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Invited commentary

Glucose and mental performance

An abundant literature suggests that intellectual performance can be improved following the intake of a glucose load, or of some carbohydrate-rich food. Improved mental performance generally correlates with the subjects' blood glucose level at the time of tests. Inconclusive studies also exist and the overall picture of glucose effects on cognition remains enigmatic.

Cognition represents a complex and multidimensional set of abilities. Validated tests assess specific dimensions of 'intelligence'. Memory, reasoning, attention and psycho–motor coordination are only a few of the functions that contribute to mental ability. Memory itself is a complex set of processes (visual, spatial, verbal, short-term, long-term, etc.) that can be investigated using very different tools.

In addition to the fundamental complexity of mental functions, intellectual performance under specific test conditions depends on multiple factors, amongst which are individual ability, motivation, general arousal, previous learning, fatigue, time of day, etc. Nutritional factors play a demonstrated role in mental test performance under particular conditions: for example, vitamin-deficient subjects, such as undernourished children, display poor performance in mental tests such as non-verbal intelligence quotient and supplementation is likely to improve their scores. The impact of nutritional factors on mental performance in well-nourished individuals is more difficult to demonstrate. Given the large number of factors that potentially affect mental responses, however, it is not surprising that the beneficial effect attributed to glucose ingestion is neither consistently nor universally reported.

Typically, studies of glucose effects investigate several aspects of post-ingestive mental performance and use a battery of tests. Most report significant effects on some measures, and non-significant effects on other measures, in the same subjects. Obviously, cognitive processes are not equally sensitive to enhancement following a given load of glucose. Positive effects on short-term memory have been reported often (for example, Manning *et al.* 1997; Korol & Gold, 1998) and other benefits have been demonstrated on rapid information processing, performance on the Stroop test, word recall, focused and sustained attention, maze learning, arithmetic ability (Benton *et al.* 1987, 1994), long-term free and cued recall tasks (Foster *et al.* 1998), etc. Among negative results, glucose produced no effect on digit span measures (Gonder-Frederick *et al.* 1987), digit recall or long-term non-verbal memory (Foster *et al.* 1998).

The rise in blood glucose that follows a glucose drink correlates with improved decision time in a reaction time task, faster information processing, better word recall, and improvement on a cognitive conflict task (Benton & Owens, 1993). This effect is not due to the correction of hypoglycaemia, since it is reproduced across a range of baseline blood glucose levels. Hypoglycaemia, however, is associated with slower reaction times. A study carried out in eighty adults confirmed that a glucose drink improved performance on a memory test and that performance was positively associated with the blood glucose level (Martin & Benton, 1999). Glucose also improves memory in patients with Down's syndrome (Manning *et al.* 1998) and Alzheimer's disease (Craft *et al.* 1992, 1996; Messier & Gagnon, 1996).

In type 2 diabetes mellitus, cognitive impairments are sometimes reported, including selective attention deficits, verbal and visuo–spatial memory deficits. Cognitive deficits in patients with poor glucose tolerance are not necessarily permanent correlates of the condition, but can be reversed by short-term (1–2 months) treatment with oral hypoglycaemic agents (Gradman *et al.* 1993). These observations suggest that at least some cognitive impairment is associated with ongoing glucose regulatory status rather than permanent anatomical functional alterations produced by diabetes. Impaired glucose tolerance has been identified as a predictor of cognitive impairment with age (Vanhanen *et al.* 1998).

In healthy subjects, variations in normal glucose regulation capacity could also affect mental functions. This has been investigated in a sample of elderly individuals on the basis of a glucose recovery index. Several cognitive tasks were affected in subjects with poor glucose control relative to subjects with good glucose control (Messier *et al.* 1997). In young healthy volunteers, glucose regulation capacity again appeared a good predictor of memory performance (Messier *et al.* 1999). Individuals with poor glycaemic control had impaired immediate and delayed memory for words as compared with controls, but this difference disappeared after the subjects were given a 50 g glucose load.

The mechanisms mediating the memory-enhancing properties of glucose are not elucidated at the present time. They could include both peripheral and central processes. In particular, glucose could act as a cholinergic agonist and as an opioid antagonist (Rodriguez *et al.* 1999) or else via its effects on insulin (Craft *et al.* 1994; Hoyer, 1997).

The study by Green *et al.* (2001) in the present issue of the *British Journal of Nutrition* presents changes in mental performance that are not correlated with the level of glycaemia, but that appear affected to some extent by expectancy effects after the subjects had ingested glucose. Although the classic correlation between blood glucose and cognitive performance was not reproduced in this study, improved responses occurred after the intake of glucose, but not after intake of the placebo. Thus, the data are not inconsistent with the previous literature, but they suggest the hypothesis that cognitive factors, such as subjects' expectancies, beliefs and attitudes, could modulate mental performance after a change in glycaemic status. This hypothesis is consistent with an abundant literature demonstrating potent effects of cognitive set in various areas of behaviour.

The question of the differential susceptibility of mental functions to the effects of glucose remains open. Recent studies suggest that the degree of cognitive demand or mental effort required by a task may predict its susceptibility to enhancement by glucose and other metabolic substrates (Donohoe & Benton, 1999; Kennedy & Scholey, 2000). Demanding mental tasks are improved following a glucose load as compared with a placebo. Easy tasks are not affected. The amount of cognitive load associated with task performance could be an index of its sensitivity to enhancement by glucose. In a reciprocal manner, blood glucose level decreases more rapidly while a subject is performing a more demanding mental task, as compared with an easier one. A period of intense cognitive processing leads to a measurable decrease in levels of peripherally measured blood glucose.

The evidence in this field supports the notion that raising the level of glycaemia can facilitate some aspects of mental performance although much research remains to be performed in order to elucidate the mechanisms involved and the selective nature of glucose effects on certain types of mental responses. The impact of cognitive factors, such as expectancy, also remains to be investigated under a variety of experimental conditions.

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