Conduction velocity in ischemic muscle: effect on EMG frequency spectrum

J. THOMAS MORTIMER, ROBERT MAGNUSSON, AND INGEMAR PETERSEN
Division of Applied Electronics, Chalmers University of Technology, and Department of Clinical Neurophysiology, Sahlgren Hospital, Gothenburg, Sweden

THE AVAILABLE INFORMATION regarding the effects of restricted blood flow on muscle action-potential conduction velocity is surprisingly small. The subject seems to be almost overlooked compared to the numerous articles concerning conduction velocity under normal conditions and conduction velocity as a function of temperature. In the only reference found pertaining to the relationship between conduction velocity and ischemia (Stålberg (5)), no definite conclusions were drawn regarding the effect of ischemia on action-potential propagation velocity.

The study of propagation velocity behavior during restricted blood flow is interesting not only physiologically but also clinically. Clinically, there are several reasons to study the behavior of the conduction velocity during restricted blood flow. First, electromyograms (EMGs) are taken from loaded muscles. Second, some muscle fibers become metabolically restricted at very low contraction rates, i.e., 5 times/sec (Folkow and Halicka (2)). Third, it has been shown in man that normal muscle blood flow becomes restricted at relatively low contraction levels (Lassen and Kamp (4); Tønnesen (6); and unpublished observations). Fourth, and most important, many measured properties of the electromyogram are directly dependent on the action-potential conduction velocity.

The present investigation concerns the behavior of the muscle action-potential conduction velocity under conditions of restricted blood flow. The results are presented and their relationship with the electromyogram is discussed. Included in the study are experiments indicating the cause for the propagation velocity changes.

METHODS

Four cats with body weights between 3 and 4 kg were used in the study. The animals were anesthetized with cloralose, 40-60 mg/kg body wt, after induction with ether.

The soleus and gastrocnemius muscles were exposed and dissected free from each other and surrounding tissue. The Achilles tendon was cut close to its insertion and split to leave an isolated tendon for each of the two muscles. The proximal insertion points were left intact. All minor blood vessels were ligated, leaving an isolated arterial and venous supply for the two muscles.

For motor nerve stimulation the motor nerve to the soleus and gastrocnemius was dissected free of surrounding tissue and cut 5-6 cm proximal to the muscles. A ring-stimulating electrode was secured approximately 1 cm distal to the cut end of the motor nerve. In all experiments a square voltage pulse was used with a duration of 0.2 msec. The stimulus voltage was kept between 3 and 5 v, which is far below that needed to excite the vasoconstrictor fibers present in the nerve (Folkow and Halicka (2)).

For direct muscle stimulation, paired fine-wire electrodes were inserted on opposite sides of each muscle, and a square voltage pulse, 0.2 msec in duration and 20 v in magnitude, was applied. The electrical activity of the muscle was recorded from concentric monopolar needle electrodes inserted in the body of the muscle approximately parallel to the muscle fibers. The input impedance of the oscilloscope differential amplifier was 10 megohms. Measurements on the conduction times were made from Polaroid photographs taken of the oscilloscope tracce. The recording surface of each electrode was elliptical with a minor diameter of 0.10 mm and a major diameter of 0.50 mm.

The contractile force of each muscle was measured by connecting the isolated tendons to separate strain gauges and recording the output on a Grass polygraph. Great care was taken to secure the femur and lower leg to ensure iso-
metric contraction. The muscle was kept in a slightly pre-stretched state, corresponding to its approximate normal resting length.

Blood flow, in the heparinized preparation, was measured by connecting the venous outflow via the isolated femoral vein to an optical drop recorder unit which in turn was connected to a Grass polygraph. The venous outflow was continuously returned to the animal via the femoral vein of the opposite leg. During the experiments care was taken to insure that the muscle was not ischemic prior to arterial blood flow clamping. Following an ischemic experiment, the muscles were allowed to rest with the arterial and venous supplies unobstructed. The rest periods between experiments varied from a minimum of 25 min to a maximum of several hours. The average resting blood flow prior to arterial clamping was 7 ml/min with a range between 4 and 12 ml/min.

