Review Article

The influence of carbohydrate on cognitive performance: a critical evaluation from the perspective of glycaemic load

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(Received 29 April 2008 – Revised 1 December 2008 – Accepted 2 December 2008 – First published online 12 March 2009)

Links between nutrition and cognition are widely acknowledged. Within the context of short-term cognitive performance, carbohydrate has been the dietary component most commonly investigated. The majority of studies investigating the influence of carbohydrate on cognitive performance have employed oral glucose drink interventions followed by measures of performance on cognitive tests. More recently, studies have investigated the effect of different carbohydrates on cognitive performance rather than just pure glucose drinks. To date, studies have not been evaluated based on a standardised measure of glycaemic response, such as glycaemic load. The present review provides a critical evaluation of eight studies that have explored the relationships between food carbohydrate and cognitive performance and allow glycaemic load to be used as a basis for comparison. The key finding is that these provide insufficient evidence to support a consistent effect of glycaemic load on short-term cognitive performance. Future studies should employ consistent test methodologies and describe food interventions in more detail to facilitate meaningful comparisons and interpretations of results.

Carbohydrate: Glycaemic load: Glycaemic index: Cognitive performance

The principle that foods can reliably modulate cognitive performance is receiving validation and experimental support(1–3). As a consequence, the link between nutrition science and cognitive psychology is developing rapidly. Since glucose is the primary breakdown product of carbohydrate and the primary source of energy for the brain, its influence on cognitive performance has been the focus of much of the research in this area(1,4–6). The majority of studies investigating the link between glucose and cognitive performance have employed placebo-controlled oral glucose drink interventions followed by performance measures on behavioural tests (for example, memory, attention) with or without accompanying blood glucose measures(7–9). Administration of cognitive test batteries is commonly accompanied by measures of subjective states using visual analogue rating scales(1,3). Although the evidence is not consistent, a number of studies have reported beneficial effects of glucose on performance measures, in particular on delayed verbal memory(10).

More recently, studies have investigated the effect of different carbohydrates on cognitive performance rather than just pure glucose drinks. Food interventions are typically described using terms such as glycaemic index (GI), glycaemic load (GL), the ratio of slowly to rapidly available glucose, the proportion of simple to complex carbohydrate, or the amount of rapidly v. slowly digested carbohydrate. Although more ecologically valid than pure glucose manipulations, different expressions used for the glycaemic potency of interventions render a direct comparison of results between studies difficult.

Both the quality (for example, type, nature, source) and quantity of a carbohydrate are important determinants of its glycaemic response. As the GI by definition compares equal quantities of available carbohydrate, it provides a measure of carbohydrate quality not quantity(11,12). The GL is the product of a food’s GI and the amount of carbohydrate per serving(13). GI imparts information about carbohydrate quantity and reflects the glycaemic response of actual food portions. In healthy individuals, stepwise increases in GL have been shown to predict stepwise elevations in postprandial blood glucose and/or insulin response to specific foods(14).

Although a number of cognition studies have employed different carbohydrate interventions, these have not been evaluated based on a standardised measure of glycaemic response. The present review critically examines studies that have

Abbreviations: GI, glycaemic index; GL, glycaemic load.
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explored the relationships between carbohydrate and cognition, from the perspective of GL as a basis for comparison.

Methodology

We first carried out an inventory of the literature to identify studies that examined effects of ingestion of foods of specific carbohydrate type on cognitive performance. The following were used as key words in PubMed: 'glyc(a)emic index', 'glyc(a)emic load', 'glyc(a)emic response', 'breakfast* [not] program*', 'carbohydrate*', 'GI', 'GL', and 'cognition', 'cognitive performance', 'cognitiveS', 'memory', 'attention'. Relevant studies cited in review articles and in papers found in PubMed were also examined. Human studies were included if the GL of interventions being compared was stated, or where there was sufficient information from which the GL of interventions could be reliably calculated, and the study included objective measures of cognitive performance. Studies that measured subjective states only (for example, mood, fatigue) or that used non-energy placebo interventions were excluded.

