Chapter 8

Glucose and Energy Metabolism in the Brain

Of all the nutrients used by the mammalian system, only glucose is able to satisfactorily maintain the metabolism of cerebral tissue. Although mannose and other sugars can also be metabolized, they must first be converted into glucose. On the other hand, fructose, another simple sugar, is capable of being utilized without conversion, but the process is a relatively slow one. And while the brain can additionally make use of ketone bodies, such as 2-hydroxybutyric acid, their low transport rate across the blood-brain barrier restricts their contribution to the production of energy (Hawkins and Biebuyck, 1979). Other substrates that support brain function are converted into glucose elsewhere in the body. Gluconeogenesis, the formation of new molecules of glucose from other components, is absent in the brain.

The brain, then, consumes glucose as an almost exclusive source of energy. Calculation of the ratio of generated carbon dioxide to consumed oxygen, referred to as the respiration quotient, approximates a value of 1. This would conform to the following formula for the oxidation of glucose:

\[
C_6H_{12}O_6 \rightarrow 6H_2O + 6\ CO_2 + \text{energy (38 mol ATP)}
\]
Hence, \( \frac{6\text{CO}_2}{6\text{O}_2} = 1 \)

There are only small reserves of brain glucose in the form of the polymer glycogen. These reserves are quickly consumed when there are interruptions in the glucose intake, as in ischemia or hypoglycemia. There is no evidence for the use of fats as an energy source in the adult central nervous system under normal conditions.

**TRANSPORT AND CONSUMPTION OF GLUCOSE**

Glucose is the only sugar which is actively transported into the brain in substantial quantities. Other sugars, such as fructose and galactose, are unable to pass the blood-brain barrier sufficiently. The glucose passes into the brain via molecular carrier mechanisms located in the endothelia of the brain capillaries. At least two transfer mechanisms have been described: a high-affinity, low capacity system and a low-affinity, high capacity system (Gjedde, 1981). They are strictly stereospecific; \( \text{D-} \)glucose is the only form transported. When hydrogen is substituted for a single hydroxyl group in the molecule, the entry of this substance (galactose, for example) is restricted. Such a "high-affinity" transport mechanism for glucose (Fig. 8.1) is independent of the presence of sodium ions (for review see Crone, 1978), although calcium ions may be involved (Elbrink and Bihler, 1975). Keller et al. (1981) reported the presence of an additional transport system in the neuronal membrane, which was apparently able to effectively regulate the use of glucose by the cell.

The clearance of glucose, that is the amount of sugar consumed by the brain per unit time, depends primarily upon its transport across the blood-brain barrier and the rate of blood flow through the brain, and not as much upon the plasma glucose level. Even after eight days of starvation, when the glucose level in the blood plasma is drastically decreased, the rate of glucose transport into the rat brain remains unchanged. Hyperglycemia may cause a substantial, but short-lived, increase in the cerebral gain of glucose. The excess amount of glucose is initially retained by the brain, but may later diffuse back into the blood.

The half-life of glucose in the brain is short, about 1.2 ± 0.2 minutes (Savaki et al., 1980), and its level is actually rather small, approximately 1.5 micromoles per gram of wet tissue (about 27 milligrams per 100 grams). Of this amount, the intracellular content of the brain cells is probably extremely low.