PERIPHERAL BLOCK OF MOTOR ACTIVITY

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Summary

It has been shown that an artificially induced muscle contraction can be blocked by rapid repetitive stimulation of the motor fibers. Muscle relaxation is essentially instantaneous following the application of the blocking signal. Block can be maintained for at least twenty minutes without apparent damage to the nerve. Recovery following block takes place within seconds. It is thought that the mechanism for this phenomenon is depletion of acetylcholine at the neuromuscular junction. Data is presented to justify this conclusion.

Introduction

Spacticity is one of the most debilitating effects of stroke and spinal cord injury. It places a severe limitation on the functional use of an extremity, and even in non-functional extremities it contributes to contractures and painful joints. Standard orthopedic approaches to correct this problem are neurectomies, myotomies, and tenotomies: all of which are destructive and irreversible following surgery. An alternate solution could be inhibition of undesirable motor activity through the application of appropriate electrical signals to the motor nerve.

Considerable work has been done that indicates the feasibility of blocking a peripheral nerve with electrical signals. Tanner /1/ demonstrated selective block of nerve fibers in an isolated frog sciatic nerve with a 20KHz signal from an audio oscillator. As the signal amplitude was gradually increased, block occurred first in the larger fibers and then finally in the smaller fibers in the nerve bundle. He showed this effect to be completely reversible, and hypothesized that it was due to local depolarization of nerve membrane. Woo and Campbell /2/ duplicated these results and also found similar results with the intact tibial nerve in cats (see Figure 1). Similar results have also been obtained in cats by Pudenz (personal communication) using constant-current

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pulse trains at repetition rates in excess of 1000 pps. Mendell and Wall /3/ used direct current to selectively block the large afferent fibers of the sural nerve of a decerebrate cat. In all of the above work, block was inferred by observing the abolition of peaks in the compound action potential.

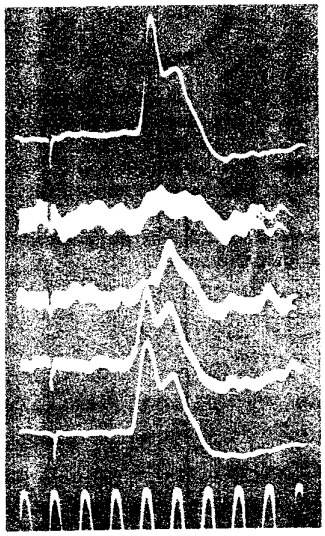

Fig. 1. Effects of 20 kc alternating current on tibial nerve conduction as shown on compound action potential of L_7 dorsal rootlet. Lowermost trace shows potential before AC is applied. The next three traces show successively higher AC voltage. The top trace is with the AC voltage shut off. Time in msec. Reproduced from Woo and Campbell /2/.

On the basis of the work cited above, studies were initiated at Rancho Los Amigos Hospital to determine the feasibility of relaxing a contracting muscle by applying an electrical signal to the innervating nerve. This paper is report on the initial phases of our work which shows that motor activity can be substantially decreased over a wide range of electrical pulse trains. A possible mechanism to explain this phenomenon is presented.

Procedure

Experiments were carried out on 10 cats. The animals were anesthetized with a pentabarbitol-sodium (Nembutol) injection I.P. and level of anesthesia maintained throughout the procedure via a catheter to the left femoral vein. An 8 cm incision was made over the fold between the semitendinosus and biceps femoris muscles, the muscles separated, and the sciatic nerve exposed. Fascia

tissue was carefully removed around the nerve in a 1 cm long section 1-2 cm distal to the muscular branch of the sciatic. The stimulating electrode was then wrapped loosely around the nerve and the flaps of the electrode sutured closed. An identical electrode serving as the blocking electrode was similarly wrapped around the sciatic 2-3 cm distal to the stimulating electrode. Each electrode consisted of two braided platinum bands 3 mm apart imbedded in a flap of dacron impregnated silastic 8 mm wide and 30 mm long. The arrangement of the electrodes on the nerve are shown in Figure 2. In certain experiments compound action potentials were recorded from the nerve 2-3 cm distal to the blocking electrode by piercing the bundle with a pair of bared teflon coated 3 mm stainless steel wires 1 cm apart. The nerve and recording electrodes were then encapsulated with silastic 385 elastomer to reduce the recording of unwanted blocking signal and muscle EMG artifact. The common peroneal, and caudal cutaneous sural branches were cut leaving only the tibial nerve intact. All electrode leads were brought out of the wound and the incision sutured closed. The calcaneus bone was cut just below the insertion of the calcaneal tendon, a hole drilled through the femur just above the knee, and a pin inserted to hold the preparation firm during stimulation. Finally the calconeal tendon was attached to a strain gage bridge network built in our lab. EMG recordings were obtained using a pair of 2 mil teflon coated stainless wires bared at the tip and inserted into the gastrocnemius using a 25 gage needle. The experimental set-up is shown in Figure 3.