Arterial blood pressure was measured from a small cannulated branch of the isolated femoral artery, giving a direct reading of the perfusion pressure to the two muscles. During dextran perfusion care was taken to keep the effective perfusion pressure of the muscle preparation at “normal” values (i.e., mean arterial pressure at 100 mm Hg).

Prior to the beginning of each experiment, a single control stimulus was delivered to the motor nerve. The resulting action potential was then used as the test reference. Similarly, a single pulse to the muscle body resulted in the control action potential for muscle stimulation. Since the recording surface of the electrode was large enough to span from 3 to 10 fibers, the resulting compound action potential represents the average electrical properties of the sampled muscle fibers. The electrode was inserted parallel to the muscle fibers; therefore the recorded compound action potential could be considered to represent the principle contribution of those fibers nearest the recording surface. (From the geometry of the electrode, and assuming a fiber diameter of approximately 70 μ, the recorded compound action potential probably represents no more than the principle effect of 10 fibers.)

The experimental procedure for the ischemic experiments was initiated by clamping the arterial supply to the two muscles and immediately beginning electrical stimulation of the motor nerve. Two frequencies of stimulation were used, 1 and 50 Hz. At the lower stimulus frequency the period of restricted blood flow lasted from 20 to 25 min. At 50 Hz the ischemic period was 30–60 sec. In both cases photographs of the compound action potential were taken at times to yield from 4 to 8 pictures spaced uniformly throughout the ischemic period. Just before the end of the ischemic period, motor nerve stimulation was stopped, a single muscle stimulus was applied, and the action potential was photographed. After the final muscle stimulus, the arterial clamp was released and single stimuli applied to the nerve and muscle at periods ranging from 30 sec to 5 min duration to record the recovery of the muscle.

The experimental procedure for the dextran perfusion was the same as the ischemic procedure with the addition of dextran to the arterial supply after the arterial blood flow had been clamped. The dextran was infused below the arterial clamp, and the muscles were perfused throughout the experiment. The venous outflow was returned to a separate container to be discarded. In all cases, nitrogen had been bubbled through the dextran solution for at least 15 min prior to its use to remove any free oxygen. The nitrogenated dextran was passed through a water bath to hold the inflowing dextran between 38 and 39 C. Three types of dextran were used in our experiments: pure dextran, perfusate (buffered to around pH 6.6), and a buffered dextran with a pH of approximately 7.4. As the numbers of experiments with each type of dextran were small, little difference could be seen. Therefore, the results for all dextran perfusions were combined under the heading “dextran perfusion.” The dextran used had a molecular weight of 70,000.

The change in conduction velocity was calculated by measuring the time from the initial rise of the stimulus pulse (which triggered the oscilloscope sweep) to a distinct amplitude peak in the compound action potential. The measurements were made at the beginning of the experiments, at the end of the ischemic periods, and at the end of the recovery period (usually about 20–30 min after the end of the ischemic period).

The percent change in conduction velocity was calculated from

\[
\text{percent change} = \left( \frac{v_1 - v_f}{v_1} \right) \times 100
\]

where \( v_1 \) is the initial or recovered conduction velocity and \( v_f \) is the conduction velocity at the end of the ischemic or dextran perfusion period. If the distance between the origin of the muscle action potential and the recording site is assumed to be constant, the above equation can be reduced to

\[
\text{percent change} = \left( 1 - \frac{t_i}{t_f} \right) \times 100
\]

Time \( t_i \) is the initial or recovered time from the stimulus artifact to a distinct peak in the compound action potential. Time \( t_f \) is similarly measured, but at the end of the ischemic or dextran perfusion period.

RESULTS

The results of the experiments are summarized in Table 1 and discussed in detail in the following text.

