

The effect of beverages varying in glycaemic load on postprandial glucose responses, appetite and cognition in 10–12-year-old school children

Emily Brindal^{1*}, Danielle Baird¹, Amy Slater², Vanessa Danthiir¹, Carlene Wilson³, Jane Bowen¹ and Manny Noakes¹

¹CSIRO Food and Nutritional Sciences, PO Box 10041, Adelaide BC, SA 5000, Australia

²Flinders University, Adelaide, SA, Australia

³Cancer Council South Australia and Flinders Centre for Cancer Prevention and Control, Flinders University, Adelaide, SA, Australia

(Submitted 10 April 2012 – Final revision received 20 September 2012 – Accepted 30 October 2012 – First published online 19 December 2012)

Abstract

Reducing glycaemic index (GI) and glycaemic load (GL) inconsistently improves aspects of cognitive function and appetite in children. Whether altering the GL by lowering carbohydrate relative to protein and fat has a role in these effects is unknown. Therefore, we assessed the differential effects of beverages varying in GL and dairy composition on appetite, energy intake and cognitive function in children. A total of forty children (10–12 years) completed a double-blind, randomised, crossover trial, receiving three isoenergetic drinks (approximately 1100 kJ): a glucose beverage (GI 100, GL 65), a full milk beverage (GI 27, GL 5) and a half milk/glucose beverage (GI 84, GL 35). For 3 h post-consumption, subjective appetite and cognitive performance (speed of processing, memory, attention and perceptual speed) were measured hourly. At completion, each child was provided a buffet-style lunch and energy intake was calculated. Blood glucose was objectively measured using the Continuous Glucose Monitoring System. Blood glucose AUC values were significantly different between the drinks ($P < 0.001$), but did not sustain above the baseline for 3 h for any drink. Mixed modelling revealed no effect of beverage on subjective appetite or energy intake. Participant sex and drink GL significantly interacted for short-term memory ($P < 0.001$). When girls consumed either milk-containing beverage, they recalled 0.7–0.8 more words compared with 0.5 less words after the glucose drink ($P \leq 0.014$). Altering GL of drinks by reducing carbohydrate and increasing protein did not affect appetite or cognition in children. Girls may demonstrate improved short-term memory after consuming beverages with higher protein and lower GL.

Key words: Cognition: Children: Satiety: Glycaemic load

Meta-analysis comparing glucose doses relative to a placebo supports the existence of an acute 'glucose enhancement effect' on memory in adults⁽¹⁾. Despite limited evidence, the administration of glucose may also alter performance in other cognitive domains such as speed of processing^(2,3). It has been hypothesised that human glucose regulation systems are important mechanisms for these effects⁽⁴⁾. If this is the case, these effects may be more pronounced in children who have much faster glucose metabolism in the brain prior to adolescence⁽⁵⁾.

The glucose enhancement effect has generally been witnessed at 1 h post-consumption of a glucose beverage. However, recent research suggests that a more prolonged glucose response may have positive effects on sustaining cognitive performance. Consequently, multiple studies have explored how reductions in glycaemic index (GI) and

glycaemic load (GL) may enhance cognitive performance, with most focusing on the effect of breakfast on children's performance and/or behaviour^(6–9). Two studies have indicated that low-GI breakfasts have favourable effects on cognitive performance in children^(6,9). In both studies, results indicated that lower-GI breakfasts may be protective against a decline in memory and attention throughout the morning (over 2 h). Generally, studies of the effects of different types of breakfast on cognitive function are limited in number and vary in experimental methods employed^(10,11). Furthermore, existing research has been criticised for failing to match the energy contents of dietary manipulations, not collecting metabolic data and assessing only limited cognitive domains⁽¹¹⁾. Nonetheless, understanding potential influences on children's cognitive function remains a high priority, given its application to learning and achievement at school, which has been

Abbreviations: CGMS, Continuous Glucose Monitoring System; CSIRO, Commonwealth Scientific Industrial Research Organisation; DHNC, Dairy Health and Nutrition Consortium; GI, glycaemic index; GL, glycaemic load; HGL, high glycaemic load; LGL, low glycaemic load; T1, 60 min post-drink; T2, 120 min post-drink; T3, 180 min post-drink; VHGL, very high glycaemic load.

* **Corresponding author:** Dr E. Brindal, fax +61 8303 8899, email emily.brindal@csiro.au

Table 1. Nutrient profile of the intervention preload of the study drink conditions (treatment)

	Test drink		
	VHGL	HGL	LGL
Nutrient profile			
Energy (kJ)	1063	1083	1088
Protein (g)	0	7	13
Fat (g)	0	8	15
Carbohydrate (g)	65	42	19
Volume (ml)	455	455	455
Weight (g)	520	487	455
Glycaemic index	100	84	27
Glycaemic load	65	35	5
Ingredients			
Glucose (g)	65	32	0
Whole milk (g)	0	200	400
Water (g)	435	215	0
Flavouring (g)	20	40	55

VHGL, very high glycaemic load; HGL, high glycaemic load; LGL, low glycaemic load.

rated a primary concern for parents of primary school-aged children in Australia⁽¹²⁾.