Tests were divided into short- and long-duration blocks. In each case, the stimulus was turned on one second before the blocking signal was applied and left on for one second after the blocking signal was turned off. For the short-duration blocks, the duration of block was one second. Long-duration blocks varied from several seconds to as much as twenty minutes. Sufficient time was allowed between runs to allow the muscle to recover from the previous run.

The stimulus parameters were 100 microsecond pulse duration and an 80 pps repetition rate, with the amplitude adjusted for supramaximal stimulation. A Grass S4 stimulator with a Grass SIU-5 isolation unit was used to supply the stimulus. The blocking signal was supplied by a battery-powered constant voltage pulse gen-

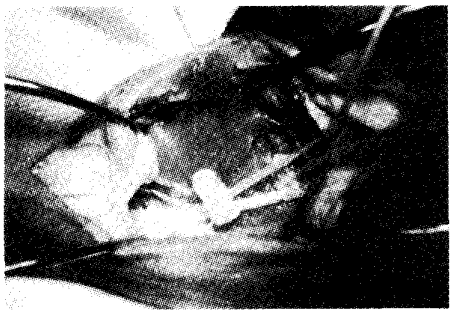

Fig. 2. Nerve-electrode preparation showing the proximal stimulating electrode at the right and the distal blocking electrode to the left wrapped around the sciatic nerve.

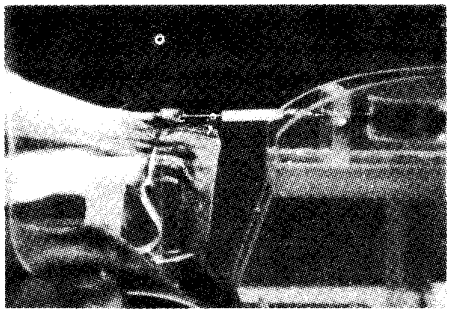

Fig. 3. Cat is shown with the calconeal tendon attached to the strain gage. A pin is placed through the femur to support the preparation.

erator built in our laboratory with variable pulse amplitude (0-10V), duration (10-1000 s) and repetition rate (10-20,000 pps).

Results

A typical short-duration block is shown in Figure 4. After the stimulus is turned on, force quickly rises to a maximal value designated by F_m. The blocking signal is turned on one second later and force rapidly drops off. Typically there will be a non-zero level of force throughout the one-second blocking interval. This force is referred to as the residual force F_r and is defined to be the measured force at the end of the blocking interval (t = 2 sec.). Following block, force again increased due to the

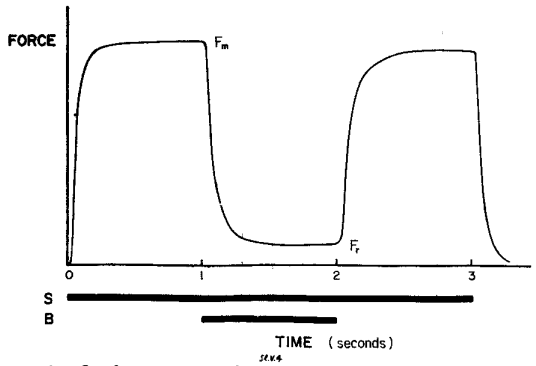

Fig. 4. Typical three second run showing force resulting from initiation of stimulus S and reduction of force after initiation of the blocking signal B. Force returns when block is removed

stimulus which has been on throughout the test. After the stimulus is terminated, the muscle relaxes and force returns to zero.

The effectiveness of the blocking signal depends upon the parameters of the pulse train applied through the blocking electrode. To quantitate the relationship between block and the waveform parameters of the blocking signal, a parameter called the blocking effectiveness B.E. has been defined as Blocking effect-

$$B.E. = \frac{F_m - F_r}{F_m} \times 100$$

iveness is therefore defined as a percentage where B.E. = 100% indicates complete block with no residual force.