Where GL data were not already stated in the original publications, these were calculated as a product of the GI of interventions employed and amount of available carbohydrate per serving: \( GL = (GI \times \text{carbohydrate (g)})/100 \). This allowed us to evaluate studies on cognitive performance from the perspective of GL.

Results and discussion

Eight studies were identified based on inclusion criteria (Table 1). Three studies were conducted in children (15–17) and three in young adults (18–20). Two were conducted in elderly subjects (21,22) of which the latter included type 2 diabetics. An overnight fast was employed in all studies. Five of the eight studies meeting the inclusion criteria used a within-subject design; three used a between-subject design. None of the studies reported whether physical activity levels or evening meals the day before test days were controlled for. In total, sixteen cognitive tests were employed. Tests involving word list recall, used as a measure of verbal episodic memory, were used most frequently (Table 1). In addition, tests of selective attention, spatial memory and immediate memory were used. In all studies, except one, cognitive testing commenced between 15 and 60 min post-interventions. In one study (16), cognitive testing began between 110 and 180 min post-interventions. In two studies, meal interventions were described in terms of \( GL^{16,20} \). For five studies, GL values were calculated (17–19,21,22) and for one (15) GL values were estimated from international GI/GL tables (23). Of the five studies in which GL values were calculated, four documented the GI of food interventions (17–19,21) and GI values (estimated) from the fifth were provided by the authors of the original publication (22). The GL values of interventions ranged from 3 to 71 (Table 1).

Thus, eight studies were compared based on GL. In one study, there was no effect of three different test foods (GL 18 v. 59 v. 71) unless controlling post hoc for \( \beta \) cell function (21). In another (GL 28 v. 50), performance on three memory tests (digit span and delayed word list and paragraph recall) was significantly better in the condition with the lower absolute GL (22). However, this finding should be interpreted with caution as the study was conducted in elderly diabetics and might not be directly applicable to healthy subjects. Furthermore, the magnitude of the difference between absolute GL values of the conditions used is similar to that in the Kaplan et al. study (21) wherein no differential effects were reported in healthy elderly subjects.

Of the studies conducted in healthy young adults, breakfasts high in slowly available glucose (GL 44) had a positive effect on verbal memory compared with breakfasts high in rapidly available glucose (GL 66) (18,19). Although in both studies the effect on memory was reported similarly (namely combined scores for immediate and delayed recall), it is interesting to note that two interventions with similar GL (44 v. 66) elicited differential effects on memory recall. Furthermore, in the latter study (19), the memory effects were only observed in subjects who had consumed alcohol the previous evening. It is unclear why this is the case. Whereas alcoholic beverage consumption has been shown to lower postprandial glycaemia before and during a meal (24), in the Benton & Nabb study (19) alcohol consumed the previous evening did not influence blood glucose levels the following morning. One explanation could be that beneficial effects observed may relate to relief of hangover or withdrawal effects of alcohol rather than to a beneficial effect of one breakfast per se.

In the third study in young adults investigating the effect of eight different breakfasts on performance (insufficient information presented to provide a reliable estimate of GL of the individual conditions), subjects with better glucose tolerance performed better on a memory task but worse on a vigilance task following a lower-GL meal (20).

However, it is important to note that an arbitrary cut-off (5 mmol/l) for fasting blood glucose was used to define whether subjects had poorer or better glucose tolerance, to provide an adequate sample size for statistical purposes. This is not aligned with international criteria used to define glycaemic states (25). Further, a between-subject design was employed.

Of the studies conducted in children, a positive effect on memory was reported in a lower-GL breakfast cereal condition (GL 7) compared with a higher-GL breakfast cereal condition (GL 23). This effect was based on combined scores from several memory tests (17). A second study showed that two different breakfast cereals (GL 15) both prevented a decline in memory over the course of the morning compared with a glucose drink and fasting conditions (15). The effect was found on a factor score composed of several memory tests. In a third, no effect on memory was reported when three different test foods (GL 3 v. 12 v. 18) were compared (16). It is interesting to note that the GL values of two conditions of the latter study (GL 12 and 18) are within a similar range to the GL in the two former studies, wherein positive effects on memory were reported (15,17).

