Journal of Cerebral Blood Flow and Metabolism
7:585–591 © 1987 Raven Press, Ltd., New York

Evidence for an Alanine, Serine, and Cysteine System of Transport in Isolated Brain Capillaries

Ivan Tayarani, Jeanne-Marie Lefauconnier, Françoise Roux, and Jean-Marie Bourre

INSERM U26, Hôpital Fernand Widal, Paris, France

Summary: Brain capillaries isolated from 2-month-old male and female Sprague-Dawley rats were used to study the transport of neutral amino acids. The uptake of alanine, leucine, and alpha-methylaminoisobutyric acid (MeAIB) was a linear function of time for the first minute of incubation. Based on these observations, an incubation time of 1 min was used to measure transport activities. The intracellular water volume of the isolated capillaries was 2.2 μl/mg protein. This value was significantly lower (1.8 μl/mg protein) when measured in the absence of sodium. L-Alanine, L-serine, and L-cysteine were taken up from the abluminal surface of brain capillaries by a sodium- and energy-dependent, carrier-mediated system. This uptake, for the most part, was not inhibited by MeAIB. System ASC (alanine-serine-cysteine) appeared to be of primary importance for the transport of these amino acids in isolated brain capillaries. The apparent K_m and V_{max} values for L-alanine uptake by ASC transport, based on the Hofstee plot presentation, were 1.3 m*M* and 0.975 nmol/μl water content/min, respectively. The results also indicate that the transport of MeAIB and 2-aminobicyclo(2,2,1)heptane-2-carboxylic acid (BCH) was limited to the sodium-dependent system A (alanine) and the sodium-independent system L (leucine), respectively. **Key Words:** Blood–brain barrier—Brain capillaries—Neutral amino acids—Transport system ASC.

In order to function normally, the brain requires a continuous supply of nutrients, such as glucose, ketone bodies, amino acids, choline, and purines. The availability of these nutrients is determined by the transport systems of the blood–brain barrier (BBB), as well as by the plasma concentrations (Hawkins, 1986). In a wide variety of animal cells, there are three major systems of transport for neutral amino acids—the A system (alanine), the L system (leucine), and the ASC system (alanine, serine, cysteins)—which may be distinguished on the basis of their sodium requirements, substrate specificities, pH sensitivities, and regulatory characteristics (Oxender and Christensen, 1963; Christensen, 1975).

In vivo and in vitro studies have shown that there is neutral amino acid transport from blood to brain through the vessel walls (Oldendorf, 1971; Yudilevich et al., 1972; Betz et al., 1975; Pardridge, 1977; Pardridge and Oldendorf, 1977) and by isolated brain capillaries (Sershen and Lajtha, 1976; Hjelle et al., 1978; Hwang et al., 1980; Cardelli-Cangiano et al., 1981; Cancilla and DeBault, 1983; Hwang et al., 1983; Audus and Borchardt, 1986). Betz and Goldstein (1978) demonstrated that there are two transport systems for neutral amino acids in isolated brain capillaries: a sodium-independent L-system, which operates both at the luminal and at the abluminal surface, and a sodium-dependent A-system, which operates only at the abluminal surface.

The ASC system, another sodium-dependent system of transport with a substrate range mostly limited to L-alanine, L-serine, and L-cysteine, has also been found in other tissues (Christensen et al., 1967; Newton et al., 1984). This system has a higher stereospecificity than the A-system, but unlike the A-system, it does not transport *N*-methylated substrates, such as alpha-methylaminoisobutyric acid (MeAIB), and it can be transstimulated

Received February 16, 1987; accepted April 23, 1987.

Address correspondence and reprint request to Dr. Ivan Tayarani at INSERM U26, Hopital Fernand Widal, 200 Rue du Faubourg Saint Denis, 75475 Paris Cedex 10, France.

Abbreviations used: ASC, alanine-serine-cysteine system; BBB, blood–brain barrier; MeAIB, alpha methylaminoisobutyric acid; BCH, 2-aminobicyclo-(2,2,1)heptane-2-carboxylic acid; Ch, choline; 3-MG, 3-O-methyl (^{3}H)-D-glucose.