TITLE: SELECTIVE HYPOOSMOTIC EFFECTS ON MYELINATED AND UNMYELINATED AXONS

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Introduction. Studies on pain mechanisms have recently shown that unmyelinated C axons are less sensitive than large myelinated A axons to glucose or oxygen deprivation.[1,2] The present study investigated the differential vulnerability of these fiber groups to a hypoosmotic stress such as arises during hypobaric spinal anesthesia.

Methods. Cervical vagus nerves of rabbit were preincubated for two hours in Ringer-bicarbonate solution containing glucose 20 mmol/l, equilibrated with 5% CO_2 - 95% O_2 at 36-38°C. The nerves were next exposed to a hypoosmotic solution for 3 hr. The osmotic strength was 0.35 of isoosmotic, achieved by adjusting the NaCl content. Finally the nerves (group I, n = 6) were allowed to recover in isoosmotic solution for a further period of 2 hr. Compound action potentials (CAP) of A and C fibers were obtained periodically by supramaximal electrical stimulation and were recorded photographically. Changes in CAP amplitude were expressed as a fraction of the last preincubation value. In another group of nerves (group II, n = 7) the recovery period of isoosmotic exposure was omitted. These nerves were used to determine the effect of hypoosmotic exposure on the sodium and potassium content of the nerve core; five concurrent controls also were processed. Significance of differences was evaluated by t-test for unpaired observations.

Results. In groups I and II, exposure to hypoosmotic solution increased the latency of the fast CAP component (A-CAP) to 189 ± 35% of the preincubation value, and extinguished the A-CAP in 15 ± 5 min (± S.D.) (Table 1). In contrast the amplitude of the slow CAP component (C-CAP) still averaged 14 ± 18% of the preincubation value at the end of 3 hr hypoosmotic exposure, and the latency increase averaged 458 ± 184%. In four of these nerves C-conduction extinguished and then partially recovered while the nerve was still in the hypoosmotic solution. When the group I nerves were transferred to isoosmotic solution for recovery, the C-CAP manifested complete reversal of the hypoosmotic effects on latency and amplitude within 2 hr; the A-CAP recovered only to 20 ± 25% of preincubation amplitude and 275 ± 60% of preincubation latency.

In group II, at the end of hypoosmotic exposure the nerve core contained (mmol/kg dry weight) Na^+ 164 ± 14, K^+ 115 ± 13. In concurrent isoosmotic controls the final core content was Na^+ 375 ± 28, K^+ 196 ± 17 ($p < 0.0005$); CAP amplitudes were A-CAP 80 ± 15%, C-CAP 92 ± 15% of preincubation values; latencies were unchanged.

Discussion. The imposed hypoosmotic stress was well tolerated by the C fibers but not by the A fibers. This was evident both in the slower and less complete progress toward extinction of conduction of the C-CAP and its much more complete recovery ($p < 0.0005$) after restoration to the isoosmotic environment. Although the electrolyte loss cannot be apportioned according to fiber type, the superior recovery of the C fibers suggests that they suffered a proportionately lesser K^+ loss. The superior functional resistance of C fibers to hypoosmotic swelling was probably not due to their small size, because a given fractional increase in the volume of axons theoretically causes the surface of the axons to expand by a factor that is the same for all axons. More likely, the intimately encircling Schwann cell found throughout the length of the C fibers afforded a support against hypoosmotic swelling that was deficient at the nodes of Ranvier of A fibers. This deficiency could render nodal axolemma locally liable to injury from osmotic swelling of the nodal axoplasm. The observed superior resistance of C fibers to hypoosmotic swelling may account for partial failure of past attempts to alleviate incurable cancer pain with intrathecal instillation of water.[3] The ability of C fibers to recover differentially during continuing hypoosmotic exposure may tend to limit the duration of a hypoosmotic spinal anesthetic.

References.

1. Fink BR, Cairns AM: A bioenergetic basis for peripheral nerve fiber dissociation. Pain in press
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3. King JS, Jewett DL, Rutkin B, Wilson CB: On attempting selective blockade of dorsal root C fibers in the treatment of chronic pain problems. Exp Neurol, 56:241-251, 1977

TABLE 1. HYPOOSMOTIC EFFECTS ON A AND C POTENTIALS

		A	C	
Amplitude*				
hypoosmolar	(3 hr)	0**	14 ± 18	13
recovery	(2 hr)	20 ± 25	110 ± 15	6
Latency*				
hypoosmolar		189 ± 35	458 ± 184	13
recovery		275 ± 60	120 ± 15	6

* % of preincubation value

** reached within 20 min