Diameter selective nerve fiber stimulation in the vagal nerve using anodal block, depolarising prepulses and long exponentially rising pulses

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Abstract

Depolarising prepulses and exponentially rising pulses are techniques for selective fiber activation, which have been demonstrated only in simulation studies. This experimental study shows selective fiber activation in a mixed nerve bundle using these two novel techniques and compare them with anodal block. Experiments were performed in vitro on the vagal nerves of pigs.

1 Introduction

When electrical stimulation is applied to a nerve, large diameter nerve fibers are activated at a lower stimulus intensity than smaller fibers. However, there are applications in skeletal muscle activation, urology and cardiology that require activation of small before large nerve fibers.

Brindley and Crags [1] used a technique called anodal block to selectively activate parasympathetic fibers without activating large somatic fibers in sacral roots. A simulation study [2] showed that it is possible to obtain diameter and fiber selective stimulation of nerve fibers by applying long, exponentially rising pulses. Another simulation study [3] showed that diameter and spatial selective stimulation can also be achieved by using subthreshold depolarising prepulses.

The vagal nerve in the cervical region is specially suited for evaluation of fiber diameter selective methods because it is composed of three groups of myelinated fibers: large fibers (≈ 10 µm), medium fibers (4-9 µm) and small fibers (<4 µm) and unmyelinated fibers [4].

This paper presents novel experimental results of selective activation of fibers of medium and small diameters using techniques of depolarising prepulses and long exponentially rising pulses and compares them with results obtained with a technique of anodal block. Maximum amplitude and pulse durations, as well as efficiency in selective activation of different fiber groups were compared between these three techniques.

2 Methods

2.1 Nerve preparation

Cervical parts of the left and right vagal nerves were excised from sacrificed pigs. The nerves were placed in the Kreb’s solution. To keep the nerve alive for as long as possible experiments were performed at room temperature (19–21 °C). To decrease the excitation threshold the Kreb’s solution was, in some cases, heated to around body temperature (35-39 °C). Experiments were performed on the vagal nerves of 9 pigs.

2.2 Stimulation and recording

A tripolar cuff electrode with contact separation of 3 mm was used for stimulation. A pentapolar cuff electrode with 5 mm contact separation was used for recording the compound action potential (AP). The lateral contacts of the recording electrode were short-circuited to improve noise rejection. The distance between the middle contacts of the stimulating and the recording cuffs was 4-5 cm. Cuff between 3.2 mm and 3.6 mm were snug fitted to nerves.

The stimulator consisted of two synchronized current sources with a common cathode. ENG signals were amplified 25000 times with a preamplifier and an amplifier (Cyber. Amp. 380 and AI 402; Axon Instruments, USA). Averaged ENG signals from 5 consecutive stimulations were monitored and recorded on a computer. The sampling frequency was 20 kHz. Recording started 1 ms before the stimulation.

2.3 Stimulation techniques

Anodal block was performed with square pulses of 600-1000 µs duration (Figure 1a). An exponentially falling edge, up to 1000 µs was added when needed, to prevent anodal break excitation.
Selective stimulation with depolarising prepulses was performed with two-step pulses (Figure 1b). Durations of the prepulse and of the excitation pulse were 400-600 µs, each. For a fixed duration of the first and the second part of a pulse the amplitude of the second part was fixed and the amplitude of the first part of the pulse varied around the excitation threshold.

Selective stimulation with long, slowly rising pulses was performed with pulse shapes as shown in Figure 1c [2]. For pulses longer than 7 ms, a compound AP was generated before the end of the stimulation pulse because of a limited distance between the stimulation and recording electrode.

![Figure 1: Pulse shapes used to obtain selective fiber activation using anodal block: square pulses (a), depolarising prepulses (b), long exponentially rising pulses (c).](image)

### 3 Results

The excitation threshold for 600 µs square pulses was for the low temperature 0.82±0.43 mA and for the high temperature 0.57±0.26 mA. Selective suppression of large or medium nerve fiber activation using depolarising prepulses could be achieved at both high and low temperatures in all tested pigs. Suppression of large fiber activation with long exponentially rising pulses could also be achieved at both temperatures. Yet, at low temperature longer pulses were applied than at the high one, because compound APs had lower velocities, and overlapping with stimulus artefact could be avoided. However, stimulation of small fibers was not possible at low temperature. Anodal block could be achieved only at high temperatures in 60% of tested pigs.

