Movement of Sodium-22, Radioiodinated Protein, and Tritiated Water from the Cisterna Magna into the Cerebrovascular Circulation*

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As Sweet¹¹ and many others have emphasized, almost all substances in the cerebrospinal fluid (CSF) are capable of movement across any of the membranes in the central nervous system (CNS), and the concept that CSF is absorbed via the arachnoidal villi or by blood vessels is oversimplified. The major research problem is to delineate the patterns of movement of the various constituents of the CSF. Since the dynamic nature of the cerebrospinal fluid-brain barrier varies with location, species, age,¹⁰ and physiological state, the problem is a difficult one. We are reporting a study on the absorption of tritiated water, radioactive sodium ion, and radioiodinated protein from the cisterna magna of monkeys in an attempt to view the separate movement of three distinctly different CSF components as an equilibrium is established between the CSF and the blood.

Method

Four monkeys (Macaca mulatta) ranging in weight from 6 to 17 lbs were anesthetized with sodium pentobarbital, and an endotracheal tube was inserted. A polyethylene catheter was placed in the brachial artery, and 23-gauge needles were inserted under direct vision into the sagittal sinus at the junction of the middle and posterior third and (using a dissecting microscope) into the vein of Labbé on the right side. The latter procedure was done through a small opening in the dura mater while the remainder of the dura was left intact. No openings in the arachnoid were seen except at the site of needle puncture. The right side of the animal was up, and there was no obvious loss of CSF. One animal was heparinized due to difficulty with excessive venous clotting.

Cisternal puncture was done; if the flow suggested an inadequate tap, the animal was not used. In one animal, the CSF was replaced by a solution containing sodium-22 as isotonic sodium chloride; in the other three animals, a mixture of sodium-22, iodin-131 labelled albumin, and tritiated water (HTO) was slowly injected into the cisterna magna. The radioactivity injected was similar in each animal at 0.1 μc/lb body weight for albumin and tritiated water, and at 0.01 μc/lb body weight for sodium-22. The total volume of CSF discarded was equal to the volume of isotope injected.

During the 90 minutes after instillation of the radioactive material, 0.5 cc samples of blood were removed at intervals from the cortical vein, the sagittal sinus, and the brachial artery. Counting of the 131-I albumin and sodium-22 was done on a dual channel well-type scintillation spectrometer. The sample was then vacuum-distilled, and the distillate was counted for tritium on a tri-carb liquid scintillation counter. Previous studies before distillation demonstrated that HTO did not count with sodium-22 and 131-I, and that after distillation the HTO was free of both.

In two animals, the brain was rapidly removed at the conclusion of the experiment (90 minutes after injection of the isotopes). The animals remained alive until the spinal cord was transected at the level of the foramen magnum. The brain was immediately sliced and blotted to remove the CSF from the surface and from within the ventricles.

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‡ Baird Atomic Model 707.
§ Packard Instrument Company.

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Samples were removed from the frontal, parietal, and occipital regions; in each sample, a cortical, middle (white matter), and medial specimen was obtained. These were again blotted, weighed, and counted, using the same technique as described for counting the blood samples.

Tritiated Water (HTO). There was extremely rapid movement of HTO from the cisterna magna into the circulation. Within 10 minutes, the sagittal sinus, vein of Labbé, and arterial blood all contained similar amounts of radioactivity. A comparison of levels of radioactivity at the three sampling sites is shown in Fig. 1.

Sodium-22. In contrast to tritiated water, radioactive sodium met a partial barrier that prevented it from spreading quickly from the CSF into the blood (Fig. 2).\textsuperscript{3,8} This barrier was incomplete, however, and equilibrium was approximated after 45 minutes. Sodium was not predominantly or solely absorbed by the vessels that drain into the sagittal sinus; in fact, in Animal 1 (not included in the graphs) this area was no more radioactive than was the peripheral blood. The cortical venous blood was very radioactive, however. Thus, it appeared that the major pathway of sodium absorption was via the brain tissue and cortical vessels rather than directly into the sagittal sinus.

Iodin-131 Labelled Albumin. The 131-I labelled albumin took longer to appear in the blood than did either sodium-22 or HTO. Figure 3 suggests that the sagittal sinus may be particularly active in the absorption of the labelled protein, although the cortical veins also contained somewhat more radioactivity than did the peripheral arterial blood.

Postmortem Brain Analysis of HTO, Sodium-22, and 131-I Labelled Albumin (Two Monkeys). Since there were so many variables and so few animals in this particular experiment, we have expressed the over-all radioactivity of the brain tissue of the two monkeys in percentages rather than in measure of concentration (Table 1). In both animals, the sodium-22 and 131-I albumin were in greatest concentration on the pial surface of the brain in the frontal and parietal lobes, and the HTO more evenly distributed throughout the brain.

Discussion

Our data on HTO agree with previous data published by others, that there is a very rapid uptake of water from the cisterna magna.\textsuperscript{2} A similar rapid establishment of equilibrium between the cerebrospinal fluid and plasma takes place following injection of radioactive water into the peripheral venous system.\textsuperscript{1} These data suggest that water can