turning the five-way valve. Those final collections in the static exercise period ranged from 18 to 56 s. Collected gases were analysed for oxygen concentration and the volumes were determined. Appropriate temperature and pressure corrections were

made and volumes were expressed at STPD. Oxygen consumption and minute ventilation were calculated for each sampling interval.

Another series of experiments, to act as a control, followed a similar procedure but the subject did not cycle; he simply sat on the bicycle seat and exerted a fatiguing hand-grip contraction at 40% MVC.

RESULTS

The respiratory responses to static exercise in the absence of dynamic activity include a modest increase over resting oxygen consumption, as illustrated in Fig. 1(a). 'Sitting' in all figures represents results from control experiments in which subjects maintained a static hand-grip contraction to fatigue while seated, without rhythmic activity, on the bicycle ergometer. Since the duration of the isometric contraction varied from subject to subject (range 138-181 s), the responses during this period were normalized by calculating them in terms of percentages of the total duration. Thereby the responses for all subjects are illustrated on a common abscissa. The increase of oxygen consumption during static contraction and its return to resting level in recovery represents the response to the increased metabolic demands of the involved muscle. The small dimension of the response (about 0.25 l of oxygen/min) is not at all surprising when the small muscle mass (about 500 g) is kept in mind.

The increase in oxygen consumption accompanying the rhythmic exercise demands is also seen in Fig. 1. As expected, during the first 7 min of cycling the oxygen uptake rose along with increasing intensity of the three rhythmic work loads. All subjects appeared to be in or very near a steady state by the end of the 7 min period of cycling, the calculated respiratory exchange ratios (R) in the last two 1 min samples of the cycling period not differing significantly. The additional consumption

of oxygen resulting from static hand-grip 'superimposed' on the cycling was small, comparable in magnitude to the increased oxygen consumption in response to the hand-grip when sitting. After the isometric tension was released, and while the subjects continued to cycle, the oxygen consumption returned to values which did not differ significantly from those found before the hand-grip (Fig. 1). When the cycling ended, the uptake of oxygen returned to resting values. As with oxygen consumption, the ventilation due to cycling rose with the severity of the load (Fig. 2). A large increase in ventilation occurred with static effort, either alone or in combination with the rhythmic exercise. The magnitude of this increased ventilation due to the 40% MVC grip was constant whether the subjects were cycling at different rhythmic loads or just sitting on the bicycle. The constancy of this effort of the static effort on ventilation is confirmed by results shown in Fig. 3, static effort producing an average increase in $\dot{V}_E$ of 20 1/min regardless of the rhythmic load. Thus, an increase in oxygen consumption of 0.25 1/min as a result of rhythmic exercise was associated with an increase in $\dot{V}_E$ of about 5 1/min in contrast the same increase in oxygen consumption due to isometric exercise resulted in an increase in $\dot{V}_E$ of 20 1/min.

The ventilatory equivalent during the isometric contraction (Fig 4) increased markedly in the control experiments when the subjects gripped while sitting on the cycle. In contrast, the typical small decrease in ventilatory equivalent with rhythmic exercise alone is seen in the 7 min of cycling before the hand-grip. The hyperventilation that occurred in response to the static effort was seen at all rhythmic work loads, but its significance progressively decreased owing to the nearly constant 20 litre increment in ventilation superimposed on higher ventilatory responses to greater rhythmic work loads.

DISCUSSION

The increases in oxygen consumption and minute ventilation during rhythmic exercise were directly related to the work load, these responses reaching a steady state in the 7 min interval of cycling which preceded the static hand-grip contraction (2,3,4).

Static effort produced a disprcportionate rise in minute ventilation relative to the increase in oxygen consumption, resulting in hyperventilation, as we have noted before in seated subjects (6). It is striking that the absolute increase in $\dot{V}_E$ elicited by the static effort is so constant at about 20 l/min despite the ventilatory commitment to rhythmic exercise (Fig. 3). Since voluntary cooperation, particularly for the hand-grip effort, is required, and since these subjects were experienced in such efforts independently of the rhythmic exercise, the possibility of the subjects providing a result (hyperventilation) that they knew should exist was present. This was, of course, impossible to eliminate in such an experiment. However, prediction of results was not discussed before the experiments, and the attention of the subject to maintaining the proper work level of the two exercise forms would almost eliminate any intentional breathing response. Most importantly, the consistency of the magnitude of ventilatory increase with grip among all subjects would suggest an unbiased response.

The inputs to the respiratory controlling centres that are effective during rhythmic exercise result in ventilatory adjustments that meet increased metabolic demands. In contrast, during static exercise ventilation increases out of proportion to metabolic needs, resulting in hyperventilation. When static effort is performed during the steady-state response to rhythmic exercise, the influence of inputs to ventilatory control related to the static effort is added to the demand resulting from rhythmic activity. In the range of rhythmic effort studied in these experiments (0-100W) the added

drive due to static effort of 40% MVC was essentially constant. The differences in ventilatory responses to static and rhythmic work suggest that different inputs are involved in control of respiration during the two different forms of exercise.

In our earlier study of the ventilatory response to static exercise (6) we concluded that pain and metabolites from the active muscles, acting either centrally or peripherally, could be excluded as primary factors in the hyperventilation. Since the ventilatory responses in this study, whether combined with rhythmic exercise or not, are the same as in the earlier one, we presume the same conclusions to hold. Coote, Hilton & Perez-Gonzalez (1) have suggested from animal experiments that reflex increase in respiration originates in the statically exercising limb and is abolished by interrupting afferents with dorsal root sections. McCloskey & Mitchell (5) confirmed these results and, by using nerve-blocking techniques, present the argument that fibres in either or both group III or group IV were responsible.

Whatever the stimuli that drive the respiratory changes accompanying rhythmic or isometric exercise (or both), the significance of those responses can be noted now. Whenever a rhythmic effort is performed, the metabolic demands are accurately reflected in the increases in ventilation. However, the addition of even a modest degree of static effort during the rhythmic exercises disrupts the match of ventilation to metabolism and produces an inefficient, energy-consuming hyperventilation.

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FIGURE LEGENDS

Figure 1: Oxygen consumption (mean values ± SEM, 1/min) of six subjects in four conditions: (1) fatiguing hand-grip contraction (Grip) while sitting on the bicycle ergometer (a); (2) grip superimposed during a period of rhythmic exercise on the bicycle ergometer at 25 W (b), 50 W (c) and 100 W (d). Time during period of cycling alone is expressed in minutes. Time during grip periods is expressed as per cent of the duration to fatigue, so normalizing duration of grip, which ranged from 138 to 181 s.

Figure 2: Minute ventilation (mean values ± SEM, 1/min) for six subjects. Time during periods of cycling alone is expressed in minutes. Time during grip periods is expressed as per cent of the duration to fatigue, as described for Fig. 1.

Figure 3: Mean minute ventilation responses to cycling with (●) and without (0) static hand-grip. Work loads are shown along the abscissa in watts and minute ventilation along the ordinate in 1/min. Zero work load represents experiments with subjects seated on the bicycle ergometer, not cycling. O, Values are taken from Fig. 2, and represent the last measurement before commencing the hand-grip effort; ● values represent the last measurement in the "grip" period, Lines were drawn by eye.

Figure 4: Ventilatory equivalent (mean values ± SEM) for six subjects. Time during periods of cycling alone is expressed in minutes. Time during grip periods is expressed as per cent of the duration to fatigue, as described for Fig. 1.

Figure 1

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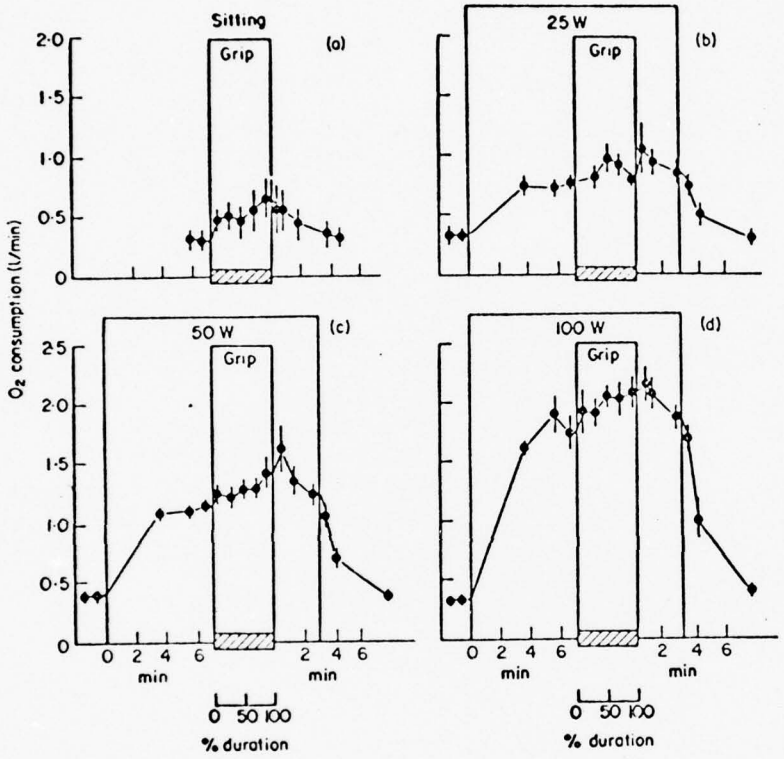