Blocking effectiveness is plotted in Figure 5 showing the relationship to the waveform parameters. Note that B.E. is plotted versus V/V_m where V_m is the least voltage required to produce a maximal contraction at a repetition rate of 80 pps. V_m, which will be referred to as the maximal voltage, is therefore a function of pulse duration. Data are ploted for nine combinations of pulse durations and repetition rates covering the range from 25 - 250 s and 1k - 10k pps. As shown in the figure, block is first seen at approximately the maximal voltage for each pulse duration. As voltage is increased, B.E. improves rapidly reaching a maximum value at about three times maximal voltage. In this case, the avarage maximum block was about 94%. Results were equally good for all four repetition rates. In three of the cases, blocking was not as effective at higher voltages: B.E. peaked at $3V/V_m$ and then dropped off at a higher voltage.

Block was also observed at lower repetition rates. Blocking effectiveness is plotted in Figure 6 for four repetition rates, all at a pulse duration od 50 microseconds. The most effective rate was 600 pps with the blocking effectiveness dropping off below 600 pps and even dropping off slightly at 800 pps. At a rate of 600 pps, the results are comparable with those obtained at rates in the range of 1k - 10k pps.

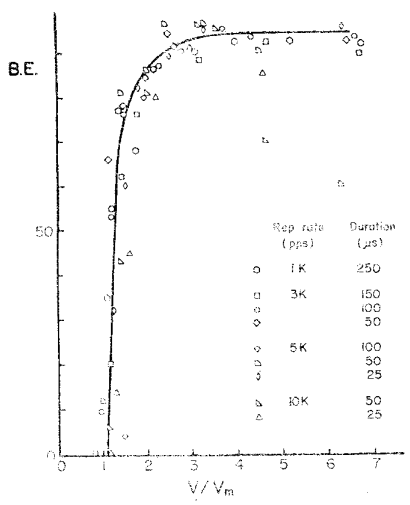

Fig. 5. Blocking effectiveness at high repetition rates is shown as a function of the ratio of applied blocking voltage to the maximal voltage. Nine combinations of repetition rates and pulse duration are plotted.

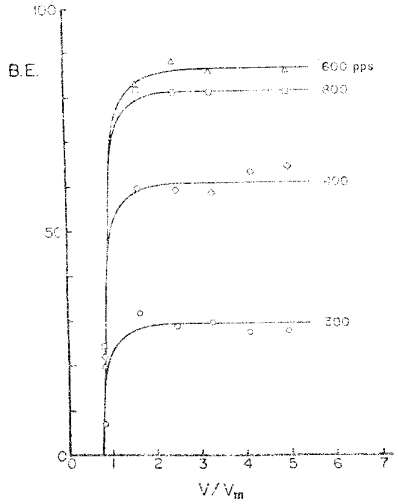

Fig. 6. Blocking effectiveness at low repetition rates is shown as a function of the ratio of applied blocking voltage to maximal voltage. Four frequencies all at a pulse duration of 50 μsec are plotted.

The rate of force fall-off following the onset of block is also a function of repetition rate as shown in Figure 7. The rate of force fall-off increases rapidly as rate is increased from 300 to 600 pps. It has also been shown that the rate of force fall-off is the same at higher repetition rates as it is at 600 pps. Furthermore, the rate of force fall-off following the onset of block is comparable with the relaxation rate of a contracted muscle when B.E. is greater than 80% which indicates that there is very little delay in the blocking effect.

Recovery following block has not been studied in detail, but it can be said that the rate of increase of force following the termination of block is slower than it is following stimulus initiation. If the 90% rise time is defined to be the time required for the force to attain 90% of its maximum value, then typical 90% rise times for the two cases would be 135 ms following stimulus initiation and 230 ms following the termination of block. The maximal force attained after block is sometimes less than that before block, but it is almost always within 80% of the maximum value before block.

It has also been shown that block can be maintained for as long as twenty minutes. (While twenty minutes has been the maximum duration attempted, there was no indication that the block

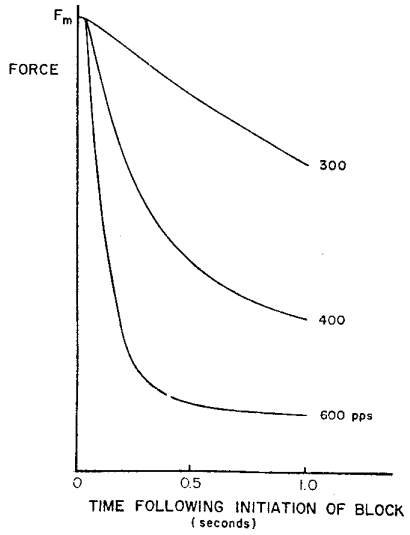

Fig. 7. Force fall-off after initiation of blocking signal for three frequencies. Note: Identical fall times were recorded at high frequencies (1k-10k pps) as that shown for 600 pps.

