

TITLE: EFFECT OF LOCAL ANESTHETIC DRUGS ON FAST AND SLOW NERVE FIBERS

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**Introduction.** This study was initiated to evaluate the relative effect of local anesthetics on motor and sensory function. Assuming that large nerve fibers (fast conducting) serve motor function and small nerve fibers (slow conducting) are involved in pain sensation, we compared the effect of the local anesthetics (lidocaine, tetracaine, etidocaine, and marcaine) on these two populations of nerve fibers.

**Methods.** We used the isolated, desheathed rabbit vagus nerve. This consists (in mid-cervical area) of unmyelinated fibers conducting at less than 1 m/s. Also present are a large number of fibers conducting at 5-15 m/s which are myelinated fibers corresponding to A gamma and/or B fiber classification.<sup>1</sup> Some experiments were done on the rabbit sciatic desheathed nerve under the same experimental conditions. These are A alpha fibers conducting at 50 m/s.

After a suitable control period the isolated nerve, at 22°, was exposed to the selected drug and concentration for a 30 min. period. Stimulation rate was 1/min. Stimulus duration was 0.05 milliseconds for A alpha, 0.1 msec for A gamma or B and 1.0 msec for C fibers. Intensity of stimulation was adjusted to maximum amplitude of action potential (AP) response. Control amplitude of AP was compared to AP at the end of 30 minutes. Washout of drug returned AP to within 90% of control. Usually, separate experiments were done for each group of fibers. No individual nerve was used for more than 2 drug concentrations with recovery to normal function between experiments.

Results were plotted as dose-response for each drug at various concentrations and a linear regression line derived from these points by least squares analysis. This computed the drug conc. for 50% nerve response. Points were also plotted on Log-Probit paper to derive standard error of drug ED50 by a graphic method.<sup>2</sup>

**Results.** All of the drugs examined caused depression of action potential in the fast fibers at a lower concentration than needed for a comparable block in the slow fibers. That is A alpha blocked before A gamma/B, and A gamma/B blocked before C nerve fibers. This is shown in the following table:

**Results:** DRUG CONC. AT 50% BLOCK OF NERVE AP

	A alpha	A gamma/B	C
Lidocaine	0.10	0.36	0.62
Tetracaine	0.009	0.012	0.024
Etidocaine		0.062	0.182
Marcaine		0.103	0.180

Conc. in millimoles

Examination of recovery records showed that as the amplitude of the AP increased with washout, the velocity of the compound AP increased, again indicating that fast fibers were blocked first and recovered last from the effects of local anesthetic drug.

Examination of the intact nerves (versus desheathed) showed the same relationship between fast and slow fibers but a larger concentration of drug was needed to achieve the same total block.

We did no experiments at rabbit body temperature but replotting of the data in experiments from de Jong's laboratory<sup>3</sup> showed the same fast-slow relationship but at a lower total drug dose.

**Discussion.** The classic teaching that small non-myelinated nerve fibers are more susceptible to local anesthetic blockade is not substantiated by these experiments.<sup>4</sup>

A most important factor in local anesthetic effect on nerve transmission is internode distance (using the concept of internode as the distance between sequentially activated areas of nerve membrane). The greater the internode distance, the more easily transmission is blocked by reducing the activation potential of the nerve membrane. Since the larger the diameter of the nerve fiber (associated with higher conducting velocity and greater internode distance), it follows that the A fibers are blocked before the B fibers, and B fibers are blocked before C fibers.

We have still not answered whether local anesthetic drugs have a differential blocking effect on motor or sensory function. But these results make it unlikely that, in peripheral nerve, it will be possible to block chronic pain and leave motor power intact by means of local anesthetic drugs.

#### References.

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