Figure 2

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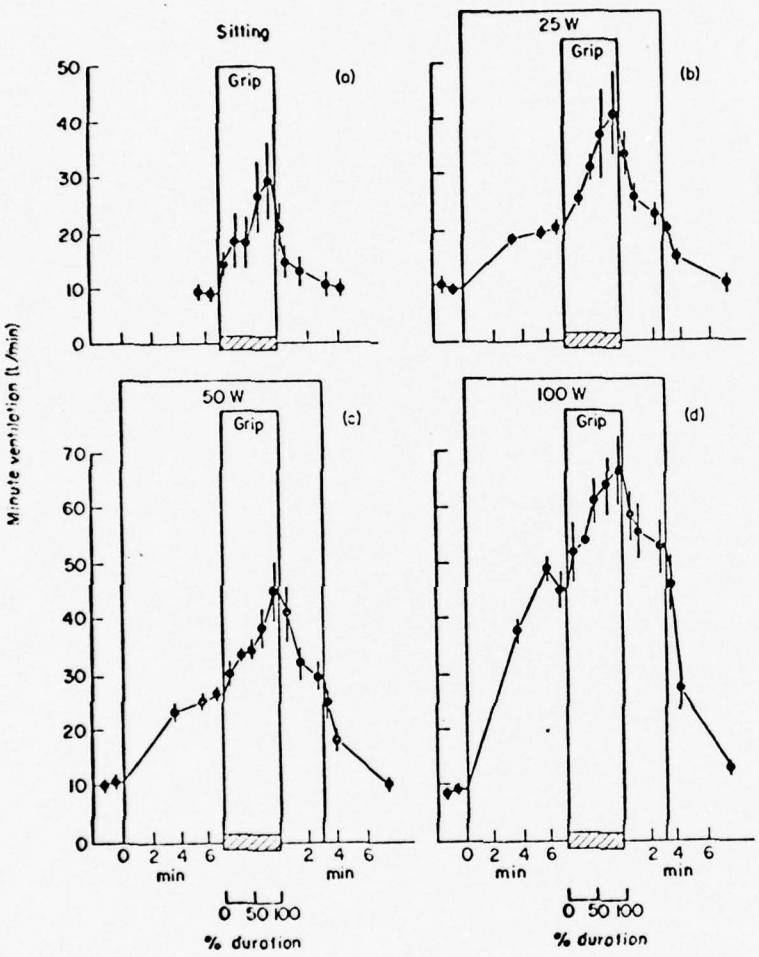
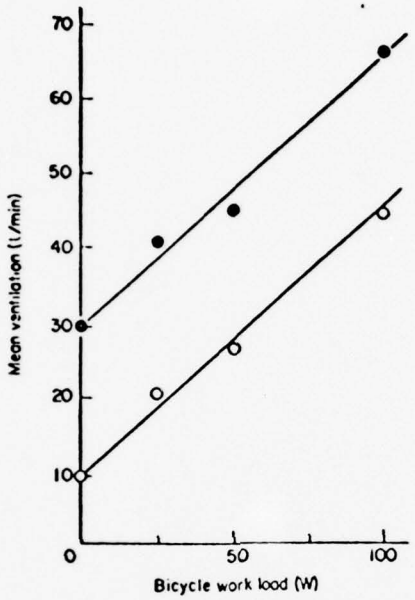
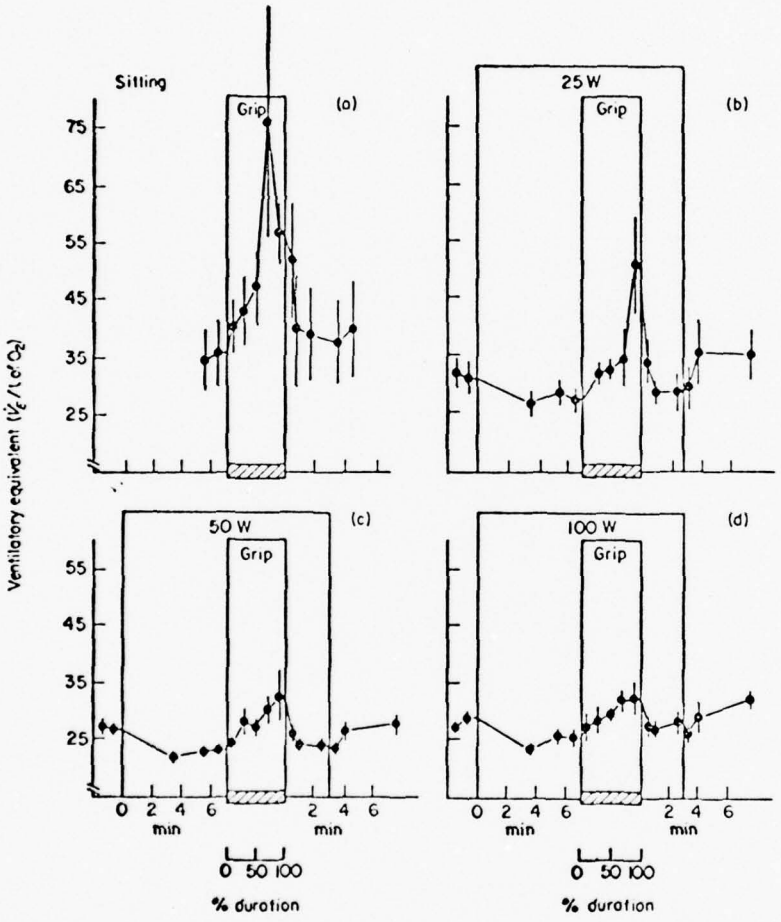


Figure 3



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Figure 4



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INVESTIGATION 13

CARDIOVASCULAR RESPONSES TO ACUTE EXPOSURE TO 2900 M DURING REST AND STATIC EXERCISE.

INTRODUCTION

The cardiovascular responses to altitude have been investigated by many researchers and the major changes are well documented. Yet there is very little information regarding regional blood flow changes in man. Durand, et al. (4) and Weil, et al. (13) have investigated the skin flow in the extremities of resting men at altitudes of 3750 m and 4300 m respectively. Roy, et al. (10) followed forearm blood flow at rest during acclimatization to 3700 m. However, no one has reported the response of whole limb flow during exercise at altitude. It was the purpose of this expedition to investigate some of the cardiovascular responses of man to altitude. This report is concerned with the responses of the central and the peripheral circulation in response to static handgrip exercise during the acute phase of acclimatization to altitude. Information is also presented on isometric function and electrolyte changes following fatiguing contractions.

METHODS

Subjects

Initially eleven healthy male and female subjects ranging in age from 19 to 50 years of age were involved in these experiments. Due to technical problems which occurred at the field station, data from two of the subjects had to be discarded. Therefore data is presented on six subjects from St. Louis, altitude 160 m and on three subjects who were residents of Calgary, altitude 1066 m. Experiments were performed at an elevation of 2900 m near

Mt. Assinboine in British Columbia. The St. Louis subjects were flown by commercial airlines to Calgary the day prior to ascent to altitude. All subjects were flown from Banff to Mt. Assinboine by helicopter. These arrangements were made so that the subjects would arrive at altitude without significant travel fatigue.

The altitude station consisted of a well equipped mountaineering hut and two ten-man insulated tents, all of which were used for either housing or experimentation. The hut or a tent was chosen for experimentation each day so that relatively constant ambient thermal conditions existed for the subjects. Electricity for instrumentation was provided by a portable generator.

All the subjects were experienced with and had been trained in the use of the hand-grip dynamometer, Clarke, et al. (3). At the beginning of each experiment the subject exerted two maximum voluntary contractions (MVC) and the sustained isometric contractions were at 10, 20 or 40% MVC.

The forearm blood flow was measured before, during and after contractions (not taken to fatigue) held for 3 min at 10% MVC and for 1½ min at 20% MVC. Forearm blood flow was measured by venous occlusion plethysmography (14). Due to problems associated with being in the field, approximately 25% of the flows were questionable and have not been reported here. Blood pressures were measured by ascultation as often as possible and heart rate was measured from a continuous recording of the ECG.

Procedures

The general procedure was that on the first (0-10 hrs) and third day (48 hrs) each subject's forearm blood flow, heart rate and arterial blood

pressure was measured before, during and after hand-grip contractions at 10 and 20% MVC, while on the second day (24 hrs) the heart rate and blood pressure were measured in response to a fatiguing contraction at 40% MVC, during which venous blood samples were taken for analysis of plasma constituents.

Peripheral Circulation

On days 1 and 3, each subject sat quietly with his or her left arm immersed in water at 34° C. for 15 min; the wrist cuff was inflated after 14 min immersion. The arm was removed from the water and thoroughly dried. Resting forearm blood flows were started 1 min after removal. The forearm blood flows, heart rates and blood pressures were measured throughout a 2 min rest period, the 3 min contraction at 10% MVC and for 3 min of recovery. The wrist cuff was deflated and the arm was replaced in the water (34° C.) for 10 min. The procedure was then repeated except that the isometric contraction was at 20% MVC for 1½ min.

Isometric Endurance

The subject was clothed comfortably and the test (right) arm was insulated by a down filled sleeve. Through an opening in that sleeve, a sterile 20-gauge cannula was placed in an antecubital vein. A sample of venous blood was drawn while the subject was at rest and the catheter and connecting tubing were flushed with sterile heparinized saline (1000 units/ liter). The subject then exerted two maximum contractions one minute apart. Five minutes later, a second resting blood sample was drawn. Then the subject began the 40% MVC to fatigue. Based upon the prior training sessions at the subject's resident altitude, samples were drawn between 30 and 50%

of the endurance time, at 80 to 100% of the endurance time and 60 and 300 seconds after the tension was released. All blood samples were immediately centrifuged and the plasma eluted and stored in a sealed container which was refrigerated by immersion in the snow bank behind the field station. Upon return to Calgary, the concentration of sodium and potassium (flame photometry), calcium (atomic absorption) and chloride (chloridometer) were measured, along with the osmolarity (freezing point depression).

All these procedures were repeated 3-5 days on return from the 2900 m altitude.

The altitude of 2900 m was chosen because it is 1) above the threshold where measurable changes have been reported for other physiological parameters and 2) not high enough to precipitate acute mountain sickness which would have complicated these experiments.

Due to the small number of subjects in each group, statistical comparisons of changes were judged to be inappropriate.

RESULTS

The resting heart rates of the six St. Louis residents increased from a resting value of 71 beats/min at St. Louis to 85 beats/min during the first 10 hrs at 2900 m (Table 1). This increase in heart rate was seen in all six subjects and was sustained for 48 to 72 hrs. The heart rates returned to the values obtained at St. Louis after 1-3 days return to Calgary, 1066 m.

In two of the St. Louis subjects, who remained at 2900 m for five days, the resting heart rate had dropped nearly to control levels by the fifth day. In contrast, the Calgary residents showed an average increase of only 2 beats/min at 2900 m.

The resting blood pressures demonstrated a similar pattern in the two groups of subjects. The St. Louis subjects increased their systolic pressure by 13 mm Hg and their diastolic pressure by 17 mm Hg; the blood pressures of the Calgary residents remained unchanged (Table 2). Even after return to 1066 m the blood pressures of the St. Louis subjects were 4 to 5 mm Hg higher, on the average, than their control values; however, this average response was due to one subject whose blood pressure remained elevated while the rest fluctuated about the control values.

Table 3 shows that the average blood flow at rest increased by 25% for both groups of subjects. During exercise the blood flow of the St. Louis residents, at 10% MVC, reached 9.0 ml/100 gm/min at 1066 m, whereas after 1-10 hrs at 2900 m the flow was 9.4 ml/100 gm/min and after 2 days at 2900 m it had increased to 10.8 ml/100 gm/min. The corresponding values for a contraction of 20% MVC were 14.0, 15.3 and 16.2 ml/100 gm/min. Smaller increases, but with the same trends, were seen in the Calgary residents.

The arterial blood pressures during isometric exercise are shown in Table 4. The resting pressures in the St. Louis residents were elevated at 2900 m compared with the resting pressures at 1066 m by 5 mm Hg. This increase was also present during the first day at 2900 m during the 10% MVC experiment (Table 4) but all other pressures for the St. Louis residents and the Calgary residents were virtually identical with their control conditions at 1066 m.