Of the five studies that measured attention, all three studies in children indicated a positive influence of lower-GL breakfasts on cognitive performance. One reported a positive effect of two breakfast cereals (GL 15) (15) and another reported a positive effect on a lower GL intervention (GL 7) (17), both effects were based on factor scores composed of several attention tests. In a third study in children, in-depth
### Table 1. The influence of glycaemic load (GL) on cognitive performance

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample</th>
<th>Design</th>
<th>Carbohydrate intervention</th>
<th>GI</th>
<th>GL</th>
<th>Blood glucose sampling</th>
<th>Domain</th>
<th>Test</th>
<th>Timing of tests post-food</th>
<th>Findings and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elderly</strong></td>
<td></td>
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<tr>
<td>Kaplan et al. (21)</td>
<td>Elderly</td>
<td>WS</td>
<td>Lemon beverage containing 50 g glucose</td>
<td>142</td>
<td>71</td>
<td>Baseline, 15, 60, and 105 min</td>
<td>Episodic memory</td>
<td>Immediate</td>
<td>WLR</td>
<td>15, 60, 105 min</td>
</tr>
<tr>
<td></td>
<td>Elderly</td>
<td>WS</td>
<td>50 g available carbohydrate from instant mashed potatoes</td>
<td>118</td>
<td>59</td>
<td>Delayed</td>
<td>Visuomotor</td>
<td>PR</td>
<td>Trails/B</td>
<td>Poor β cell function predicted greater improvements in performance after the foods</td>
</tr>
<tr>
<td></td>
<td>Elderly</td>
<td>WS</td>
<td>50 g available carbohydrate from pearled barley</td>
<td>36</td>
<td>18</td>
<td>Selective attention</td>
<td>Counting words or names while watching a videotape game</td>
<td></td>
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<tr>
<td><strong>Papakonou et al. (22)</strong></td>
<td>T2D</td>
<td>WS</td>
<td>50 g available carbohydrate from a low-GI meal: pasta (42.5 g) with tomato sauce (6 g) and cheese (1.5 g)</td>
<td>55</td>
<td>28</td>
<td>5, 15, 62, 100, 138 min</td>
<td>Episodic memory</td>
<td>Immediate</td>
<td>WLR</td>
<td>15, 62, 100 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50 g available carbohydrate from a high-GI meal: white bread (42.5 g) with tomato sauce (6 g) and cheese (1.5 g)</td>
<td>100</td>
<td>50</td>
<td>Delayed</td>
<td>Semantic memory</td>
<td>PR</td>
<td>VPS from WMS</td>
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<td></td>
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<td>250 ml water (control)</td>
<td>–</td>
<td>–</td>
<td>Selective attention</td>
<td>Task from test of everyday attention</td>
<td>Trails A/B</td>
<td>Performance on delayed WLR, PR and digit span better after the pasta (GL 28) compared with the white bread (GL 50) treatment No difference between pasta and white bread treatments on other tests</td>
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<tr>
<td><strong>Young adults</strong></td>
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<tr>
<td>Benton et al. (18)*</td>
<td>Young adults</td>
<td>BS</td>
<td>50 g high-SAG biscuit containing 34 g carbohydrate of which the glycaemic fraction is 28 g</td>
<td>42</td>
<td>12</td>
<td>Baseline, 30, 60, 90, 120, 150, 180, 210 and 240 min</td>
<td>Episodic memory</td>
<td>Immediate</td>
<td>WLR</td>
<td>30, 90, 150, 210 min</td>
</tr>
<tr>
<td></td>
<td>Young adults</td>
<td>BS</td>
<td>50 g high-RAG cereal bar containing 31 g carbohydrate of which the glycaemic fraction is 21 g</td>
<td>66</td>
<td>14</td>
<td>Delayed</td>
<td>WLR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>Sample</td>
<td>Design</td>
<td>Carbohydrate intervention</td>
<td>GI</td>
<td>GL</td>
<td>Blood glucose sampling</td>
<td>Domain</td>
<td>Test</td>
<td>Timing of tests post-food</td>
<td>Findings and comments</td>
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<tr>
<td>Benton &amp; Nabb (19)†</td>
<td>Young adults</td>
<td>BS</td>
<td>50 g biscuits containing 34 g carbohydrate of which glycaemic fraction is 27 g (SAG breakfast)</td>
<td>42</td>
<td>11</td>
<td>20, 50, 80, 140, 200, 230, 260, 310, 380 and 410 min</td>
<td>Episodic memory</td>
<td>Immediate</td>
<td>WLR</td>
<td>30, 90, 150, 210, 270, 330, 390 min</td>
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<tr>
<td></td>
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<td></td>
<td>49 g breakfast cereal containing 34 g carbohydrate of which glycaemic fraction is 21 g (Choco-Krispies) (RAG breakfast)</td>
<td>66</td>
<td>14</td>
<td></td>
<td></td>
<td>Delayed</td>
<td>WLR</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td>49 g breakfast cereal containing 34 g carbohydrate of which glycaemic fraction is 21 g (Coco-Pops) (RAG breakfast)</td>
<td>NS</td>
<td>NC</td>
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<tr>
<td>Nabb &amp; Benton (20)‡</td>
<td>Adults</td>
<td>BS</td>
<td>Eight breakfasts varying in macronutrient content and GL</td>
<td>GI range 50–90</td>
<td>GL range 12–53</td>
<td>Baseline, 20, 50, 95, 140 min</td>
<td>Episodic memory</td>
<td>Immediate</td>
<td>WLR</td>
<td>30, 75, 120 min</td>
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<td></td>
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<td>Fasting condition</td>
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<td></td>
<td>Delayed</td>
<td>WLR</td>
<td></td>
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<tr>
<td>Ingwersen et al. (17)</td>
<td>Children</td>
<td>WS</td>
<td>35 g All Bran breakfast cereal with semi-skimmed milk</td>
<td>42</td>
<td>7</td>
<td>Not measured</td>
<td>Episodic memory</td>
<td>Immediate</td>
<td>WLR</td>
<td>10, 70, 130 min</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>35 g Coco Pops breakfast cereal with semi-skimmed milk</td>
<td>77</td>
<td>23</td>
<td></td>
<td>Episodic memory</td>
<td>Delayed</td>
<td>WLR</td>
<td></td>
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<td></td>
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<td></td>
<td>Selective attention</td>
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<td>Picture recognition</td>
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<td></td>
<td>Detection task</td>
<td>(visual digits)</td>
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</tbody>
</table>
Table 1. Continued