Conduction Velocity Under Ischemic Conditions

During repeated stimulation of the ischemic muscle, there was consistently found a significant decrease in muscle fiber conduction velocity. The decrease in conduction velocity was found to be greater in the gastrocnemius than in the soleus. As calculated from nerve stimulation, the average decrease in conduction velocity for the gastrocnemius was found to be 34% (number of measurements, \( n = 14 \), and \( \bar{sd} = 6.7\% \)). For the soleus the average decrease in conduction velocity was found to be 21% (\( n = 9 \) and \( \bar{sd} = 7.2\% \)). As calculated from direct muscle stimulation, the average decrease in conduction velocity for the gastrocnemius was 38% (\( n = 6 \) and \( \bar{sd} = 9.8\% \)) and for the soleus was 28% (\( n = 5 \) and \( \bar{sd} = 6.8\% \)).

Figure 1 shows the results of a single ischemic experiment.
and is representative of all experiments performed during ischemic conditions. Figure 1A is the time course of contractile force for the two muscles during a period of ischemia and subsequent recovery period. The Roman numerals on the time axis indicate the times at which the pictures in Fig. 1B were taken. The photographs show the decrease and recovery of the conduction velocity throughout the experiment. The conduction velocity change can clearly be seen by observing either the shifting of the peaks in the compound action potential or the change in spacing between peaks in the same tracing. In Fig. 1C is graphed the change in conduction times as calculated from the oscillograms of Fig. 1B.

After the ischemic stimulation period of the experiment, when the muscles were at rest and the muscle blood flow had been returned, there was noted occasionally a transient
increase in conduction velocity. This transient increase was seen in 4 of the 9 soleus experiments and in 2 of the 14 gastrocnemius tests. The increase in conduction velocity was higher in the soleus than in the gastrocnemius. The velocity increase in the soleus was approximately 10% and in the gastrocnemius approximately 3%.

After return of muscle blood flow, recovery of the conduction velocity in both muscles proceeded at approximately the same rate with the soleus being slightly faster. The average recovery time was between 3 and 4 min; the maximum time was 10 min for a large transient increase in the soleus conduction velocity to decay back to the resting value. The minimum recovery time (1 min) followed a 30-sec ischemic period in which the motor nerve was stimulated at 50 Hz. (During this 30-sec ischemic experiment, the conduction velocity for the soleus decreased by 12% and the gastrocnemius decreased by 31%.)

**Contractile Force During Ischemic Period**

During the course of this investigation, the contractile force was not a variable under study but merely used as an indicator of the relative physical state of the muscle. Therefore, the following presentation will be restricted to general observations.

During low-frequency stimulation (1 Hz), the contractile force fails at approximately the same rate in both red and white muscle. This observation was made by calculating the time for the contractile force to fall to one-half its initial value. The time was approximately 9 min. At the end of the ischemic period the contractile force of the gastrocnemius was roughly 5% of the initial value and of the soleus about 10% of its initial value.

During high-frequency stimulation of the motor nerve (50 Hz), the gastrocnemius fails much faster than the soleus. The contractile force of the gastrocnemius is about 5% of its initial value at the end of 30 seconds. During the same time, the soleus begins to show a force decay after 25 sec and is at about 90% of its initial value after 30 sec of stimulation. If the stimulation is continued for an additional 30 sec, the gastrocnemius force decays to about 3% of its initial value (i.e., falls an additional 2%), while the soleus falls to about 20% of its initial value.

Recovery of the soleus contractile force proceeds much faster than that of the gastrocnemius. Following cessation of stimulation and return of muscle blood flow, the soleus fully recovers in about 5 min while the recovery of the gastrocnemius takes 10–15 times longer.

**Conduction Velocity During Dextran Perfusion**

During repeated stimulation of the dextran perfused muscle, only slight changes in the muscle conduction velocity were noted on the average. As measured from nerve stimulation, the conduction velocity of the gastrocnemius decreased on the average by 11% (n = 7 and SD = 16.7%). For the soleus there was an increase in conduction velocity. The average value of the increase was 6% (n = 7 and SD = 11.6%). As calculated from direct muscle stimulation, the average decrease in conduction velocity for the gastrocnemius was 12% (n = 6 and SD = 13%). For the soleus the conduction velocity was found to increase by an average value of 4% (n = 4 and SD = 15%).