The physiological significance of the pressure and flow changes both at rest and during isometric exercise are illustrated by the tissue resistance changes. The tissue resistances (PRU 100 gm) were calculated by dividing the mean arterial pressure (Table 4) by the average blood flows. For example, at 1066 m the St. Louis residents had resistances of 2131 during rest, 727 during 10% MVC and 493 during 20% MVC and those values fell on the 3rd day at 2900 m to 1835, 617 and 422 respectively, a consistent fall of about 15%. Similar changes were found in the Calgary residents. The exception to this trend occurred, also in both groups, during the first day at 2900 m during the 10% MVC contraction where a slight increase in tissue resistance was seen. In this case, the St. Louis residents increased their tissue resistance by 26 PRU/100 gm while the Calgary residents increased theirs by 40 PRU/100 gm (Table 5).

The isometric performance at 2900 m was assessed by two means: the maximum tension developed and the endurance time of a 40% MVC contraction to fatigue. No change in MVC was seen in any of the subjects regardless of the length of stay at 2900 m. The duration of the 40% MVC contraction was reduced by an average of 9.4% after 48-50 hours at 2900 m when compared to 1066 m control experiments. This reduction in duration was not consistent for all subjects.

The changes in plasma osmolality, sodium, calcium and chloride concentrations all showed that the St. Louis residents hemoconcentrated both at 1066 m and 2900 m (Tables 6 and 7). However as is evident from the results in Table 7, the Calgary subjects hemodiluted. In spite of these differences the plasma potassium concentrations increased during the fatiguing contractions in both groups. These changes are best exemplified by the osmolality changes: in the St. Louis group the average resting

value was 292 m osm/Kg H_2O which increased to 311 m osm by the end of the contraction whereas the Calgary subjects' plasma osmolality dropped from 295 to 282 under the same experimental conditions. The results of these experiments have not been subjected to statistical analysis due to the small numbers in each group of subjects.

DISCUSSION

There were two striking features concerning the physiological responses of our subjects when they were transported rapidly to the modest altitude of 2900 m. First, our subjects who were normally resident at an elevation of 160 m showed increases in resting heart rate and blood pressure of 14 beats/min and 16 mm Hg respectively. In addition, both the heart rates and blood pressures of these subjects were erratic. Second, some adaptation to the altitude of 2900 m must be incurred by residence at 1066 m since our subjects from Calgary showed no changes in either heart rate or blood pressure.

The increases in heart rate and blood pressure are consistent with the findings of other investigators at much higher altitudes. Increases in resting heart rates have been reported as 20 beats/min at 4350 m (11), 20-30 beats/min at 4300 (6) and 5-20 beats/min at 3800 (in 2 of 4 subjects) (8). Alexander, et al. (1) reported a fall of resting heart rate by 2 beats/min after 10 days at 3100 m but unfortunately did not report on changes in the acute phase of acclimatization. In the few reports available blood pressure was not consistently increased in all subjects. Klausen (8) reports that some subjects had an increase of 12-27 mm Hg in resting mean blood pressure on the first day at 3800 m and Grollman (6) found an increase of 11-20 mm Hg on the first day at 4300.

The alterations in peripheral blood flow at rest do not agree with the findings of other investigators (4, 10, 13). Roy, et al. (10) reported a steady decline in forearm blood flow over 7-8 days at 3700 m and that that fall was reversed when the subjects breathed 100% oxygen. Eckstein and Horsley (5) reported a reduction in peripheral blood flow when subjects breathed a gas mixture with only 7.5% oxygen; however, the flow was unchanged at rest while breathing 11.5% oxygen. Comparing our results from 2900 m with those of Roy, et al. (10) at 3700 m, the major differences in the circumstances of these two field experiments appear to lie in the altitude and the control over limb temperature. The use of the water bath to ensure that the arm was at a constant temperature in each of our experiments may explain the discrepancy between present results and those of Roy, et al. (10). Although Durand, et al. (4) and Weil, et al. (13) demonstrated a reduction in skin flow with exposure to altitude, this may reflect body temperature changes and need not necessarily be related only to hypoxia, as they suggest. If Roy, et al.'s (10) results are due to the reduction only in skin flow as put forward by Durand, et al. (4) and Weil, et al. (13), hypoxia would have to have had little or no effect on skeletal muscle at rest in man. This has been shown not to be the case in animals. Vogel, et al. (12) has demonstrated that rabbits breathing 8% oxygen for 30 min increase their resting muscle blood flow three fold over animals breathing 21% oxygen. Further evidence for hypoxia stimulating muscle blood flow is presented in Table 7. The 15% reduction in tissue resistance is a constant at rest and during isometric exercise after 48 hrs exposure to 2900 m. This suggests that the level of hypoxia at 2900 m is sufficient to have a vasodilator effect both at rest and during exercise. The consistent increase in resistance

at 10% MVC on the first day at 2900 m is not easily explainable. It may be related to the presence of a slight excess of bicarbonate as a result of hyperventilation, serving to buffer the metabolic dilators.

Since hypoxia is reported to dilate muscle vessels (12) a problem arises in the explanation of the blood pressure rise. If all the large muscle bed is dilated, then a marked constriction of other vascular beds must occur to result in an elevated blood pressure (Tables 2 and 4). Such vasoconstriction has been reported to occur in the skin of man (4, 13), and in the renal and splanchnic beds in animals (12). All the cardiovascular changes could be explained by an increase in sympathetic activity as suggested by Vogel, et al. (11). Pace, et al. (16) and Cunningham, et al. (15) have reported marked increases in urinary norepinephrine excretion during the early stages of acclimatization to 3850 m and 4600 m.

The evidence on electrolyte changes in the plasma are intriguing. Regrettably, we were unable to measure blood flows during the 40% MVC held to fatigue, so that the total efflux of electrolytes during the contraction cannot be calculated. But the fact that the St. Louis subjects hemoconcentrated during the contraction while the Calgary subjects hemodiluted suggests that residence at 1066 m results in some metabolic adaptation in muscular tissue. However, there is no question that for this and other unexpected aspects of our findings a more extensive investigation, on larger numbers of subjects, is required.

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Table 1: Resting Heart Rate Response to Acute Exposure to 2900 m.

Condition	At Resident Altitude	0-10 hrs at 2900 m.	24-72 hrs after return to 1066 m.
St. Louis Residents 160m n=6	71.3	84.8	71.2
Calgary Residents 1066 m n=3	69.6	71.7	69.3

Heart rates were averaged from 2-3 minutes of ECG tracing taken from subjects quietly sitting in a chair.

Table 2: Resting Blood Pressure Values During Acute Exposure to 2900 m

Condition	At Resident Altitude	0-10 hrs at 2900 m.	24-72 hrs after return to 1066 m.
St. Louis Residents alt 160m n=6			
Systolic	126	139	131
astolic	77	94	89
mean	93	109	104
Calgary Residents alt 1066 n=3			
Systolic	115	112	114
Diastolic	76	76	76
mean	89	88	89

Da' points represent mean values from all subjects in each group. The individual values we taken from averages of 3 to 5 measurements on each subject. The pressures were measured by ascultation and the mean values were calculated according to $\bar{X}BP = D + \left(\frac{S-D}{3}\right)$

Table 3: Blood Flow Response to Isometric Exercise

@ 2900 m

St. Louis Residents n=6	Rest	10% MVC	Rest	20% MVC
Control 1066 m	2.9	9.0	3.2	14.0
0-6 hrs 2900 m	3.5	9.4	3.2	15.3
50-100 hrs 2900 m	3.4	10.8	3.4	16.2
Calgary Residents n=3				
Control 1066 m	2.6	8.9	2.7	15.1
1-10 hrs 2900 m	3.0	8.0	2.8	15.1
50-60 hrs 2900 m	3.2	9.6	3.5	15.9

The above values represent means from the individual averages. The resting values for each subject are averages of five flows prior to the onset of the contraction. The 10% MVC flows values are averages of the last minute and the 20% MVC are averages of the last 40 sec of exercise. The values are in ml/100gm/min.

Table 4: Blood Pressure Response to Isometric Exercise @ 2900 m

St. Louis Residents n=6	Rest			10% MVC			20% MVC		
	Sys	Dia	X	Sys	Dia	X	Sys	Dia	X
control 1066 m	132	88	103	138	95	109	143	102	115
1-6 hrs 2900 m	139	94	109	145	104	118	141	104	115
50-100 hrs 2900 m	134	89	104	138	97	111	141	101	114
Calgary Residents n=3									
control 1066 m	114	76	89	121	91	102	122	90	100
1- hrs 2900 m	115	77	90	119	86	97	119	92	101
50-60 hrs 2900 m	112	76	88	120	83	95	117	84	95

The individual data points represent averages of three pressure readings taken by ascultation during the period when the flows were measured in Table 3. The values are in mm Hg.

Table 5: Tissue Resistance Changes Due to Isometric Exercise @ 2900 m

	Rest	10% MVC	20% MVC
S Louis Residents n=6			
72-120 hr 1066 m	2131	727	493
1-6 hr 2900 m	1869	753	451
50-100 hr 2900 m	1835	617	422
Calgary Residents n=3			
Resident at 1066 m	2053	688	397
1-10 hr 2900 m	1800	728	401
50-60 hr 2900 m	1650	594	358

These values were calculated from the data presented in Tables 3 and 4 . The formula used was PRU 100 gm tissue = BP/ ml/100gm/sec

Table 6: Effects of Acute Exposure to 2900 m on Plasma Sodium and Potassium Changes in Response to a Fatiguing Static Contraction

	Na^+ meq/L		K^+ meq/L	
	72-120 hrs at 1066 m	46-50 hrs at 2900 m	72-120 hrs at 1066 m	46-50 hrs at 2900 m
St. Louis Residents n=4				
Rest	136	135	3.6	3.3
30-50%*	137	134	5.2	4.9
80-100% *	141	138	6.3	5.1
60 sec post	137	138	3.7	3.4
300 sec post	133	134	3.2	3.2
Calgary Residents n=3				
Rest	137	137	3.8	3.4
30-50%*	136	137	4.9	4.3
80-100%*	138	134	4.8	4.3
60 sec post	136	139	3.7	3.3
300 sec post	138	134	3.6	3.4

*This data has been normalized for the time periods representing the percentage of each individual's time to reach fatigue. These antecubital venous contcentrations are averages of individual duplicate analyses. The exercise test was that of a 40% MVC hand-grip. The handling of the samples and means of analyses are described in the text.

Table 7: Plasma Electrolyte Changes at 46-50 hr of Exposure to 2900 m in Response to a Fatiguing Static Contraction.

	Osmolality	Na^+	K^+	Cl^-	Ca^{++}
	m osm/Kg H_2O		m eq/L		
St. Louis Residents n=4					
Rest	292	135	3.3	101	4.40
30-50%*	294	134	4.9	102	4.68
80-100%*	311	138	5.1	104	4.90
60 sec post	302	138	3.4	104	4.77
Calgary Residents n=3					
Rest	295	137	3.4	104	4.58
30-50%*	291	137	4.3	104	4.57
80-100%*	282	134	4.3	103	4.52
60 sec post	294	139	3.3	103	4.64

*This data has been normalized for the time periods representing the percentage of each individual's time to reach fatigue. These antecubital venous concentrations are averages of individual duplicate analyses. The exercise test was that of a 40% MVC handgrip. The handling of the samples and means of analyses are described in the text.

