VOLUME REGULATORY INFLUX OF SODIUM ACROSS THE BLOOD-BRAIN BARRIER DURING ACUTE HYPEROSMOTIC STRESS IN THE LITTLE SKATE (RAJA ERINACEA).

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Brain interstitial fluid volume is determined by the total tissue content of extracellular ions, chiefly Na and Cl. In response to hypernatremic dehydration, the brain of the little skate gains sufficient NaCl to restore interstitial fluid volume to normal (Cserr, Bradbury, Mackie & Moody. Am. J. Physiol. 245:R853-R859, 1983). This volume regulatory response is complete within 35 min and is based on an increase in the permeability of the blood-brain barrier to electrolytes (Mackie, DePasquale & Cserr. Bulletin. MDIBL 23:41-42, 1983). This reports examines the mechanism of the osmotically induced increase in barrier permeability to Na.

The permeability of the blood-brain barrier was studied in anesthetized skates injected im with isotonic saline (15 ml/kg) (isosmotic) or with 56 mosmol/kg NaCl (10 ml/kg) or fructose (15 ml/kg) in saline (hyperosmotic). Terminal plasma osmolality varied from 930 to 1025 mosM. The unidirectional blood-to-brain transfer constant, K_1, for influx across the blood-brain barrier was measured for ^{22}Na and, as a marker for nonselective changes in barrier permeability, for ^{14}C-mannitol using the integral technique of Ohno, Pettigrew & Rapoport (Am. J. Physiol. 235:H299-H307, 1978). Tracer measurements were made over a 30 min period beginning 5 min after im injection of saline, NaCl or fructose. In isosmotic skates, values of K_1 for ^{22}Na (in ml plasma$\cdot$g brain$^{-1}\cdot$min^{-1}x10^4) for telencephpalon, medulla and cerebellum were 7.3$\pm$0.7, 7.7$\pm$1.0 and 14.3$\pm$1.8, respectively (N=6). K_1 increased linearly with osmolality in all three brain regions. The increase in Na permeability was the same (3×10^{-5} ml$\cdot$g$^{-1}\cdot$min$^{-1}\cdot$mosM^{-1}) whether osmolality was elevated with NaCl (N=17) or fructose (N=12). It was also unaffected by pretreatment with the "loop" diuretic bumetanide (1 mg/kg iv) (N=18). K_1 for ^{14}C-mannitol also increased linearly with osmolality during hypernatremia (N=29), although the increase was less ($1.2\pm0.1 \times 10^{-5}$ ml$\cdot$g$^{-1}\cdot$min$^{-1}\cdot$mosM^{-1}) than the comparable change for Na.

The observations that bumetanide does not inhibit the osmotically stimulated increase in barrier permeability to sodium and that barrier permeability to mannitol also increses with osmolality suggest that Na uptake by the skate brain during hypernatremia is due to a passive increase in blood-brain barrier permeability. Dependence of the osmotically induced increase in permeability on molecular size, i.e. the increase in permeability was greater for Na than for the larger molecular weight mannitol, is consistent with a pore model of barrier opening.

The vertebrate blood-brain barrier consists of two membranes, the parenchymal capillary endothelium and surrounding glial endfeet. In elasmobranchs perivascular glial cells are joined by tight junctions and barrier function resides in this membranes (Bundgaard & Cserr. Brain Res.

226:61-73, 1981), whereas all other vertebrates have an endothelial barrier (Cserr & Bundgaard. Am. J. Physiol. R:277-R288, 1984). Our functional studies of the skate blood-brain barrier indicate that the permeability of the glial barrier, like that of an endothelial barrier (Rapoport. J. Physiol. 170:238-249, 1964), is increased by exposure to hyperosmotic stress. (Supported by PHS NS 11050.)