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample Design</th>
<th>Carbohydrate intervention</th>
<th>GI</th>
<th>GL</th>
<th>Blood glucose sampling</th>
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<th>Findings and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wesnes et al. [15][§] Children 14 M 15 F 9–16 years Mean 12 years</td>
<td>WS</td>
<td>30 g breakfast cereal with milk containing 29 g total carbohydrate including 16 g as complex carbohydrate (Cheerios) 45 g breakfast cereal with milk containing 38 g total carbohydrate including 25 g as complex carbohydrate (Shreddies) Orange-flavoured glucose drink containing 38 g of carbohydrate as glucose</td>
<td>NS 15</td>
<td>Not measured</td>
<td>Episodic memory Immediate Delayed Selective attention</td>
<td>WLR SR WLR</td>
<td>0, 60, 120, 180, 240 min</td>
<td>Breakfast cereal conditions reduced declines in attention over the morning by more than half, and prevented the decline altogether for immediate word recall</td>
<td></td>
</tr>
<tr>
<td>Benton et al. [16] Children 10 F 9 M Mean 6 years</td>
<td>WS</td>
<td>25 g cornflakes, 115 ml semi-skimmed milk, two spoons sugar, one waffle, one tablespoon maple syrup 60 g scrambled egg, one slice bread, 8 g low-fat spread, 10 g jam, 125 g low-energy yoghurt 30 g ham, 40 g cheese, 30 g bread, 8 g low-fat spread</td>
<td>– 12 3</td>
<td>Not measured</td>
<td>Episodic memory Immediate Delayed Sustained Reaction to frustration</td>
<td>Picture recall SR SR Difficult video game (ten sessions)</td>
<td>110–180 min</td>
<td>Performance on half of the trials of the difficult video game was poorer in those who had consumed the cornflakes breakfast (GL 18) but not the other breakfasts When eating the ham and cheese breakfast (GL 3), significantly more time was spent working on the classroom task at hand compared with the other breakfasts</td>
<td></td>
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</tbody>
</table>

