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Title : THE MARGIN OF SAFETY FOR TRANSMISSION IN FAST AND SLOW NERVE FIBERS

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Introduction. A recent study of the differential effect of local anesthetic drugs on fast and slow conducting nerve revealed that in all instances fast conducting nerve was blocked at lower concentrations of drug than slow conducting nerve.[1] Since such drugs are associated with a decreased inward sodium current on activation of the nerve membrane[2] we studied the effect of decreasing the sodium current directly by perfusing with a sodium deficient solution, and by use of tetrodotoxin (TTX). By this we hoped to differentially assess the safety margin of transmission in each group of fibers. Safety margin is defined as to how much activation current exceeds that needed for threshold stimulation.[3]

Methods. We used the isolated desheathed rabbit vagus or sciatic nerve. We defined as fast fibers (A) those whose conduction velocity ranged from 25-50 meters/sec, slow conducting (C) those whose velocity was 1.0 meter/sec or less and a group of fibers (B) conducting at 5-15 meters/sec. At least 10 mm of nerve was desheathed and exposed to test solutions, recording and stimulation were from the nerve immediately outside the test area. Stimulation was adjusted to produce maximum amplitude of action potential (AP) as visualized on a recording oscilloscope. Stimulation duration was 0.05 msec for A, 0.1 msec for B and 1.0 msec for C. The nerve at 22°C was repeatedly flushed with Hepes-Liley solution (pH 7.4) for a 30 min control period. Then test solution was applied for 30 minutes and the AP amplitude compared to control period AP. Washout of this test solution returned AP to 90% of control value. Sodium deficient solution was made by substituting choline chloride for sodium chloride in the Liley solution. TTX was dissolved in regular Liley solution.

Results were plotted as log dose-response for sodium concentrations and TTX concentrations. A linear regression curve was derived from these points by least squares analysis.

Results. As the sodium concentration in the perfusing solution was decreased fast conducting fibers (A) were blocked first and at a higher sodium concentration than B fibers and B fibers were blocked at a higher concentration than C fibers. The fast conducting fibers in the sciatic nerve (A) which have a higher conduction velocity than the fastest conduction fibers in the vagus nerve were blocked at the highest sodium concentration. The results with TTX were the same:

Concentration at 50% Block of AP

	Na Conc	TTX Conc
A(sciatic)(34.90 m/sec)	84.69	
A(vagus)(26.82 m/sec)	70.31	
B(vagus)(6.63 m/sec)	44.88	0.04
C(vagus)(0.95 m/sec)	34.41 mM	0.06 μM

In general, all fibers showed marked slowing of conduction before blockade; also the first blocked fiber in a mixed nerve was the last to recover.

Discussion. In contrast to the classical statement that small fibers are more susceptible to drug blockade than large nerve fibers because of their larger surface area to volume ratio[4] we have found that small slow nerve fibers are more resistant to block. Our results in these experiments verified our results with the local anesthetic drugs.[1] Reduction of the inward activating sodium current in both groups of fibers is more likely to cause transmission failure in the large fast-conducting fibers. The TTX experiments showed the same results as with the sodium deficient solutions.

This study shows that in the peripheral mixed nerve small non-myelinated nerve fibers, as a group, have a larger margin of safety for nerve transmission than large myelinated fibers and the faster (and larger) the nerve fiber the smaller the margin of safety for transmission.

References.

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