INVESTIGATION 14

THE EFFECT OF HANDGRIP SPAN ON ISOMETRIC EXERCISE PERFORMANCE.

INTRODUCTION

The absolute strength of the hand-grip is markedly different for individuals (2, 8). In a recent study of 100 men (10), we found their average strength was 49.8 kg but the scatter of strength was large, ranging from 31.0 kg to 71.6 kg. In another study of 83 women (9), the average strength was 28.3 kg with a range of 19.1 kg to 47.5 kg. In those studies, the two poles of the hand grip dynamometer were not altered. In trying to assess the reason for those wide variations in muscular strength, one possible cause might simply be the dimension of the hands. A similar argument can be advanced for the wide variation in isometric endurance. The average endurance of a contraction at a tension of 40% of the maximal voluntary contraction (MVC) was 136 sec (range 75 to 220 sec) for men and 162.7 sec (range 53 to 332 sec) for women.

In the present study we have investigated the absolute strength and the isometric endurance of individuals with different sizes of hands and when the distance of the poles of the handgrip was varied. Our interest ranged from the practical consequences of exerting absolute tensions to the fundamental problems of varying the length of sarcomeres on the responses of the EMG and the cardiovascular system.

METHODS

Subjects

Two male and two female volunteers served as subjects in these experiments; their physical characteristics are listed in Table 1. All

subjects were informed of all experimental procedures and were physically examined, including a stress test (ECG) before taking part in these experiments. Care was taken during the study to assure that the weight reported in Table 1 for these subjects was maintained during the experimental period.

Strength and endurance

Isometric strength and endurance were measured on a portable strain gauge handgrip dynamometer similar to one described previously by Clarke, Hellon and Lind (3). The distance separating the poles of the grip could be adjusted to any of 5 preset distances, these distances being 4.4, 5.0, 5.6 and 6.6 cm measured from the inside of the finger bar to the outside of the palm bar. On any one day, strength was first measured with the grip span set at any of these present distances as the largest of 2 brief (< 3 sec) maximum efforts with an interval of 3 min between contractions. Using the same separation distance, a tension set at either 25, 40, 55 or 70% of the maximum tension was held until, through fatigue, the target could no longer be maintained. The length of time the target could be held, then, was the endurance time.

Measurements

The blood pressure was measured by auscultation of the inactive arm before, after and as frequently as possible during the fatiguing isometric contractions.

The heart rate was measured over a 15 sec interval from a continuous recording of the ECG before, during and after the fatiguing contractions.

The EMG was measured from 2 silver/silver chloride disc electrodes placed on the medial surface of the forearm. Care was taken to place the electrodes in the same position for each subject on different days.

The raw EMG was amplified through a specially designed EMG amplifier

with an input impedance of 10^8 ohms and a frequency response which was flat from DC to 4000 Hz and then recorded for future analysis on a Sangamo-Tandberg Series 100 FM recorder.

Training

Prior to the experimental procedures outlined below, each subject was trained daily to exert his maximum isometric strength and to hold tensions of 25, 40, 55 or 70% MVC to fatigue. On any one training day, maximum strength and the endurance for a series of 5 fatiguing contractions at any one of these tensions was measured; 3 min were allowed between contractions. Training was assumed to be complete when the day-by-day variation of the first and subsequent contractions in a series at any tension was reduced to less than 5%. In practice, this required a training period of 6 to 8 weeks on any one subject.

Procedures

To determine the distances between the 2 poles of the handgrip dynamometer to be used for each subject in the later experiments, the isometric strength was measured with the distance between the poles at 4.4, 5.0, 5.6 or 6.6 cm. From these results, 3 dimensions of hand-grip were chosen for each subject represented as the extremes of distance (4.4 and 6.6 cm) and that distance at which each subject developed his or her greatest isometric strength.

Two series of experiments were performed. First, on any one day, each subject performed one fatiguing contraction at either 25, 40, 55 or 70% MVC at one of the three handgrip sizes. Each experiment was replicated, and the experimental conditions were randomized. Finally, the surface EMG was examined during brief (3 sec) contractions at tensions between 10 and 100% MVC for all 3 handgrip spans. On any one subject, the brief contractions

were all performed on the same day with a 2 min interval between them. In all these experiments the subjects sat with their arms bare to the shoulder. Room temperature was maintained at 23 $\pm$ 0.5^{o} C.

EMG analysis

The recorded EMG was analyzed in a Linc computer. The amplitude was assessed as the average of the half wave rectified EMG over a 1.5 sec sampling period. To analyze the frequency of the EMG, a full wave Fast Fourier Transform (FFT) was performed over 6 serial 250 ms time periods over the frequency range of 4 to 508 Hz. From this analysis, the average (center frequency) of the power spectra was calculated and averaged to give the average frequency over the 1.5 sec sampling period. The details of this procedure are given elsewhere (11).

RESULTS

Strength

The maximum voluntary strengths (MVC), measured for each subject with differing dimensions of the handgrip dynamometer, are shown in Fig. 1. The greatest strength for 3 of the subjects was recorded when the two poles of the dynamometer provided a hand-grip size of 5 cm, and for the remaining subject it was 5.6 cm. For all 4 subjects, the strength decreased at grip spans above and below these dimensions.

Isometric endurance

The isometric endurances of the handgrip muscles measured at 25, 40, 55 or 70% MVC at each grip span is shown in Fig. 2. Each point in this figure represents the mean of 2 determinations on each of the 4 subjects at each tension. There was no systematic difference between the endurance determined

at optimal muscle length (○) or with the narrow (△) or wide (●) grip spans at any of these relative tensions (panel A). However, in terms of the absolute strength exerted by the handgrip muscles (panel B), because of the difference in maximum strength associated with differing dimensions of the handgrip dynamometer, the endurance at any set load was longest for contractions performed at the optimal grip span.

Blood pressure and heart rates

For any muscle length both the blood pressure and heart rate increased linearly during the fatiguing contractions at any of the 4 tensions we examined. Figures 3 and 4, therefore, illustrate only the blood pressures and heart rates recorded at the end of the fatiguing isometric contractions. There was no significant difference between the blood pressures recorded at the end of contractions at any tension examined for any given grip span (Fig. 3).

In contrast, the highest heart rate recorded at the end of the fatiguing contraction was directly related to the tension exerted (Fig. 4). However, at any one tension, the lowest heart rates were recorded during contractions at the optimal grip span. Thus the heart rate at the end of a fatiguing contraction at a tension of 25% MVC (the average absolute tension was 12.2 kg) with the handgrip span set at 6.6 cm was equal to that at the end of a fatiguing contraction at 55% MVC (the average absolute tension was 32.8 kg) exerted with the handgrip span set at the optimal length.

EMG

The EMG recorded during the brief (3 sec) isometric contractions at various tensions up to maximum is shown in Fig. 5. Because of the large difference in the EMG amplitude between subjects, and the additional day to day variation in EMG amplitude in any one subject during the experiments

where the subjects went to fatigue, we have normalized the EMG amplitude in terms of the amplitude for a brief MVC here, and in Fig. 6. Under all experimental circumstances, EMG amplitude was linearly related to tension. Further, the absolute EMG amplitude was the same for any grip span at 100% MVC. Thus, in relative terms, at any % MVC the EMG amplitude was the same for the optimal (○), wide (●) and narrow (△) grip spans (Fig. 5a). However, because of the difference in absolute strength with different hand dimensions, for any given sub-maximal tension, the EMG amplitude was lowest for contractions at the optimal handgrip size (Fig 5b). In contrast, the frequency of the EMG was the same for any given tension or any handgrip size. During the fatiguing contractions, the EMG amplitude increased linearly during the contractions (Fig. 6) by between 25 and 30%. However, there was no difference in the pattern of response or magnitude of the response between the 3 handgrip sizes. In a similar manner, the frequency of the surface EMG (Fig. 7), which decreased linearly to fatigue for any of the 4 tensions examined, was unaffected by the handgrip span.

DISCUSSION

The effect of handle size on the tension exerted during contractions of the handgripping muscles has been well documented in the literature (5, 7, 12).

In the present investigation we found the optimal distance of the 2 poles of our dynamometer, to permit the greatest handgrip strength, to be approximately 5 cm. Increasing or decreasing the span of the grip by 0.6 cm could result in a loss of as much as 20% in isometric strength. The mechanism for this loss of strength is undoubtedly mainly due to the

variations in muscle length with different degrees of handgrip closure, while a certain variation of mechanical advantage and wrist angle with different finger positions must be noted (1).

In contrast, when isometric endurance was measured at any given fraction of the maximum strength the endurance was the same at all grip spans. Thus, when the muscles of the forearm are at different lengths, this appears to have an effect only on the maximum strength and not the endurance at the same fraction of that strength. However, in terms of the absolute tension exerted during those contractions, the endurance was 30-35% longer for any sustained submaximal tension when the contractions were performed at the optimal length for the muscle.

The blood pressure response was independent of the tension exerted and of the grip span for all 4 subjects reported here. Since the blood pressure response is considered to be reflex in origin and driven by a metabolite released by the active muscles (4) it appears that grip span does not affect that reflex function. The increases in the heart rate were directly related to the tension exerted, as reported by others (6). But the heart rate response was influenced by the grip span as well, being lowest when contractions were performed at the optimal hand span which allowed development of the highest strength.

In relative terms, the EMG amplitude and frequency were not influenced by the degree of handgrip closure either during brief or sustained contractions. However, in terms of absolute strength, at any one sustained submaximal tension, the EMG amplitude at the onset and the rate of change of amplitude and frequency during fatiguing contractions were lower for contractions at optimal muscle length.

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TABLE 1

General Characteristics of Subjects

Subject	Sex	Ht. (cm)	Weight (kg)	Age (Yrs)
JP	M	187.9	118.2	27
MC	M	184.8	68.9	24
CW	F	167.6	61.3	28
DB	F	168.9	56.7	24

FIGURE LEGENDS

Figure 1: This figure shows the maximum voluntary strength measured for male (panel A) subjects JP (●) and MC (X) and female (panel B) subjects DB (△) and CW (○) as a function of the dimensions of the hand dynamometer.

Figure 2: This figure shows the average isometric endurance of all 4 subjects for contractions exerted at 25, 40, 55, or 70% MVC for 3 different grip spans, set at a narrow separation distance (△), a wide separation distance (●), and at that distance where each subject exerted his or her maximum isometric strength (○). Endurance is shown as a function of both the relative (panel A) and absolute (panel B) isometric strength.

Figure 3: This figure illustrates the average blood pressure response for all 4 subjects at the end of fatiguing isometric contractions exerted at 25, 40, 55, and 70% of their maximum strength for the narrow (△), wide (●) and grip span set for the greatest strength in the muscle (○).

