

# Selective nerve stimulation in an acute rabbit model

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## Abstract

*Artificial muscle activation by electrical stimulation of motor nerves is characterized by poor force gradation and a relative fast onset of muscle fatigue. Force gradation would improve and the onset of fatigue would be delayed by primarily activating the small-diameter motoneurons. In this study the effects of selective small fiber activation stimulation was investigated in an acute rabbit model. Acute animal experiments were conducted using an isometric setup of medial gastrocnemius. The muscle was activated through a tripolar cuff electrode placed on the tibial nerve. Selective small fiber activation was obtained using selective anodal blocking. The study shows that orderly recruitment can be obtained in the rabbit. However the nerve responses to stimulation are different from what has been described in cat and dog. Break excitation occurs at relative low currents and can only be prevented by extending the pulse with a relative long gradual decay.*

## 1. Introduction

Electrical stimulation of motor nerves to activate muscles is used to restore function in patients with an upper motoneuron lesion. However the performance of this concept is rather limited. One of the problems is the inverse recruitment order of motor units compared to physiological recruitment. In physiological muscle contraction the recruitment order is in the order of increasing size, but electrical stimulation recruits large motor units before small motor units (inverse recruitment). Inverse recruitment leads to a relative fast onset of muscle fatigue and poor force gradation [1]. The onset of muscle fatigue should be delayed and force gradation should improve by primarily activating small motoneurons. Selective small fiber activation finds also application in the control of bladder and bowel [2]. Bladder emptying induced by electrical stimulation of the ventral sacral nerve roots to activate the urinary bladder is hindered by simultaneous activation of the urethral closure mechanism. Since the bladder is activated by small diameter nerve fibers and the external urethral sphincter is innervated by larger ones, selective small fiber activation would result in selective bladder activation and would improve bladder emptying. The same applies for bowel emptying where sacral root stimulation lead to activation of both the rectum and the external anal sphincter. At least 3 different methods are known that allow for selective small fiber activation: selective anodal blocking, high frequency stimulation

and slowly rising pulses [2]. The goal of this study was to investigate whether selective small fibre activation could be obtained in a rabbit model using the 3 different stimulation methods.

## 2. Methods

Acute experiments were conducted on anaesthetized rabbits (adults, New Zealand White, weight: 3-5 kg). Anaesthesia was introduced by intramuscular injection of Dormicum® (0.4 ml/kg) and was maintained by intramuscular injection of both 0.1 ml Dormicum® and 0.3 ml Hypnorm® every 20 minutes. The sciatic nerve and its peroneal and tibial branches were exposed. A tripolar cuff electrode (inner diameter: 1.6 mm, contact separation 3mm, contact width 0.5 mm) was placed on the tibial nerve while the sural nerve was cut.

The triceps sura were fully exposed and the nerve branches to the soleus, the lateral gastrocnemius as well as all other branches of the tibial nerve were cut, leaving only the innervation of the medial gastrocnemius (MG) intact. The calcaneal bone was cut and the Achilles tendon was freed from the underlying tissue. All tendons contributing to the Achilles tendon were cut except the one from the MG. The Achilles tendon, still attached to a piece of calcaneal bone, was wrapped around a kevlar thread which was hooked on a force transducer. The femur was clamped and positioned in a rigid frame such that the muscle was aligned with the force transducer. The exposed muscle was kept at a temperature of about 36 °C using a heating lamp and was kept moist with warm saline.

EMG was recorded using two wire electrode inserted into the muscle. The EMG-signal was amplified, filtered and sampled at 5 kHz.

A force transducer was firmly mounted on a 'crank'-operated micro slide. This allowed to set the muscle length. The force signal was amplified, lowpass filtered and sampled at 2 kHz.

The electrode was connected to a custom made computer controlled stimulator consisting of two synchronised current sources. The electrode had a central cathode, flanked by two anodes so that the cathodal current equalled the sum of the two anodal currents. Any arbitrary pulse shape could be generated but only mono- and biphasic square pulses plus monophasic square pulses with a gradual decay have been used in this study. The muscle length was set, before each recruitment curve, to a length which produced the maximum twitch force in response to a suprathreshold stimulus pulse.