In addition to any potential association between GI/GL and cognitive outcomes, low GI/GL could have the added advantage of keeping children feeling full. The glucostatic hypothesis suggests that carbohydrate is potentially implicated in the regulation of energy intake⁽¹³⁾. Throughout the post-breakfast period, low-GI meals, which prolong the release of glucose, may also be associated with decreased hunger and improved satiety. One review of the literature indicated that fifteen of sixteen studies suggested that lower GI is associated with lower hunger and/or greater satiety in adults⁽¹⁴⁾. In children, a low-GI relative to a high-GI breakfast has also been found to be related to lower pre-lunch hunger ratings and lower energy intake⁽¹⁵⁾.

Given the findings in the present literature and limited number of studies exploring the effects of different breakfasts on cognition and satiety, the present study was designed to assess differential effects of beverages varying in GL on appetite, energy intake and cognitive function in children. Glycaemic load (rather than GI) was the focus of the present trial, because it is more accurately associated with glycaemic response – the potential mechanism for cognitive effects. It was hypothesised that lower-GL beverages would be associated with improved cognitive performance. Given the literature suggesting that lower-GI foods are associated with greater satiety in adults, it was predicted that lower-GL breakfasts would be related to prolonged satiety throughout the morning. Finally, it was predicted that low-GL beverages would result in lower energy intake at a buffet lunch relative to a glucose drink.

Subjects and methods

Study design

The present study employed a randomised three-way repeated-measures crossover design. Delivery order of the different drinks was randomised using randomization.com

The dietary conditions varied in GL, which was manipulated through the addition of dairy milk to a pure glucose beverage

to create three conditions: very high glycaemic load (VHGL)-pure glucose; high glycaemic load (HGL)-half milk, half glucose; and low glycaemic load (LGL)-pure milk (Table 1). Dairy milk was used to manipulate GL because it contains a unique source of carbohydrate (lactose) which has a naturally low GI. As well as providing important micronutrients, dairy products are also a rich source of protein. Both lactose and protein have resulted in significantly higher feelings of satiety in obese adults⁽¹⁶⁾. Therefore, it is possible that the unique nutrient composition of dairy products is potentially beneficial for both children's cognitive performance and appetite.

The study was performed at the Commonwealth Scientific Industrial Research Organisation (CSIRO) clinical research unit in the September/October 2008 (*n* 20) and December/January 2008/2009 (*n* 20) school holiday periods. Written consent was provided by all participants and their caregiver(s). Ethical approval to complete the study was granted by the CSIRO Human Nutrition Research Ethics Committee. The trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12608000324314).

Study population

A total of forty children (twenty-one female, nineteen male) aged between 10 and 12 years (11.6 (SE 0.13) years) were recruited to participate in the randomised clinical trial. A majority of children (*n* 30, 75%) were classified to be of normal weight status for their age and sex, according to the International Obesity Taskforce grade⁽¹⁷⁾, with nine (22.5%) classified as overweight (Table 2). No sex differences were observed for age or anthropometric data. All children who started the trial completed it.

To be eligible for the study, children could not be on a prescribed diet, have a known allergy to dairy foods (or be lactose intolerant) or be diagnosed as having diabetes, learning difficulties or attention deficit hyperactivity disorder.

Table 2. Baseline characteristics of participants (*n* 40) (Mean values with their standard errors; number of participants and percentages)

	Mean	SE
Age (years)	11.6	0.13
Weight (kg)	44.82	1.47
Height (m)	1.52	0.012
BMI (kg/m ²)	19.2	0.44
Weight status*		
Thinness grade 1		
<i>n</i>	1	
%	2.5	
Normal weight		
<i>n</i>	30	
%	75.0	
Overweight		
<i>n</i>	9	
%	22.5	
Obese		
<i>n</i>	0	
%	0	

* Categorised using the international grade given by the International Obesity Taskforce⁽¹⁷⁾.

Procedure

Children attended the clinical research unit for over four consecutive days. The first of these was a familiarisation day, where children practised the cognitive tests, tasted a sample of the buffet lunch they had selected and had their glucose monitors fitted by a registered nurse.