Figure 4: This figure illustrates the average heart rate response for all 4 subjects at the end of fatiguing isometric contractions exerted at 25, 40, 55, and 70% of their maximum strength for the narrow (△), wide (●) and grip span set for the greatest strength in the muscle (○).

Figure 5: This figure illustrates the normalized EMG amplitude and center frequencies during brief (3 sec) isometric contractions of the handgrip where the span was set at the optimal (○), narrow (△) and wide (●) grip spans.

Figure 6: This figure shows the average EMG amplitude measured at the onset and throughout the fatiguing isometric contractions at 25 (○), 40 (●), 55 (□) or 70% (■) MVC at each of the 3 grip spans.

Figure 7: This figure shows the center frequency of the surface EMG at the onset and throughout the fatiguing isometric contractions at tensions of 25 (○), 40 (●), 55 (□) and 70% (■) MVC for each of the 3 grip spans.

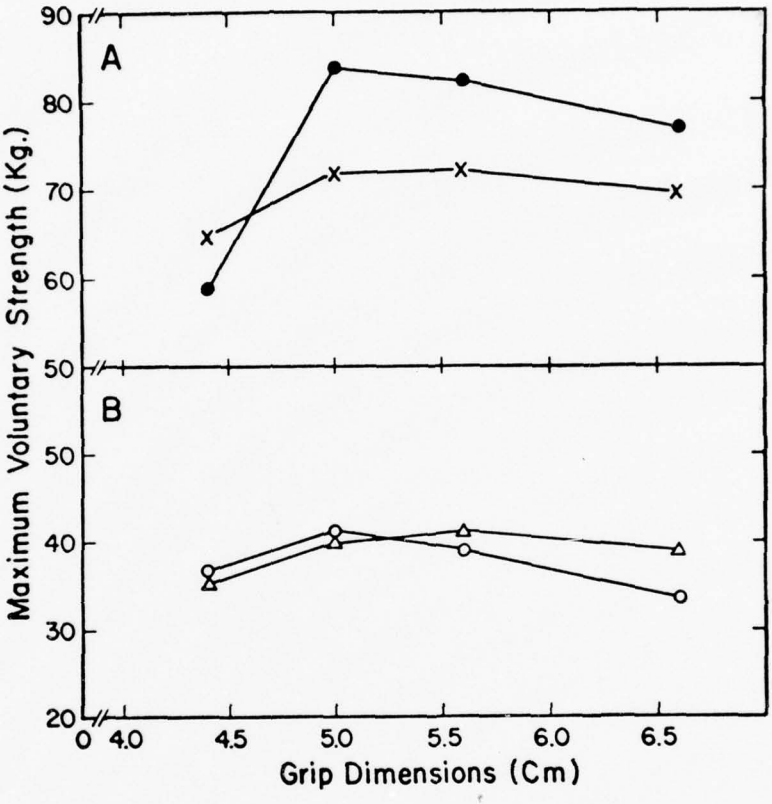

90
80
70
60
50
A
B
50
40
30
20
0
4.0
4.5
5.0
5.5
6.0
6.5
Maximum Voluntary Strength (Kg.)
Grip Dimensions (Cm)

FIGURE 1

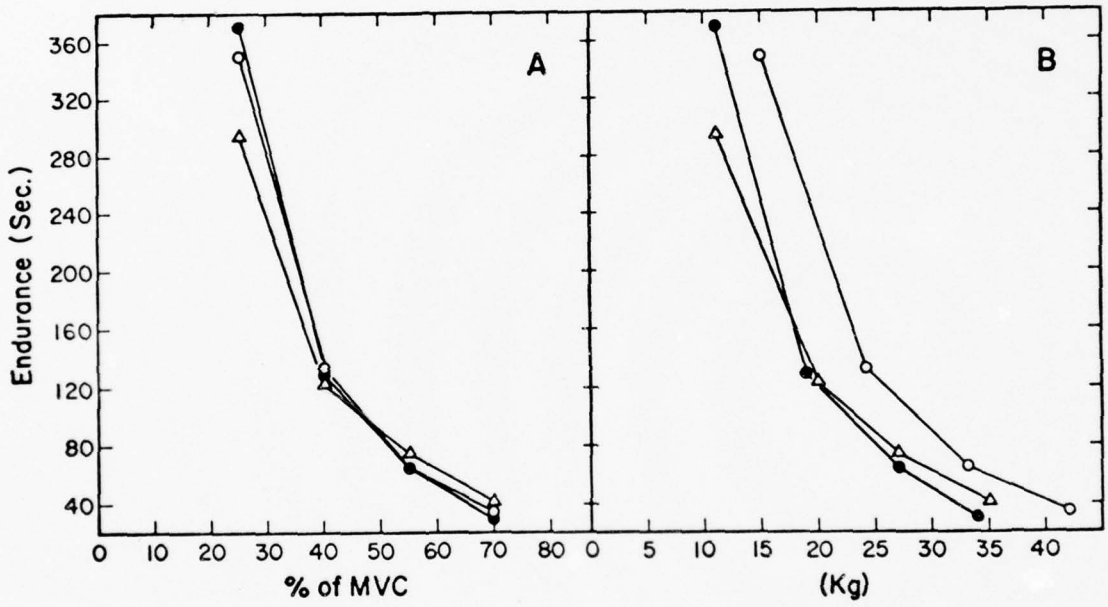

Endurance (Sec.)
360
320
280
240
200
160
120
80
40
A
B
0 10 20 30 40 50 60 70 80
% of MVC
0 5 10 15 20 25 30 35 40
(Kg)

FIGURE 2

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THE INVESTIGATION OF METABOLIC AND CARDIOVASCULAR RESPONSES TO --ETC(U)
JUL 76 A R LIND, H BARCROFT, J S PETROFSKY AF-AFOSR-2362

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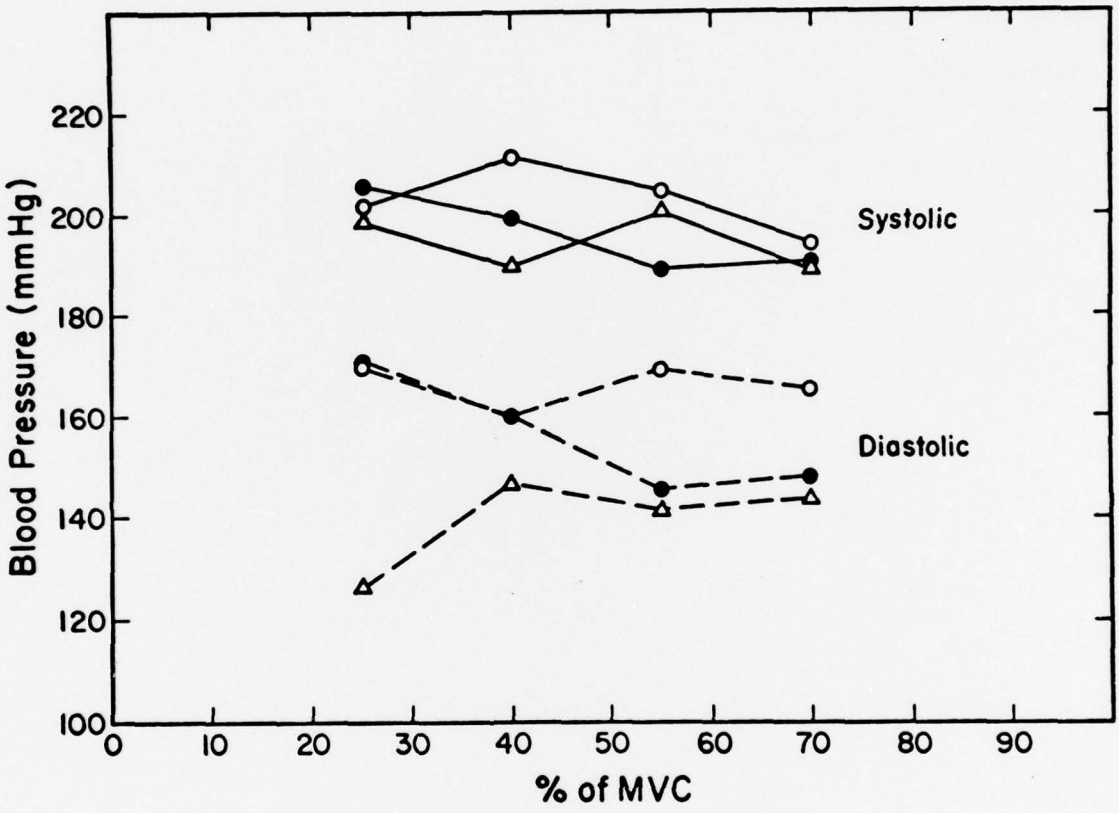

Blood Pressure (mmHg)
220
200
180
160
140
120
100
0
10
20
30
40
50
60
70
80
90
% of MVC
Systolic
Diastolic

FIGURE 3

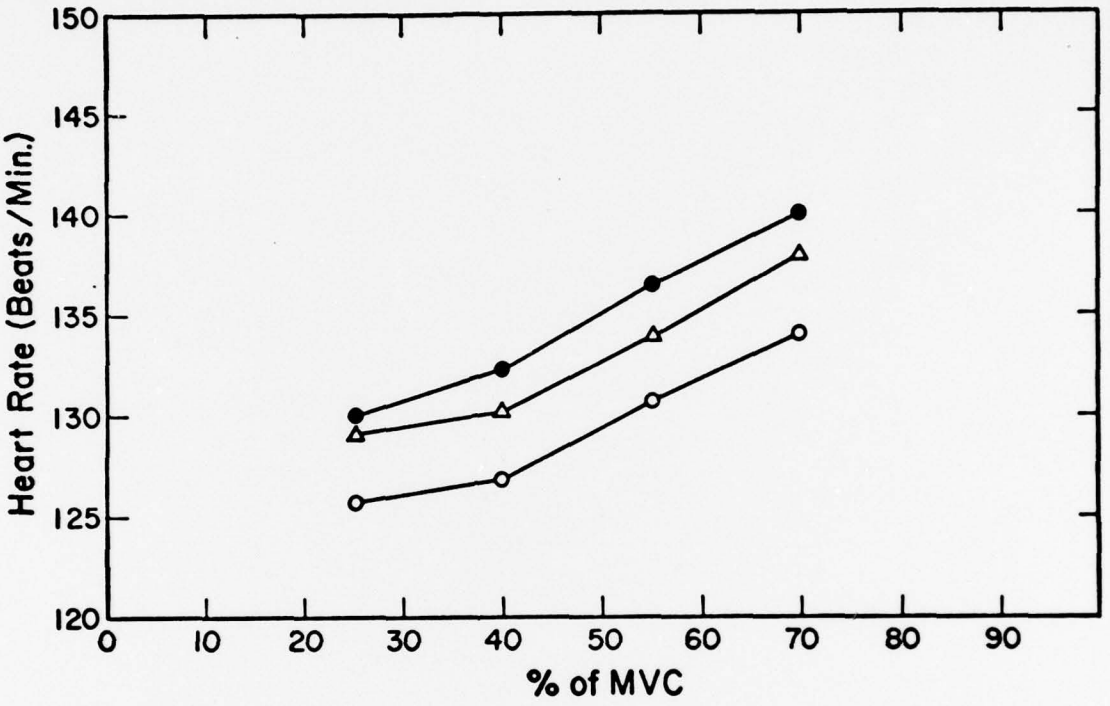

150
145
140
135
130
125
120
Heart Rate (Beats/Min.)
0
10
20
30
40
50
60
70
80
90
% of MVC