Series of single pulses with varying amplitude and pulse duration have been applied to induce muscle twitch contraction. Five successive twitches were used to obtain an average twitch at each pulse amplitude.

### 3. Results

#### High frequency stimulation

##### Slowly rising pulses

No selective stimulation could be demonstrated using slowly rising pulses. The goal was to raise the threshold of the largest fibers above the threshold of the smaller fibers by applying a subthreshold stimulation pulse or prepulse. Various subthreshold levels (80%, 85%, 90%, 95%) and pulse durations (400  $\mu$ s, 600  $\mu$ s, 800  $\mu$ s)\_\_\_\_\_

##### Selective anodal blocking

Selective activation of the small diameter nerve fibers could be obtained by a combination of excitation and selective anodal blocking. The different responses to stimulation are most easy to interpret by analysing the EMG-response of the activated muscle. A typical set of EMG traces is shown in Fig.1. The first few traces (0.05, 0.07 and 0.29 mA) show the response to a monophasic 1.2 ms wide square pulse. It shows an increasing EMG amplitude with increasing stimulus amplitude as more motorunits are recruited. At 0.30 mA a third phase emerges in the EMG which is even more pronounced at 0.35 mA.

This can be attributed to anodal break excitation. Stimulation now leads to 2 action potentials, one at the onset of the 1200 ms pulse and one at the onset. The effect of the 2 action potentials was also visible in the force signal which suddenly jumped to double the peakforce due to this doublet activation.

To confirm that the 3rd phase was caused by anodal break excitation the pulse has been extended with a gradual decay of 3 ms. This prevented the break excitation (0.35 mA\*). The next trace is the response to a 1.90 mA, 1.2 ms square pulse. The break excitation is still present but the primary response is a little reduced as the largest fibers are blocked. Increasing the the amplitude to 3 and 4.03 mA causes the EMG response to shift to the right. This is because most of the fibers will be blocked by the anodal current but break excitation occurs at the end of the pulse.

To confirm that break excitation occurs at the end of the pulse, the pulse duration has been increase from 1.2 ms to 2.0 ms (**a**) and 2.5 ms (**b**). It can be seen that the delay of

the EMG response increases with increasing pulse duration indicating that the break excitation occurs at the end of the pulse.

Trace **d** is the response to 4.03 mA, 1.2 ms pulse duration plus a 2 ms gradual decay. The break response is nearly eliminated but not completely. Complete elimination can only be obtained with a gradual decay of 3 ms (**e**). Trace **f-l** show responses with to pulses with

a decreasing pulse duration (**f**: 800  $\mu$ s; **g**: 500  $\mu$ s; **h**:  $\mu$ s; **i**: 400  $\mu$ s; **j**: 300  $\mu$ s; **k**: 200  $\mu$ s; **l**: 250  $\mu$ s). The EMG-response stays flat until a pulse duration below 300  $\mu$ s is used. At a pulse duration of 250  $\mu$ s a small response can be seen. This response is larger at 200  $\mu$ s.

### 4. Discussion and Conclusions

In contrast to other studies [4] no selective activation of small nerve fibers could be demonstrated in this study when using high frequency stimulation and slowly rising pulses. The main difference between this study and the others is that in this study a rabbit model has been used while a cat model has been used in the other. Perhaps the nerve membrane kinetics differ between cat and rabbit.

Selective small fiber activation could be obtained using a combination of excitation and selective anodal blocking. This could successfully be used to obtain orderly recruitment of the MG-muscle. However the nerve responses to stimulation are different from what has been described in cat, dog and human. In comparable experiments using cat and dog, anodal blocking always occurred at a lower current amplitude than break excitation.

In addition, break excitation could be prevented in cat and dog using a gradual decay of 300-600  $\mu$ s. In the rabbit, typically a gradual decay of 3 ms is needed to prevent break excitation. This finding is another indication that the nerve membrane kinetics of rabbit differ from those of cat and dog.

### References

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