**DISCUSSION**

In the opinion of the authors, the present experiments show that there is a decrease in action-potential conduction velocity during repetitive firing of an ischemic muscle. The change is more pronounced in white muscle than in red muscle.

It may be argued that the results of these experiments could be attributed to a dropout of certain muscle fibers, but this explanation is unacceptable for the following reasons:

1) The recorded compound action potential represents the summed response of several individual action potentials. Slight differences in phase between the individual action potentials will cause a smoothing in the peaks of the summed response. Therefore, if fibers were to drop out, one would expect the peaks to become sharper rather than rounder or smoother. Figure 1B clearly demonstrates that the peaks do not sharpen but broaden.

2) If dropout of muscle fibers were to occur, one would expect to see discrete changes in the compound action potential during the experiment. All changes noted in action-potential shape during the course of an experiment were of a continuous nature.

---

**TABLE 1. Experimental results**

<table>
<thead>
<tr>
<th>State of Muscle Circulation and Period</th>
<th>Stimulus Frequency, Hz</th>
<th>Percent Conduction Velocity Change</th>
<th>Approximate Recovery Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Gastrocnemius</td>
<td>Soleus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nerve Stim</td>
<td>Muscle Stim</td>
</tr>
<tr>
<td>Ischemic, 20 25 min</td>
<td>50</td>
<td>22</td>
<td>6.8</td>
</tr>
<tr>
<td>Ischemic, 30 sec</td>
<td>50</td>
<td>22</td>
<td>6.8</td>
</tr>
<tr>
<td>Ischemic, 60 sec</td>
<td>50</td>
<td>22</td>
<td>6.8</td>
</tr>
<tr>
<td>Dextran perfusion, 20–25 min</td>
<td>50</td>
<td>22</td>
<td>6.8</td>
</tr>
</tbody>
</table>

$\Delta V =$ the averaged change in conduction velocity; $S =$ the SD of the averaged data; $X =$ no data taken on that parameter; and a blank indicates the parameter could not be calculated, because there was only one value of data taken.
The only distinct change consistently occurring in the recorded signal during these experiments was a shifting and spreading of the action potential on the time axis. The shifting was continuous and so pronounced in some cases that positive peaks shifted to the previous location of a negative peak without changing the basic shape of the recorded signal. This type of shifting is clearly seen by comparing the soleus action potentials in the photographs of I or II with IV in Fig. 1B.

A change in action-potential conduction velocity will result in an increase in the duration of the recorded action potential. (The length of time a potential change is detected at a stationary position depends inversely upon the velocity with which the potential change is traveling.) If the muscle activity is recorded as in standard electromyography, a change in the action-potential duration results in a shift in the frequency spectrum (Cenkovich and Gersten (1)). If one assumes a constant pulse rate (which is quite reasonable at a maximal isometric contraction) during a period of increasing action-potential duration, the overall effect would be a shifting of the high-frequency end of the spectrum to the lower frequencies and an increase in the energy in the low-frequency end of the spectrum.

During a maximal isometric contraction, the blood flow in normal muscles is restricted, and in the human biceps blood flow is completely blocked (unpublished observations).

Arranging the above facts in a sequential manner, one would expect to find the following changes during a maximal isometric contraction: 1) restriction in muscle blood flow producing ischemia; 2) under repeated contraction the ischemic muscle fibers show a decay in conduction velocity; 3) the decrease in conduction velocity appears as an increase in action-potential duration, and 4) the increased duration results in a shifting of the EMG frequency spectrum toward the lower end, plus an increase in the low-frequency energy.