For the next 3 d, children arrived in a fasted state at the clinical research unit between 07.45 and 08.00 hours (Fig. 1). From midnight prior to their arrival at the clinic, children and their caregivers were instructed to consume only water and to refrain from any rigorous exercise. Upon arrival, clinic staff confirmed participants' adherence to these instructions. A nurse then checked the site where the glucose monitor sensor had been inserted and attached the Continuous Glucose Monitoring System (CGMS) unit. Each day, the CGMS took 60 min to initialise. After this period, a blood glucose reading from a glucometer was required to calibrate the monitor. Then, two other finger pricks were taken throughout the testing day. This was the minimum number of finger pricks that could be used throughout testing for calibration of the CGMS. All calibrations were within the acceptable tolerance of the CGMS, according to manufacturer's standards.

Children completed baseline assessments of appetite and cognition through a computer-delivered battery during the 60 min CGMS initialisation period. Each time children completed this battery, tests appeared in the same order. Children took roughly 20 min to complete all sections.

After final CGMS initialisation, children were given a test drink and allocated 10 min to consume it. All test drinks were served in a concealed container with a black straw and identified as a 'milkshake'. On two occasions, the children failed to consume the glucose-only test drinks and data for these cases were excluded from all analyses. All other children completed the entire drink within the allocated time.

After consuming the test drink, cognitive and appetite measures were administered at each hour for 3 h. Approximately, 3.75 h after the consumption of the test drink, testing was concluded with the presentation of the buffet-style lunch. No time limit was imposed on the lunch. Children received the same buffet-style lunch each day and were asked to eat *ad libitum* until they were 'comfortably full'.

The buffet lunch consisted of de-crusteds sandwiches (seven per child) cut into bite-size portions, an 800 ml bowl of dessert and a bottle of water (500 ml). Prior to the study, children selected a preferred sandwich filling (matched on energy density) and either a custard or yoghurt for dessert. Variety within the lunch was limited to minimise any artificial increases in consumption⁽¹⁸⁾. Sandwiches were portioned and desserts were presented in a large bowl in an attempt to mask the amount consumed and minimise the tendency of the children to eat their usual quantity. All foods were offered simultaneously on a tray.

Children remained supervised by the research staff throughout the entire testing period. Caregivers were not present during the testing periods. Between testing points, quiet activities were provided to entertain children, including playing board games and watching short films.

Outcome measures

Blood glucose. MiniMed CGMS monitors (Medtronic Mini-Med, Inc.) were used to collect blood glucose values throughout the study periods. CGMS monitors use interstitial fluid to calculate blood glucose levels at every 10 s and store an average of these values at every 5 min⁽¹⁹⁾. Incremental AUC, peak blood glucose value (mmol), time to peak (min) and time taken to return to baseline (min) were calculated based on blood glucose data generated from the CGMS using the CGMS communication station to download data (MEDTRONIC MINIMED software 3.0C program, Medtronic Minimed, Inc.).

Cognitive constructs. A total of six cognitive constructs were assessed using individually completed tasks administered in a group setting (described in detail in the Supplementary Appendix A, available online). The constructs assessed were speed of processing, attention switching, perceptual speed, short-term and working memory and inspection time, and were designed to cover a range of areas potentially affected by the different breakfasts. At each testing session, a unique version of each test was presented in randomised order.

Appetite. Based on previous studies⁽²⁰⁾, a subjective appetite scale was used to assess children's appetite. This scale had four items: 'How hungry do you feel?', 'How satisfied do you feel?', 'How full do you feel?' and 'How much do you think

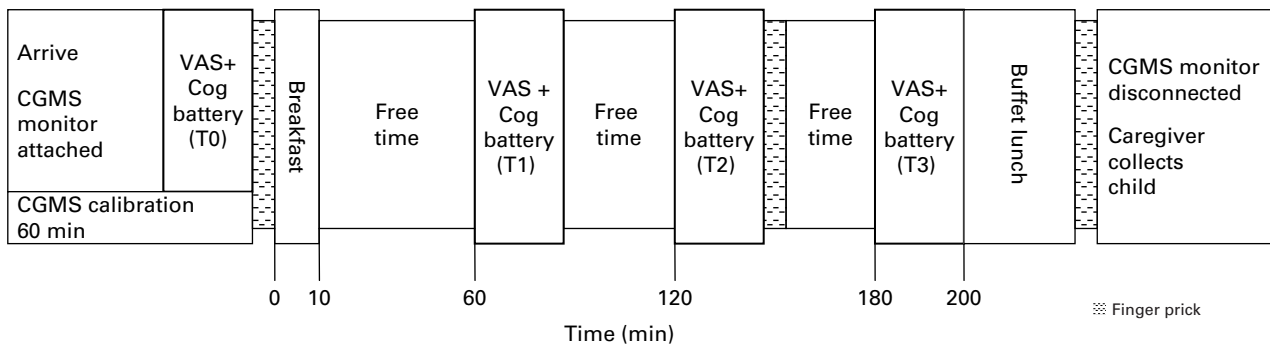


Fig. 1. Study protocol for each testing day. CGMS, Continuous Glucose Monitoring System; VAS, visual analogue scale; Cog, cognitive; T0, baseline; T1, 60 min post-drink, T2, 120 min post-drink; T3, 180 min post-drink.

you can eat?'. Each question was presented on a computer as a visual analogue scale. Opposing extremes were described at either end of a 100 mm horizontal line (e.g. 'not hungry at all' to 'never been more hungry'), and participants indicated their level of hunger by dragging the cursor to a point appropriate to how they felt at that moment. Scores for each item ranged from 0 to 100 (measured in mm).

