Cognitive performance and glucose

Dear Sir:

A recent report by Kaplan et al (1) suggested that glucose enhances cognitive performance. This work is supported by extensive evidence that modest increases in circulating glucose concentrations enhance the formation of new memories in rodents and humans (reviewed in reference 2). Glucose enhances memory for several different tasks in rodents. In humans, glucose enhances memory in healthy young and elderly persons and in persons with Alzheimer disease or Down syndrome (2). The effect of glucose on cognitive functions across species and tasks suggests that glucose might act on the areas of the brain important for memory formation, which may be in addition to glucose’s being the major source of energy for the central nervous system. This suggestion is supported by the observation that microinjections of glucose into the septohippocampal system of rats enhance mnemonic functioning (3). In this context, it is interesting to note that glucose is critical for the production of acetyl-CoA, a precursor of acetylcholine (4), and that decreases in glucose concentrations result in decreases in brain acetylcholine (5). Thus, one strong possibility is that glucose enhances memory processes by increasing acetylcholine synthesis and release (2). This is substantiated by the observation that glucose can modify the effects of cholinergic drugs on various behavioral and neural measures (2). Furthermore, extracellular brain glucose concentrations vary with neuronal activity, indicating that glucose may be critical in modulating memory functioning (6). This is supported by the report that hippocampal acetylcholine release is increased in rats during a spatial task (2).

Insulin receptors are present in brain cells and may play a role in brain cognitive functions (7), including learning and memory. Insulin is also a potent stimulator of endothelial nitric oxide formation (8) and an inhibitor of tumor necrosis factor α (TNF-α) synthesis (9). One of the functions of insulin in the brain could be to stimulate nitric oxide formation and at the same time to down-regulate TNF-α synthesis so that neurons are protected from the neurotoxic actions of TNF-α (10) and memory formation is aided. Thus, one important function of insulin, insulin receptors, and glucose in the brain may be to protect neurons from the death signals of TNF-α. This is in addition to the role of glucose in improving memory. The finding that hyperinsulinemia improves memory in patients with Alzheimer disease (11) supports this view. Furthermore, nitric oxide is also believed to play a role in memory formation. On the basis of this evidence, I suggest that there is a close interaction between glucose, insulin, insulin receptors in the brain, endothelial nitric oxide, TNF-α, and neuronal survival and memory formation.

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REFERENCES