GI, glycaemic index; M, males; F, females; WS, within-subject; WLR, word list recall; PR, paragraph recall; Trails/B, trail making part B adult form; T2D, type 2 diabetics; VPS, verbal paired associates; WMS, Wechsler Memory Scale; Trails A/B, trail making part A and B adult form; BS, between-subject; SAG, slowly available glucose; RAG, rapidly available glucose; NS, not specified; NC, not calculated; RIPT, rapid information processing task; SR, spatial recall; NWM, numeric working memory.

* GL values were calculated as a product of the GI and the glycaemic fraction (sum of SAG and RAG). Other tasks were performed but their results were not reported.
† An arbitrary cut-off of 5 mmol/l (fasting blood glucose) was used to define ‘good’ and ‘poor’ glucose regulators. Given that the data were presented from the perspective of macronutrient compositions, it is difficult to provide a reliable interpretation of results in terms of GL. With regard to the vigilance test, ten cases were removed from the sample as they had responded in an indiscriminate way and produced a long series of errors. The results of simple and choice reaction times of the vigilance task were not reported.
‡ Published GI values were based on breakfast cereals consumed with 250 ml milk. Results pertain to factor scores. All data from individual tests were not presented.
(correlation) analyses indicated that those consuming a lower GL were less likely to display lapses of attention\(^{(16)}\). Furthermore, when performance on a commercial video game was compared between three test foods (GL 3 v. 12 v. 18), performance was reportedly lower following one of the test foods (GL 18) but not the other two\(^{(16)}\). The two further studies performed in an elderly population reported no differential effects of GL on attention\(^{(21,22)}\).

Besides memory and attention, almost no other tests were used in these studies. Effects of GL on other cognitive domains such as executive function remain unstudied. Indeed, many tests were selected without a clear rationale, and in four of the eight studies included in the present review, cognitive data from at least one test were not reported or not alluded to\(^{(15,18–20)}\). One study, conducted with children, also monitored childhood behaviour as perceived by teachers as a subjective measure of cognitive performance\(^{(16)}\). In the lowest GL condition (GL 3), more time was spent working on a classroom task at hand compared with two other conditions (GL 12 and 18).

Five studies included blood glucose measures. In two of the studies that reported a beneficial effect on memory, blood glucose levels had returned to baseline before a treatment effect was observed\(^{(18,19)}\). In addition, in three studies without blood glucose measures\(^{(15,16,22)}\), cognitive effects were mostly reported between 2 and 4 h after the intervention, which is probably also after the return of blood glucose levels to baseline. In the study by Kaplan et al.\(^{(21)}\), overall performance did not differ with consumption of the different test foods, all of which elicited significant differences in glucose response curves. Findings such as these indicate that blood glucose per se might not be a reliable biomarker of performance measures, and question the traditional and intuitively appealing hypothesis that ingested glucose improves memory by directly increasing uptake of glucose to the brain.

In the study by Kaplan et al.\(^{(21)}\), inter-individual differences in glucose tolerance have been posited as important in mediating nutritional effects on cognitive function. Elderly subjects have been shown to have poorer glycoregulatory control than young subjects which may account for memory enhancement following a glucose drink in elderly subjects compared with younger counterparts\(^{(15,18–20)}\).

In the study by Kaplan et al.\(^{(21)}\), in the present review, poor β cell function predicted improvements in memory performance of healthy elderly subjects. Differences in glycaemic response between children and adults are also worthy of consideration. However, there appears to be no published studies that allow objective comparison of glycaemic response between these two population samples.

Taken together, these results show that there is insufficient evidence to support a consistent effect of GL on short-term cognitive performance. There are several factors to bear in mind when interpreting these findings. First, a small number of studies with non-homogeneous population samples met the criteria for which behavioural measures could be compared based on GL. Second, there is a considerable amount of inter-study methodological variability. Moreover, there appears to be a lack of a compelling mechanistic hypothesis upon which GL might affect behaviour.