#### 3.1 Anodal block

An example of anodal block of the large fibers in left vagal nerve is shown if figure 2. The experiment was performed at 37 °C. The vagal nerve was stimulated with 600 µs square pulse. The excitation threshold for the 600 µs square pulse was 0.17 mA. When the nerve was stimulated with 2.5 mA a high peak at T<2 ms of the large fibers could be noticed. When the nerve was stimulated with 4 mA, the amplitude decreased for 50%. Several more peaks in the compound AP can be noticed. They represent contributions of medium and small-size fibers. Propagation velocities of these four fiber groups were ≈57 m/s, 40 m/s, 12 and 7 m/s.

#### 3.2 Depolarising prepulses

An example of selective fiber activation in a right vagal nerve using depolarising prepulses is shown in Figure 3. Duration of the prepulse and the stimulation pulse was 600 µs each. The experiment was performed at 37 °C. The excitation threshold for a 600 µs square pulse was 0.7 mA. Figure 3a shows the ENG response to stimulation with square pulse of 600 µs and 6 mA. Large, medium and small myelinated fibers, whose contributions are marked with arrows, were activated. Figure 3b shows stimulation with a subthreshold depolarising prepulse with an amplitude of 0.6 mA. The same fiber groups were stimulated but stimulation was delayed for the duration of the prepulse. Figure 3c shows stimulation with a suprathreshold depolarising prepulse of 0.75 mA. Activation of the large fibers was suppressed. There are however small amplitude responses generated with both parts of the pulse marked with asterisks. The first peak, that is contribution of large fibers, was overlapping with the stimulation artefact. The contributions of the medium and small fibers were not affected. Figure 3d shows stimulation with a depolarising prepulse of 1.0 mA. A response of the medium fibers was suppressed. The large nerve fibers were activated already during the
prepulse and their compound action potential was shifted to the left.

### 3.3 Long exponentially rising pulses

An example of blocking of a compound action potential of large nerve fibers with exponentially rising pulses is shown in Figure 4. The experiment was performed at 21 °C on a left vagal nerve. The maximum amplitude at the end of the pulse was 2 mA. When the nerve was stimulated with a 1 ms pulse, both large and medium fibers were activated. Stimulation with 3 ms pulses caused partial deactivation of large nerve fibers. Stimulation with 5 ms and 7 ms further decreased the contribution of large fibers but also affected the contribution of the medium nerve fibers.

Figure 3: Stimulation with a square (a) and a two-step pulse (b). Blocking of large (c) and medium (d) nerve fibers using depolarising prepulses. Arrows point to the APs of large, medium and small myelinated fibers.

was stimulated with a 1 ms pulse, both large and medium fibers were activated. Stimulation with 3 ms pulses caused partial deactivation of large nerve fibers. Stimulation with 5 ms and 7 ms further decreased the contribution of large fibers but also affected the contribution of the medium nerve fibers.

![Figure 4](image.png)

**Figure 4:** Blocking of the large and medium fibers with long exponentially rising pulses.

**Discussion and Conclusions**

This paper shows that it is possible to obtain diameter selective nerve fiber stimulation using anodal block and depolarising prepulses. Long exponentially rising pulses can suppress activation of large fibers but also affect smaller fiber groups. In anodal block, selective block of large fibers was achieved with anodal current that hyperpolarizes the membrane while in the later two cases membrane accommodation was achieved with a cathodal current that depolarises the membrane. Therefore, suppression mechanisms in the latter two cases should be similar. Of the three techniques, long exponentially rising pulses require the longest pulse duration, whereas anodal block requires the highest current to block the compound AP. Selective nerve fiber activation using depolarising prepulses offers a compromise between the pulse duration and the current amplitude. However, it can be achieved for a very limited range of currents. In contrast to Deurloo et al. [2], depolarising pulses were supra- and not subthreshold. Although the prepulses were suprathreshold for the whole nerve bundle, they might be subthreshold for most of fibers in the nerve bundle. The highest selectivity in activation large or medium fibers can be achieved with depolarising prepulses and the worst selectivity was achieved with exponentially rising pulses.

**References**


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