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Lipid Synthesis by Rat Brain Microvessel Endothelial Cells in Tissue Culture

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Abstract. Lipid synthesis and its regulation by serum lipoproteins at the microvascular blood–brain barrier were studied using primary cultures of microvascular endothelial cells from rat brain. These cells are capable of synthesizing all their lipids (neutral lipids, phospholipids, glycolipids) from the water-soluble compounds, glucose, acetate, acetoacetate and beta-hydroxybutyrate. The ketone bodies, especially acetoacetate, are the preferred substrates for lipid synthesis. The incorporation patterns of acetate, acetoacetate and beta-hydroxybutyrate are very similar, indicating that these precursors contribute to lipid synthesis via the same metabolic route. However, the metabolic pathway is different for glucose, which is preferentially incorporated into phospholipids. The existence of an inverse relationship between lipid synthesis and the serum lipoprotein concentration suggests that cultured cerebral endothelial cells are capable of taking up lipids, principally cholesterol, contained in the serum lipoproteins. Cellular lipids would thus be supplied both by intracellular lipid synthesis and by serum lipoproteins. The difference between cholesterol synthesis rates in cultured cerebral endothelial cells and in isolated brain microvessel cells could be partly explained by the fact that the lipoprotein concentration is much lower in the culture medium than in rat serum.

Key Words: Blood–brain barrier; Cell cultures; Cerebral endothelium; Cholesterol; Ketone bodies; Lipids; Lipoproteins.

INTRODUCTION

The structure that forms the blood–brain barrier (BBB) consists of brain microvessel endothelial cells. These endothelial cells are bound together by tight intercellular junctions that, combined with the presence of few pinocytotic vesicles, form a barrier that restricts the movement of most polar molecules, lipoproteins and proteins, from blood to brain (1–3).

The transport of plasma lipids (free fatty acids, cholesterol, triglycerides and phospholipids) into and through the brain microvessel endothelial cells is impeded by the tight binding of these compounds to plasma proteins or lipoproteins. The reported data are conflicting with regard to blood–brain transport of these different lipids (4, 5). Serougne et al (5) showed that labeled dietary cholesterol enters brain, which suggested that cholesterol may cross the BBB. However, the process occurs very slowly.

The presence of lipoprotein receptors on brain capillaries has not yet been demonstrated, but Brecher and Kuan showed the presence of acid lipase in rabbit brain microvessels. This finding suggested that lipoprotein-associated cholesterol esters could be internalized by receptor-mediated endocytosis and subsequently hydrolyzed by the acid lipase (6). However, most of the cholesterol taken up may be needed for

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