FIGURE 4

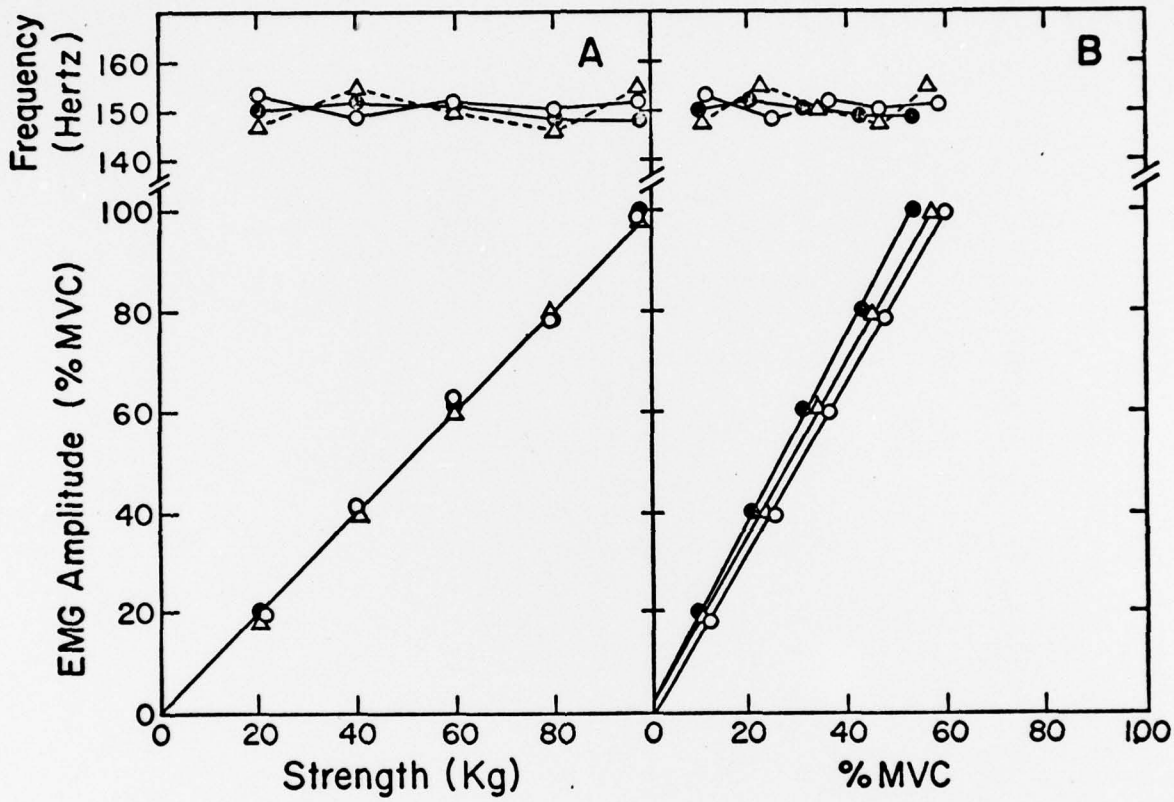

Frequency (Hertz)
160
150
140
A
B
EMG Amplitude (% MVC)
100
80
60
40
20
0
0
20
40
60
80
0
20
40
60
80
100
Strength (Kg)
% MVC

FIGURE 5

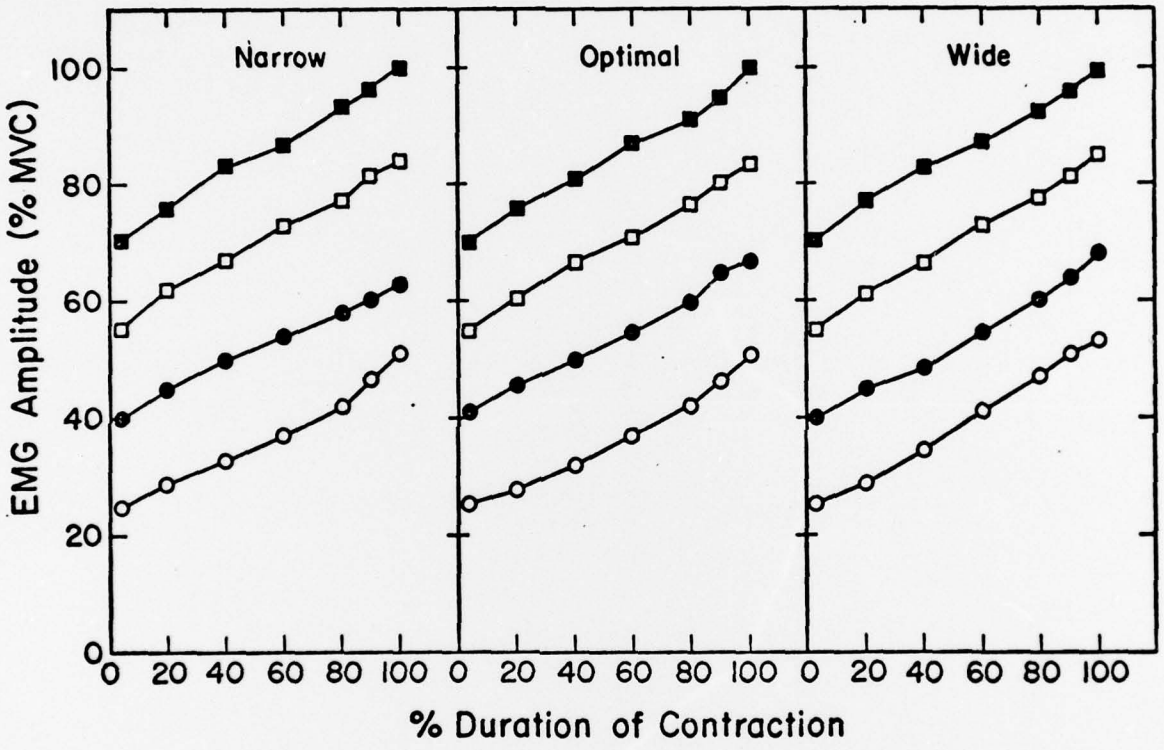

Narrow
Optimal
Wide
EMG Amplitude (% MVC)
0
20
40
60
80
100
0 20 40 60 80 100 0 20 40 60 80 100 0 20 40 60 80 100
% Duration of Contraction

FIGURE 6

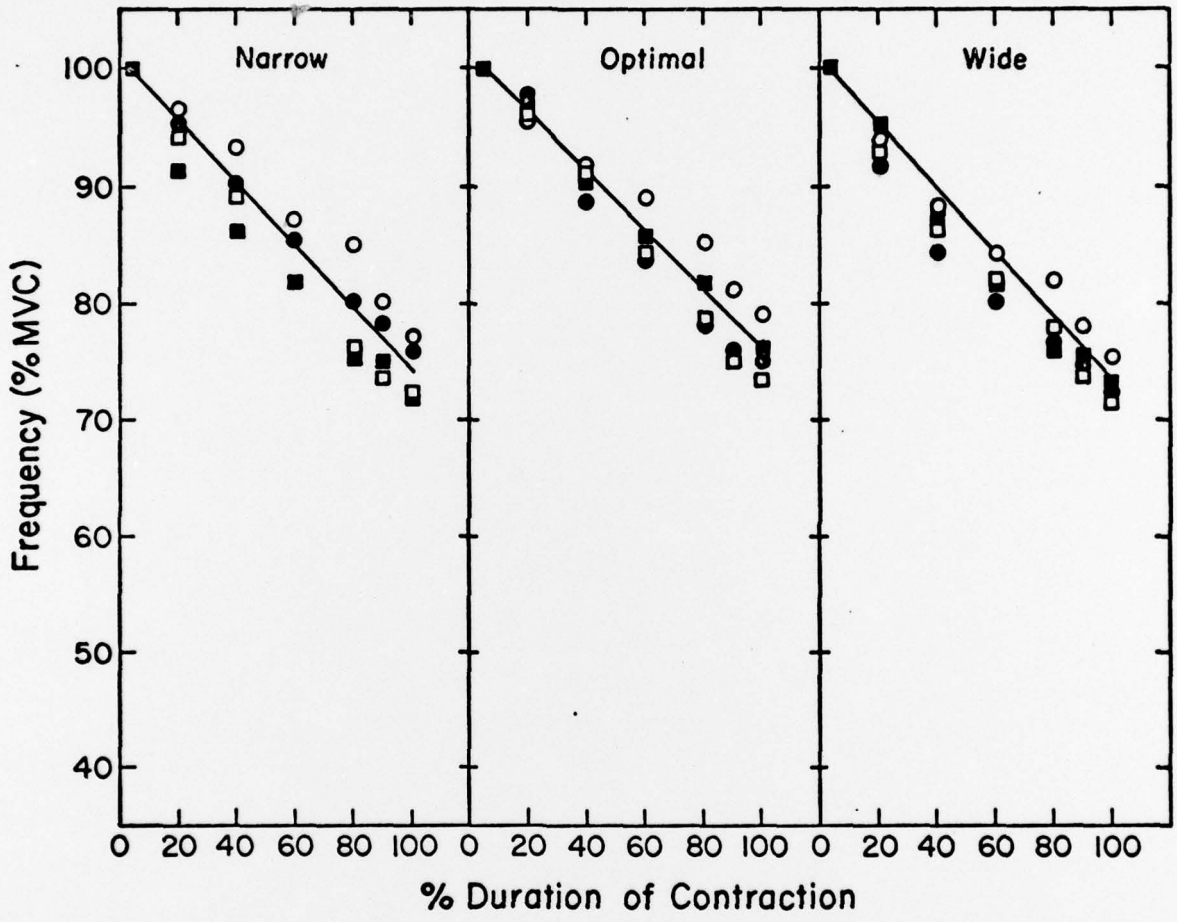

Narrow
Optimal
Wide
Frequency (% MVC)
100
90
80
70
60
50
40
0 20 40 60 80 100 0 20 40 60 80 100 0 20 40 60 80 100
% Duration of Contraction

FIGURE 7

INVESTIGATION 15

THE LACK OF INFLUENCE OF REACTIVE HYPEREMIA ON EXHAUSTING RHYTHMIC OR STATIC EXERCISE.