As apparent from Table 1, there is a considerable amount of inter-study methodological variability with regard to dietary restrictions the day before testing, the use of between- or within-subject design, the cognitive domain examined, the number and type of cognitive tasks in a given test battery, the temporal distribution of cognitive tests, and the temporal distribution of blood sampling. This variability serves to complicate direct comparisons of results across studies. Indeed, inter-study variability in methodological designs is frequently acknowledged as an inherent source of uncertainty when interpreting results within the general realm of nutrition and cognitive performance\(^{(4,6,27,28)}\). Furthermore, it is unclear whether glucose activity or the composition of food consumed the evening before testing was controlled for, both of which could influence glycaemic responses\(^{(29)}\). Meals with a low GI produce better glucose tolerance the following morning compared with evening meals of a high GI\(^{(30,31)}\), and acute physical exercise can increase muscle uptake on the following day\(^{(32)}\). As a compromise between the need to minimise respondent burden and the need to impose strict standardisation procedures before the test day, it is generally recommended that the same meal of choice be consumed the evening before each test day, and to avoid rigorous physical activity\(^{(20)}\).

Despite methodological differences in the studies reviewed, the results described above allow us to speculate on the involvement of various physiological processes in the observed cognitive effects.

The capacity of the brain to store energy is limited and is strictly regulated within narrow boundaries\(^{(33)}\). Further, as brain activity is unaffected by variation in brain extracellular glucose levels (except in the case of extreme hypoglycaemia), changes in brain extracellular glucose following changes in blood glucose are unlikely to affect overall brain function\(^{(5)}\).

In light of this, several hypotheses by which glucose might influence cognitive function have been proposed\(^{(5,34)}\). There is convincing evidence that astrocytes might play an important role in energy regulation. These star-shaped glial cells, which surround neurons and lie in close proximity to the cerebral vasculature, are believed to constitute a likely site of glucose uptake as it crosses the blood–brain barrier\(^{(35)}\). It is hypothesised that during neuronal activation, glucose is taken up by astrocytes, converted into lactate (by glycolysis), which is then released into the extracellular space to be taken up as an energy substrate by neurons\(^{(36)}\). The discovery of monocarboxylate (for example, lactate) transporters on both astrocytes and neurons\(^{(37)}\) lends support for this hypothesis.

As many of the brain’s neurotransmitters are derived from glucose metabolism (for example, acetylcholine is derived from acetyl CoA, γ-aminobutyric acid (GABA) is derived from glutamate), glucose may also influence cognitive function by enhancing neurotransmitter synthesis during periods of neuronal activity\(^{(38)}\). It has been hypothesised that neurons rely on glial supplies of tricarboxylic acid intermediates for this process\(^{(34)}\).

A proposed peripheral action of glucose on memory could involve a neural signal triggered when glucose is transported into cells\(^{(5)}\). This supposition is supported by the fact that peripheral injection of fructose, a monosaccharide sugar which does not cross the blood–brain barrier, and which does not elicit a significant rise in blood glucose, was shown to improve memory in rats\(^{(39)}\). Further, injection of 3-O-methylglucose, a glucose analogue which has the same affinity for glucose transporters, but which is not metabolised once inside cells, was also shown to improve memory in rats\(^{(39)}\).
GL is influenced by several factors that relate to the food itself (i.e. food components such as the nature of starch, content of fat, protein and fibre), eating behaviour (i.e. rate of ingestion, frequency of food intake, composition of a meal) and physiological factors (i.e. gastric emptying rate, intra- and inter-individual variation in glycaemic response and hormonal responses). It is plausible that hormonal responses in particular have the potential to affect brain function and behaviour either through peripheral or central mechanisms. A vagotomy in rats was shown to attenuate memory-enhancing effects of peripherally injected peptide hormones, suggesting that gastrointestinal hormones could activate a detection mechanism which could relay neural signals to the central nervous system to influence cognitive processes. Recent evidence suggests that circulating ghrelin crosses the blood–brain barrier from the periphery where it binds to neurons, alters neuronal morphology, and affects the generation of long-term potentiation and behavioural outputs.