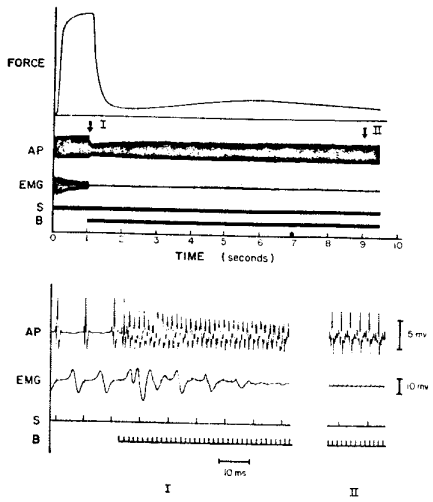

Fig. 8. a) The first 10 seconds of a 20 minute run of constant block showing the force, compound action potential AP, gastrocnemius EMG activity, stimulating signal S and blocking signal B at repetition rate of 600 pps. b) Part I shows extended time scale during initiation of blocking signal. Part II shows extended time scale eight seconds after initiation of block. Note compound action potential frequency change from 600 pps in Part I to 300 pps in Part II.

could not have been maintained for a longer period of time). The initial ten seconds of one long-duration run is shown in Figure 8. In this case, the repetition rate of the blocking signal was 600 pps. Throughout block, the residual force was less than twelve percent. The increase in residual force during the first few seconds of block is typical of all long-duration blocks. In this case, the residual force peaked about five seconds following the initiation of block and then began to decrease. While not

shown in the figure, the residual force continued to decrease reaching zero after seven minutes and remained at zero throughout the remainder of the twenty-minute block. It appears that the time to the peak in the residual force may be related to the voltage level of the blocking signal; i.e., the greater the voltage, the earlier in time the peak occurs. Complete recovery of normal nerve conduction, even after the long-duration blocks, occurs within six seconds after the termination of block.

There has been no indication of nerve damage; at all times, the nerve has continued to conduct following block. Fibrillation studies have been performed on three cats by an electromyologist eight days after long-duration blocks. He concluded that there was no damage due to the blocking currents. In each of the three cats, "worst case" blocking conditions were used: 50% duty cycle at amplitudes of ten times threshold.

Also shown in Figure 8 are compound action potentials recorded from the nerve distal to the blocking electrode and myoelectric signals recorded from wires imbedded in the gastrocnemius muscle. Both are shown with an expanded time scale at the initiation of block (I) and eight seconds after initiation (II). There is considerable activity in the nerve during block even though force and myoelectric activity drop off. It is interesting to note the change in the character of the compound action potential eight seconds later as compared with immediately following block. Right after block, the potential is synchronous with each pulse; whereas, it is synchronized with every other pulse at eight seconds. Myoelectric activity falls off rapidly following the initiation of block and is not even apparent after eight seconds. At this time, there is still a non-zero force. The total absence of myoelectric activity in the gastrocnemius may imply that the residual force is due to the soleus or plantaris.

Discussion

It is convenient to separate the discussion of block of motor activity into those at repetition rates greater than 1000 pps and those below 1000 pps. It is quite clear that the cause of block at rates below 1000 pps is not due to cessation of nerve conduction. The compound action potentials recorded during block in Figure 8 clearly show that the nerve fibers are conducting at a

very rapid rate while, at the same time, the force and the myoelectric activity are very small.

It is our opinion that the decrease in motor activity with blocking rates below 1000 pps is due to a failure in transmission at the neuromuscular junction. This phenomenon initially reported by Wedensky /4/ has been studied recently by numerous investigators. Independent work by Otsuka, et al. /5/ and Brooks and Thies /6/ showed that failure occurs because of a rapid diminution in the amount of acelytcholine ACh released per pulse at the motor nerve endings. Similar results were reported by Elmquist and Quastel /7/ who went on to show that during repetitive stimulation, there is a rapid decline in ACh release per impulse followed by a plateau which diminishes slowly with time. At 47 pps, this plateau which is about one-third of the initial value, is reached after approximately 100 ms or five pulses. They explained their findings on the basis of a two compartment model of presynaptic transmitter storage and release which is similar to one originally proposed by Birks and MacIntosh /8/. On the basis of these reports, it is certainly plausible to assume that the rapid decline in force during block at rates of 300 - 600 pps can be attributed to depletion of ACh at the junction.