INTRODUCTION

It has been claimed (7 , 8) that the performance of exhausting exercise can be greatly enhanced if the exercise is begun at the start of reactive hyperemia. Those authors reported an increase of endurance performance related to an increase of the duration of previous circulatory occlusion, whereby occlusion for 10-14 minutes resulted in an increase of endurance capacity by nearly 7-fold. The main explanation offered was that the increased blood flow during reactive hyperemia permitted a better metabolic scene of supply and demand for continued muscular function. But that argument did not seem to us to stand close scrutiny, in physiological terms. Subsidiary arguments presented seemed even less valid. In a brief report, Collier and Percival (3) challenged the findings reported above; they found no increase in the working capacity of 9 students when the work was done in the presence of hyperemia following arterial occlusion for 5 min.

The experiments described here were intended to re-examine the possibility that fatiguing exercise performed in the presence of an initially increased blood flow due to prior circulatory occlusion could go on for longer.

METHODS

Five young men and women volunteered to act as subjects. The methods and procedures and their attendant dangers were explained to each subject in detail. All subjects signed a statement of informed consent following a medical examination, including a cardiovascular stress test.

Both Nukada (8) and Muller (7) used an unusual ergometer on which

the sole subject of each author was tested. We had no such ergometer. We decided to examine our subjects during exhausting rhythmic exercise on a bicycle ergometer and during fatiguing static effort on a hand-grip dynamometer. Three of the subjects were well trained in both kinds of exercise, while the other two subjects were only partially trained.

Since Muller (7) showed data in which the duration of endurance performance in normal circumstances was of the order of 5 minutes, the belt tension of the bicycle ergometer and the muscular tension on the hand-grip dynamometer were adjusted for each subject to result in fatigue in a similar time. Also Muller's results showed endurance time to double following a previous circulatory occlusion of 5 minutes duration, while after 10 minutes occlusion the endurance increased by 4 to 7 fold depending on the level of training. In consequence, each of our subjects, performed fatiguing 1) rhythmic and 2) isometric exercise with endurance times of *about* 5 minutes with normal circulation. They also undertook the same levels of rhythmic and isometric exercise immediately following circulatory occlusion for both 5 and 10 minutes. Each experiment was replicated. The order of performance of these experimental activities was randomized for each subject and on each occasion.

Blood flows are difficult to measure during rhythmic exercise, but, with some limitation, can be readily measured during isometric exercise. The forearm blood flows of 3 of the subjects were measured during static effort at 10, 20 and 40% of the maximal voluntary contraction (MVC); at 10% MVC, no fatigue occurs while at 20 and 40% MVC, fatigue occurs, on average, in about 8 and 2.5 minutes respectively. Blood flows were measured 1) before during and after static effort at 10 and 20% MVC for 3 min and at 40% MVC for 2 min with free circulation to the arm and 2) during and after static effort at the same tensions and for the same durations of the contractions which began immediately after circulatory occlusion for 5 and

10 minutes. Since static effort results in an increase in both arterial systolic and diastolic pressures (4 , 6) the forearm blood flow was also measured 3) after the release of circulatory occlusion of the test arm when the contralateral arm performed static effort at the same tension as in items 2) above, and 4) in the resting arm following 5 and 10 minutes occlusion of the circulation. The order of each of those 4 treatments were presented haphazardly for each subject.

RESULTS

The symbols in Fig 1a show the endurance times for each subject while the mean endurance for all 5 subjects on the bicycle ergometer is shown by the heavy uninterrupted line. The load on the ergometer was selected to yield individual endurance times between 4 and 7 minutes. The time scale on the abscissa represents the duration of circulatory arrest to both legs; bicycling began immediately as the cuffs were deflated. The mean endurance time for all the subjects was 325 sec with no previous occlusion. After 5 or 10 min circulatory arrest the mean values were 348 and 319 sec respectively. The results for 3 of the subjects showed some variability but in a haphazard fashion with no trend of response. The data are shown again in Fig 1b in terms of the proportional changes, following occlusion, to the values found with no previous occlusion of the circulation. Obviously, the changes are not large and are haphazard. They contrast with the 3 curves shown for the results of Muller's (7) subject who worked at the rates shown in association with each curve--the hatched line shows the findings after the subject was trained.

In a similar fashion, Fig 2a shows the individual and mean endurance times of our subjects in response to a hand-grip isometric contraction.

Figure 2b represents those results proportionately, as for Fig 1b; again, the findings from Muller's subject are superimposed. Except for one of our subjects, there was less variability in isometric endurance than there was for endurance on the bicycle ergometer. There was no evidence that previous circulatory arrest either helped or hindered muscular function.

Figure 3 shows the forearm blood flows, measured on 3 subjects during isometric contractions performed with a normal circulation or during reactive hyperemia. For the sake of clarity, results from each subject are shown, one at each tension, in Fig 3. In each panel of Fig 3, the procedure was the same except for the tension and its duration. Figures 3a, 3b and 3c, respectively, represent the changes in forearm blood flow associated with contractions at 10%, 20% and 40% MVC. In each panel is shown 1) the reactive hyperemia for that subject following 5 min of circulatory arrest, 2) the increments of forearm blood flow during the isometric contraction without (✳) and with (O) previous circulatory arrest for 5 min. It is clear that for all 3 subjects, the blood flow through the forearm was higher for the first minute during the contraction following occlusion than it was without circulatory arrest. But any circulatory benefit was lost in the same time (about 1 min) that the reactive hyperemia took to dissipate; thereafter the blood flow during the contractions at all tensions was the same. The findings for each subject at all the tensions followed the same pattern.

In the final series of experiments, two subjects first exercised to exhaustion on the bicycle ergometer: their average endurance at 12 kpm/min was 380 sec. On repeating the work during the reactive hyperemia following 5 min circulatory occlusion the average endurance was slightly lower, at 367 sec. In another experiment, the legs were again occluded for 5 min and exercise was begun at 12 kpm/min, but was maintained at that level for

only 190 sec, when the level of work was reduced to 10.5 kpm/min and the exercise was continued to fatigue, 286 sec later, with a total working time of 476 sec. That is, with this procedure, the endurance time was 109 sec longer (30%) than when the exercise following occlusion was kept at the constantly higher level of 12 kpm/min. Similar findings followed experiments of this type with isometric rather than rhythmic exercise.

DISCUSSION

Our results on 5 subjects are at complete variance with the findings reported by Nukada (8) on one subject, or Muller (7) on his subject. No functional benefit accrued to our subjects who performed either dynamic or isometric exercise during reactive hyperemia, even when the preceding circulatory arrest was maintained for 10 min, conditions in which Muller's subject was reported to extend his endurance by 250-650% depending on his degree of training. The largest change of any of our subjects was +17% in one subject and -7% in another during rhythmic exercise, and +19% and -13% during isometric exercise. Average values never exceeded a 4% change, which is within the expected range of day-by-day variation in endurance to either kind of exercise.

It is hard to envisage any good physiological reason why previous arrest of the circulation should greatly enhance muscular function. The concept that the increased blood flow in reactive hyperemia may be beneficial to concomitant muscular activity might, at first sight, be considered as an attractive possibility. But it must be kept in mind that at least half of the reactive hyperemia to a limb goes to the skin vessels (2). Furthermore, it is clear that vasodilatation of the vessels in muscles occurs within seconds of muscular activity (4 ,5). If, during a bout of rhythmic

or isometric exercise following occlusion, any of the increased blood flow does go to the muscle its nutritive value must be nil since it does not prolong the exercise. Certainly, as shown in Fig 3, the increased blood flow through the whole forearm is small and shortlived.

The tissues will be denuded of oxygen within 3 minutes of circulatory arrest but the oxygen content of the tissues will be as rapidly or possibly even more rapidly restored in the resting arm once the circulatory occlusion is released (1). Muller's concept that the anoxia during occlusion dilated the capillaries, thereby permitting an unusually rapid diffusion of metabolites from the active muscle into the abnormally dilated capillaries scarcely fits our current understanding of curculatory events. Our experiments conclusively show that there is no maintenance of a consistently and unusually high limb blood flow when muscular exercise begins in the presence of a reactive hyperemia.

It is even more difficult to understand Muller's claim that when exhausting work was begun at a high level the muscular endurance is longer if the work was continued at that high level than if it were reduced to a lower level (but still fatiguing) part-way during the bout of exercise. The results of our experiments follow the edict of common sense that if, part-way through a bout of exercise, the severity of muscular activity is reduced, the endurance time of the exercise is increased.

The conclusions of this series of experiments are simply that our results are contradictory to those of Nukada (8) and Muller (7) and support those of Collier and Percival (3). It remains possible that the kind of exercise indulged by the sole subject in these earlier reports was sufficiently unusual to induce the reported findings. But the physiological principles involved makes those earlier reports unexpected and unlikely, particularly in the face of the present findings.

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FIGURE LEGENDS

Figure 1: The left panel shows the absolute endurance times of cycling for each subject (and the average, ●). Zero on the abscissa indicates that the subjects had no previous impediment of the circulation to the legs. The other two points on the abscissa show that the circulation to the legs was arrested for 5 and for 10 minutes and was released immediately before cycling began. The right panel shows the same data normalized; also shown in this panel are 3 curves representing the endurance of Muller's subject (7) with normal circulation to the legs and after 5 min of circulatory occlusion.

Figure 2: Showing the endurance times of our subjects (and the average, ●) to isometric contractions. The circumstances are exactly as explained for Fig. 1.

Figure 3: Showing the increase in forearm blood flow after 5 min circulatory occlusion (●), during sustained isometric contractions (*) and during sustained isometric contractions performed during reactive hyperemia after 5 min arterial occlusion (o). The results are from a different subject in each panel, and the isometric tension exerted was different on each occasion, as indicated.