The alterations in the EMG spectrum just described quite accurately depict the end results obtained by Kadefors, Kaiser, and Petersén (3) in their experiments with the maximally contracted biceps. In their experiments the subject voluntarily contracted the biceps muscle to its maximum strength for 30 sec. Therefore, as far as the muscle blood flow is concerned and if one assumes a firing rate of 50 Hz in the maximally contracted muscle, their experimental conditions in man and ours in animal are quite similar. In their article, Kadefors et al. calculated the change in action-potential duration which would yield the shift in spectrum they noted. By one method of calculation they found the duration to shift from 3.2 to 5.0 msc. Since the duration is inversely related to the velocity, one can take the reciprocal of these values and find the relative change in conduction velocity. This procedure yields an expected decrement in conduction velocity of 36%. Using the values from their locus diagram, they found the initial and final durations to be 11 and 16 msc, respectively. These numbers yield an expected velocity decrease of 32%. By either calculation the change in conduction velocity quite closely approximates the changes we have found of 34-38% for the gastrocnemius and are close to the 21-28% found for the soleus.

In our calculation of conduction velocity change, we have used two different methods of stimulation. The values found through direct muscle stimulation are slightly higher than those found through motor nerve stimulation. The cause for this appears to be due to changes in the synaptic conduction time, a subject for a later paper.

The period of restricted blood flow varied from 30 sec to 20 min. In the shorter periods, 30 sec and 1 min, a stimulation rate of 50 Hz was used. During the longer periods, averaging 20 min, the muscle was stimulated at 1 Hz. In the high-frequency stimulation experiments the muscle fibers would contract 1,500 times for each 30 sec, and at the lower rate the muscle fibers would contract an average of 1,200 times during the experiments. Therefore, as far as the blood flow and the number of repeated contractions during the ischemic period are concerned, the two experiments are quite similar. This is borne out in terms of the changes in conduction velocity.

Using the same experimental procedure as in the ischemic muscle experiments but continuously perfusing the muscles with a nitrogenated dextran solution produced a significantly smaller change in the action-potential conduction velocity. During dextran perfusion, the decrease in conduction velocity was 11% for the gastrocnemius as measured by nerve stimulation. This is opposed to the 34% decrease with the perfusion. Measured by direct muscle stimulation, with and without the dextran perfusion, the values found were 12 and 38% decreases in conduction velocity, respectively.

In the soleus muscle during dextran perfusion there was found a 6% increase in conduction velocity as opposed to the 21% decrease without perfusion. The changes in conduction velocity as measured by direct muscle stimulation in the soleus were a 4% increase with dextran perfusion and a 28% decrease without perfusion.

To make a qualitative judgment on the differences between the mean values of the conduction velocity changes for the ischemic and dextran perfusion experiments, a t test was employed. The true variance for each group of data was assumed unknown and unequal to the group of data it was being compared with. In Table 2 are shown the data and the results of the calculations. The significant point to note is that the calculated t is, in all cases, larger than $t_{0.05,3}$.

### Table 2. Tabulation of data for statistical comparisons

<table>
<thead>
<tr>
<th></th>
<th>Ischemic</th>
<th>Dextran Perfused</th>
<th>Calculated $t$</th>
<th>$t_{0.05,3}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Change in Conduction Velocity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nerve Stimulation</td>
<td>$-34$</td>
<td>$6.7$</td>
<td>$14$</td>
<td>$-11$</td>
</tr>
<tr>
<td>Soleus</td>
<td>$-21$</td>
<td>$7.2$</td>
<td>$9$</td>
<td>$+6$</td>
</tr>
<tr>
<td><strong>Muscle Stimulation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrocnemius</td>
<td>$38$</td>
<td>$9.8$</td>
<td>$6$</td>
<td>$12$</td>
</tr>
<tr>
<td>Soleus</td>
<td>$-28$</td>
<td>$6.8$</td>
<td>$5$</td>
<td>$+4$</td>
</tr>
</tbody>
</table>

$\Delta V$ is the mean of the population, $\sigma = standard deviation$, and $n = size of the population.$ The quantities $t$ and $v$ are calculated from the data, and $t_{0.05,3}$ is found in standard tables containing the Student $t$ distribution.
which indicates that the means of the two compared populations are statistically different at a 99.5% significance level.