The results shown in Figure 7 are consistent with the concept of ACh depletion. The rate of depletion would certainly be affected by the avarage firing rate in the fibers. The faster fall-off at 600 pps can be attributed to a more rapid depletion of ACh at the neuromuscular junction.

It is also possible to explain the transient rise in force during long-duration blocks on this basis (Refer to Figure 8). While it is difficult to draw conclusions from the compound action potential, it does appear on gross examination of the recordings that the avarage firing rate drops from an initial rate of 600 pps to 300 pps eight seconds after block. The rise in force may be a result of this shift in the firing rate. If it is assumed that the 300 pps firing rate is maintained, then the decline following the rise would be expected due to the continuous depletion of available ACh.

The mechanism producing block at blocking rates greater than 1000 pps is not as clear because of the difficulty in interpreting the compound action potential during block. At these rates,

the recordings from the nerve are similar to those shown in Figure 1. It is certainly clear that the compound action potential due to the stimulus does disappear. Tanner /1/ postulated that a segment of the nerve in the region of the blocking electrode was rendered incapable of conducting action-potentials and implicitly assumed the blocking signal did not introduce firing of the nerve fibers. The similarity of the blocking results above 1000 pps in our study with those at 600 pps when the fibers are firing very rapidly, raises the question of whether there is really a different mechanism operating in the two cases.

Investigations by Woo and Campbell /2/ lend support to the theory that the mechanism of motor activity block is ACh depletion at rates greater than 1000 pps as well as below. They showed that during block, using a 20 kHz sinusoidal current, the individual fibers are firing rapidly but asynchronously due to the blocking signal. They did this by measuring action potentials from individual fibers during block. They found that even though the compound actionpotential was abolished, individual fibers were conducting pulses at rates up to 500 pps. Some of their results are shown in Figure 9. Note that the rate of firing increases as the amplitude of the blocking signal is increased, however, they did reach a point where conduction ceased; i.e., the stimulus was truly blocked and no action potentials were induced in the nerve as suggested by Tanner /1/. Casey and Blick /9/ have also shown that the compound action potential is not a reliable indi-

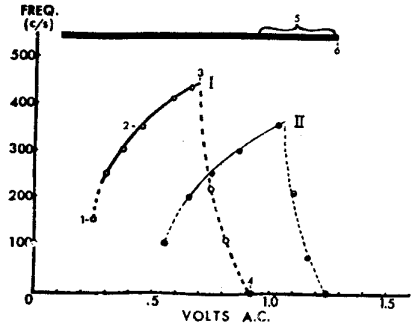

Fig. 9. Graph showing relationship of avarage frequency of firing for two fibers during block of compound action potential with 20 kHz sinusiodal current. Solid lines, rhythmic firing; broken line, arhythmic firing. Reproduced from Woo and Campbell /2/.

cator of nerve activity; i.e., fibers may still be firing even though the compound action potential has been abolished.

Extension of these results to blocking signals of the type used in our studies have been obtained by computer simulation of the Hodgkin-Huxley differential equations describing nerve conduction. The input to the simulated system has been a train of current pulses at various repetition rates. Output data yield results very similar to those shown in Figure 9. This work will be reported at a future time.

Conclusion

It has been shown that peripheral block of motor activity can be accomplished without damage to the nerve by applying a train of current pulses to the nerve over a wide range of repetition rates. Results of investigations by other authors as well as our own data supporting the hypothesis that muscle relaxation is due to inducement by the blocking signal of firing rates in the motor fibers far in excess of normal physiological rates which results in rapid fatigue. It is proposed that fatigue occurs because of ACh depletion at the neuromuscular junction. Pure nerve block may occur at voltage levels five to six times the maximal voltage as reported by Woo and Campbell /2/. Further work is currently underway in our laboratory to clarify the basic mechanism of block and the results of these investigations will be published in the near future. It is felt that these investigations will not only lead to a better understanding of how to block motor activity, but also will provide insight into the cause of fatigue during functional neuromuscular stimulation. In addition, a series of patient studies are currently underway to determine if similar blocking phenomena as described in this study are repeatable in humans.

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