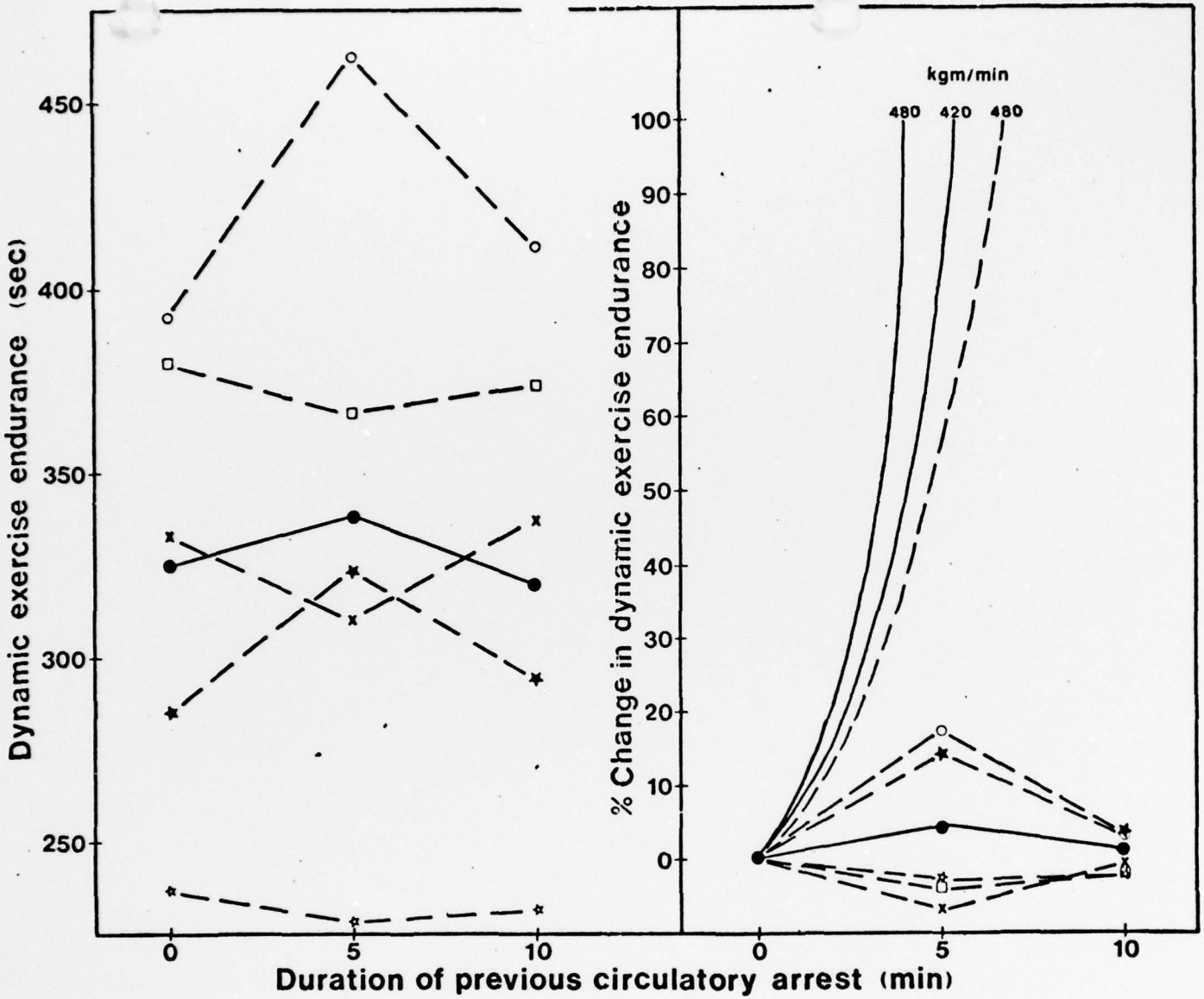

Dynamic exercise endurance (sec)
450
400
350
300
250
% Change in dynamic exercise endurance
kgm/min
480
420
480
100
90
80
70
60
50
40
30
20
10
0
0
5
10
0
5
10
Duration of previous circulatory arrest (min)

Figure 1

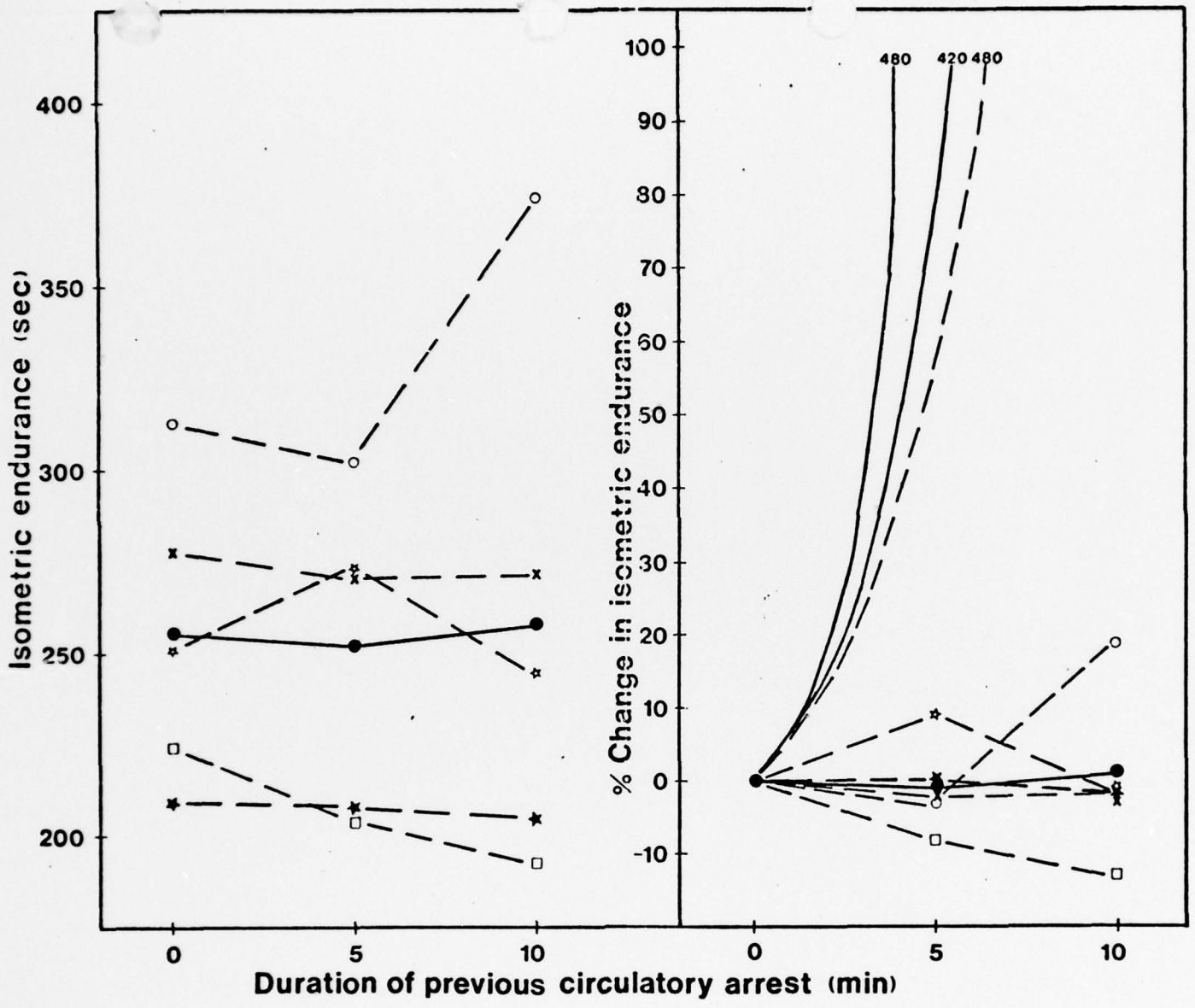

Isometric endurance (sec)
400
350
300
250
200
% Change in isometric endurance
100
90
80
70
60
50
40
30
20
10
0
-10
480
420
480
0
5
10
0
5
10
Duration of previous circulatory arrest (min)

Figure 2

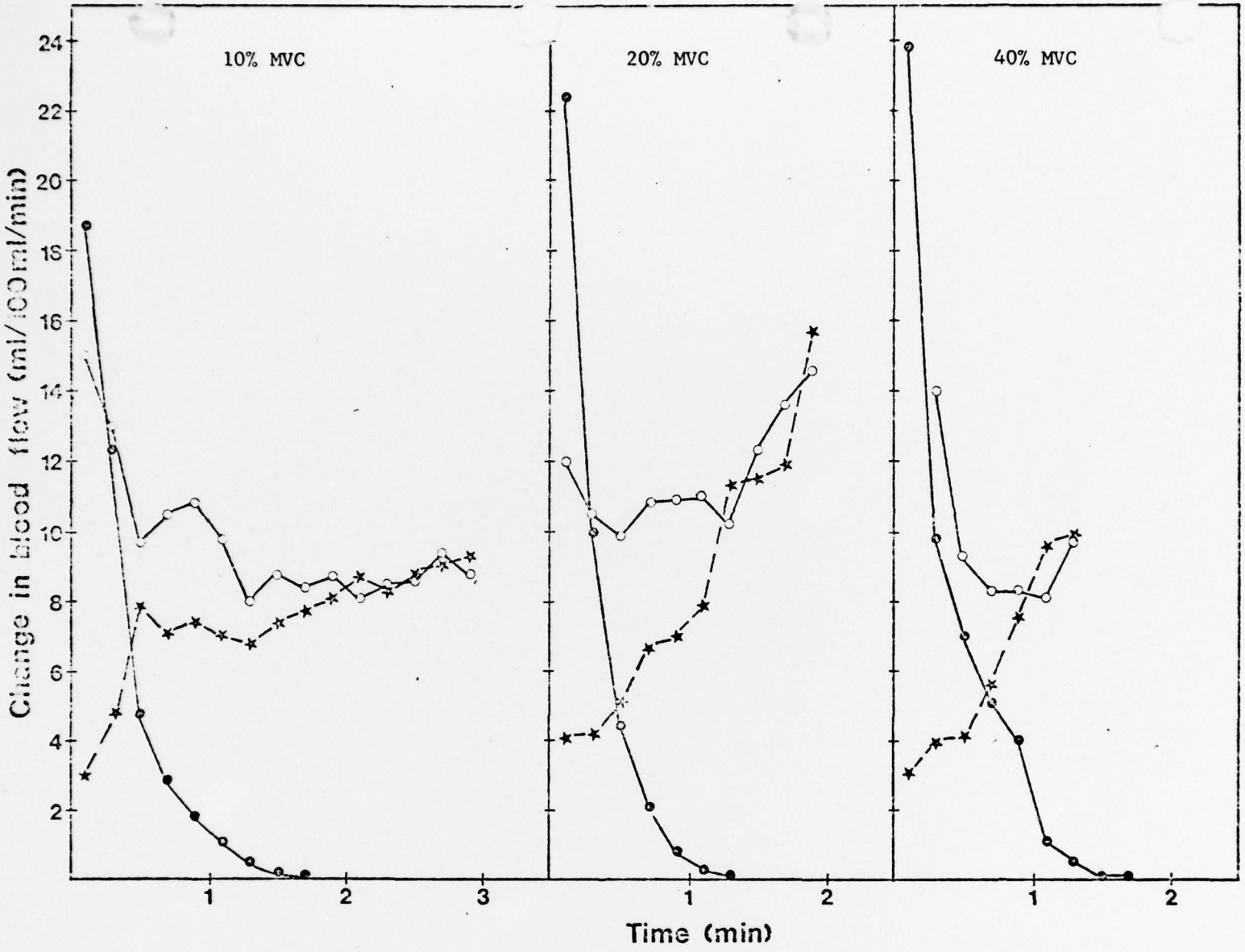

10% MVC
20% MVC
40% MVC
Change in blood flow (ml/100ml/min)
24
22
20
18
16
14
12
10
8
6
4
2
1
2
3
1
2
1
2
Time (min)

Figure 3