In light of the significant difference in conduction velocity changes with and without dextran perfusion, one must conclude that the cause for the velocity decrease in the ischemic muscle is its inability to remove the chemical by-products of contraction. It is strongly suspected that the important substance to be removed is lactic acid.

Transient increases in conduction velocity were seen in about 25% of the experiments. The increase in conduction velocity only occurred during the recovery period following an ischemic contraction or during the dextran perfusion period. The implication is that the dextran perfusion or increased blood flow is possibly removing something from the muscle tissue beyond its natural concentration. In this case, the substance could again be lactic acid.

The transient increase results in a shorter recorded action-potential duration. This, in turn, is seen in the EMG frequency spectrum as a transient increase in the high-frequency energy. These transient increases in the high-frequency portion of the spectrum have been observed during the recovery period following a maximal isometric contraction (Kadefors, Kaiser, and Petersén (3) and unpublished data).

In conclusion: 1) repeated stimulation of ischemic red and white muscles results in a continuous delay of the action-potential propagation velocity. The decrease in conduction velocity is more pronounced in the gastrocnemius than in the soleus. Under our experimental conditions the average decrease for the gastrocnemius was 38% and for the soleus 28%. In the gross EMG this decay in propagation velocity appears as a general shift in the frequency spectrum toward the lower frequencies plus an increase in low-frequency energy.

2) During the low-frequency stimulation experiments (1 Hz), the contractile force of the ischemic muscles fails at about the same rate in both red and white muscles. However, during high-frequency stimulation (50 Hz) the white muscle fails much sooner than the red muscle.

3) During the recovery period (return of natural blood to the muscle) there was occasionally noted a transient increase in conduction velocity. The transient change was seen in 4 of 9 experiments with the soleus and in 2 of 14 experiments with the gastrocnemius. The increase was more pronounced in the soleus than in the gastrocnemius. In the gross EMG this is seen as a general shift in the frequency spectrum toward the higher frequencies.

4) Recovery of the conduction velocity to its normal resting value proceeds at approximately the same rate in both red and white muscle, following the return of natural blood flow. The average time is between 3 and 4 min.

5) There appeared to be no correlation between conduction velocity recovery time and contractile force recovery time in the gastrocnemius. Upon return of the muscle blood flow, the contractile force of the soleus recovered much faster (approximately 5 min) than that of the gastrocnemius. The average recovering time for the gastrocnemius was 10-15 times longer.

6) Prolonged stimulation of a dextran-perfused muscle resulted in a significantly smaller change in conduction velocity as compared to the ischemic experiment. During ischemia the conduction velocity decrease in the gastrocnemius was 3 times greater than during dextran perfusion. In the soleus the conduction velocity increased slightly during the dextran perfusion as opposed to the 28% decrease during ischemia.

7) Under our experimental conditions the maintenance of normal conduction velocity is dependent on the blood flow for removal of metabolic by-products and not for an energy supply. This conclusion is based on the striking difference observed with dextran perfusion and the lack of correlation between conduction velocity recovery and contractile force recovery times.

It is suggested that the metabolic by-product causing velocity changes is lactic acid.

The authors express their most sincere gratitude to Professor Björn Folkow, Department of Physiology, University of Göteborg, for the very generous use of his facilities. We are indebted to Mrs. Margareta Hallbäck, also of the Department of Physiology, for her invaluable assistance throughout the course of this investigation.

This investigation was supported by grants from the Swedish Council for Applied Research and the Swedish Medical Research Council.

Present address of J. T. Mortimer: Dept. of Biomedical Engineering, Case Western Reserve University, Cleveland, Ohio 44106.

Received for publication 20 October 1969.

REFERENCES