Insulin also crosses the blood–brain barrier from the periphery; improvements in cognitive function have been observed following the infusion of insulin in healthy adults. The corticosteroid hormone cortisol has also been suggested as a potential mediator of an association between glucose and cognition. Receptors binding cortisol are abundant in the hippocampus, a brain region strongly implicated in delayed memory, and there is evidence from both animal and human studies that glucocorticoids (for example, cortisol) influence memory. However, as several gastrointestinal hormones are typically released in response to food consumption, it is unclear to what extent all of them would exert an effect simultaneously.

Besides these, other factors could influence cognitive performance via an indirect effect on blood glucose or otherwise. Circulating glucose is higher after a palatable meal than after a meal composed of the same constituents presented in a non-palatable form. Furthermore, potential fluctuations in performance due to fatigue, hunger, physical discomfort, changes in mood and motivation are also acknowledged. Thus, cognitive testing should ideally be accompanied by subjective measures of some or all of these states. As subjective evaluations of performance can interact with expectations and compensatory effort, these should ideally be measured as well.

Whereas a general consensus on likely underlying mechanisms appears far from being attained, the above-mentioned hypotheses and confounding factors illustrate that there is not a clear-cut relationship between glycaemic response, brain glucose and performance measures. This may account, at least in part, for an inconsistent effect of GL on short-term cognitive performance observed in the present review. Furthermore, studies investigating the effect of carbohydrate at the psychophysiological level using event-related potentials have not been able to provide further insights to help understand behavioural outcomes.

To our surprise, few studies fulfilled the criteria to allow a comparison of performance measures from the perspective of GL. Of the studies selected based on our search criteria, two were excluded as both employed non-energy placebo-controlled interventions for comparisons. In addition, two were excluded as interventions were described as having a high or low GI without specifying the absolute values, and there was insufficient product information documented to allow a reliable estimation of their GI from international tables.

Nevertheless, it is interesting that the results of the two latter studies indicate evidence of a beneficial effect of an oatmeal breakfast cereal (low to medium GI) compared with a ready-to-eat breakfast cereal (high GI) on tests of immediate memory (backward digit span only; in girls but not in boys) and on tests of attention. The beneficial effect on attention was only detected in two of four outcome measures of the auditory version of an attention test, not in a visual version.

The GL values estimated in the present review represent the best possible estimate based on available information. Whereas information on GI values (In the majority of studies, GI values were predicted from international tables. In some studies, it was not apparent whether GI values were predicted or measured) and available carbohydrate content were provided in the majority of studies, in some cases, GL values were predicted from international GI/GL tables. In one study, GL values were calculated based on the amount of carbohydrate rather than the amount of available carbohydrate per se, an effect that could result in overestimation of GL values. In addition, the mode of expression of available carbohydrate is a source of variation between studies.

Finally, the above-mentioned studies refer to acute interventions. The extent to which any beneficial cognitive effects reported would persist following habitual consumption over a longer period is less clear. To date, few studies have investigated the effects of longer-term consumption of carbohydrate on cognitive performance. One study investigated the effect of 14 d consumption of inulin compared with a placebo in healthy adults. No differential effects on attention were found. In another, saccharide intake (estimated using a 3 d food diary) was positively correlated with verbal memory recall in middle-aged adults and, in a third, saccharide intake (as assessed by FFQ) was related to better self-reported memory functioning, after controlling for health and demographic factors.

**Conclusion and recommendations**

At present, there is insufficient evidence to demonstrate a consistent directional effect of GL on short-term cognitive performance. Future studies should employ consistent methodologies to facilitate meaningful comparisons and interpretation of results. Such methodologies should include, as a minimum, a clear rationale for the selection of a given cognitive domain and/or test, sufficient detail about the carbohydrate composition (for example, GI, specification of carbohydrate type and supplier if possible) to allow reliable estimation of glycaemic response of the interventions employed, more transparency with regard to reporting of pre-test day standardisation procedures and more transparency when reporting results. Further, studies should include consideration of mechanistic hypotheses with respect to rationales and interpretation of results. This would facilitate comparison of findings across studies and help towards elucidation of underlying mechanisms to provide more robust scientific substantiation of claims in this area.

**Acknowledgements**

The present review was supported by Unilever, which has an interest in developing food products to improve cognitive...
References