Factor analyses revealed that these four items represented the same construct. Negatively worded items were reverse coded so that high scores on the composite measure represented high levels of appetite. Cronbach's α coefficients were 0.874–0.954 (across conditions), suggesting good internal consistency for the scale. Consequently, a total appetite score rating was created (minimum 0, maximum 400).

Energy intake at lunch. For each child and testing day, the amount eaten was calculated as the difference in the weight of each of the lunch items pre- and post-exposure to the buffet. Weight was then converted to an energy (kJ) value using FoodWorks (Xyris 5.0, 2007; Xyris Software Inc.).

Statistical analysis

All statistical analyses were performed using SPSS for Windows 16.0 (SPSS, Inc.). In order to test for differences between conditions, a maximum likelihood mixed-model using first-order autoregressive matrices was constructed. To test the hypotheses, test drink condition (VHGL; HGL; LGL) and testing session (60 min post-drink (T1); 120 min post-drink (T2); 180 min post-drink (T3)) were entered in the model as within-subjects variables. Preliminary analyses indicated some sex differences in the outcomes and, consequently, a two-way interaction between participant sex and drink condition was included in all models. These were the only two higher-order interactions considered in the model. Significant interactions were tested *post hoc* using pairwise comparisons with Bonferroni adjustments.

All models controlled for participant sex, BMI *z*-score, age and day of testing. Day of testing was a categorical variable, with three levels representing which day testing occurred on, and it was included to limit any potential effects of testing fatigue throughout the testing week. Relative glucose

tolerance was calculated using a median split of the blood glucose responses to the glucose drink and was entered into the analysis of appetite, cognition and energy intake, given the potential importance of glucose tolerance⁽²¹⁾. For outcomes where the score represented a change from baseline, baseline values were also included as covariates.

Results

Blood glucose

Descriptive data for each of the measurements of blood glucose can be seen in Table 3 and Fig. 2.

Differences between time to peak (min) for each drink condition were not significant ($F(2,34.2) = 1.97$, $P = 0.16$). Incremental AUC values ($F(2, 34.7) = 23.40$, $P < 0.001$) and peak values ($F(2,34.3) = 32.64$, $P < 0.001$) differed significantly between each drink condition. Values were in the direction expected according to their GL, with the VHGL drink having the highest peak and incremental AUC and these values decreasing for the HGL and LGL conditions.

Drink condition significantly affected the time (in min) it took for the participants' blood glucose values to return to (and below) their baseline measurements ($F(2,36.1) = 31.22$, $P < 0.001$). The VHGL took the longest time to return to baseline, followed by the HGL drink, with the LGL drink being the quickest. There was a significant interaction effect between participant sex and the drink condition ($F(2,36.2) = 4.45$, $P = 0.019$). *Post hoc* testing revealed a significant sex difference ($P = 0.01$) for the VHGL drink, where girls (adjusted mean 112.63 (SE 9.96)) returned to baseline slower than the boys (adjusted mean 73.68 (SE 9.90)). For boys, the difference in the time taken to return to baseline was not significantly different between the LGL and HGL beverages ($P = 0.74$). All other comparisons of the drink conditions were significant for both boys and girls (all $P \leq 0.045$).

Cognitive function

The mean cognitive function change scores for the six measures assessed throughout the testing period for each test drink are shown in Table 4.

Table 3. All blood glucose (BG) measures in response to each test drink (treatment) (Adjusted mean values with their standard errors and number of subjects†)

	VHGL			HGL			LGL		
	<i>n</i>	Mean	SE	<i>n</i>	Mean	SE	<i>n</i>	Mean	SE
Baseline BG (mmol/l)	35	5.84 ^a	0.13	38	5.61 ^{a,b}	0.10	39	5.34 ^b	0.10
Peak BG (mmol/l)	35	7.79 ^a	0.22	38	7.02 ^b	0.13	39	6.11 ^c	0.08
iAUC (mmol × 3h)	32	108.77 ^a	14.61	38	52.45 ^b	6.16	38	14.57 ^c	3.46
Time to peak (min)	34	28.38 ^a	1.70	38	26.98 ^a	1.59	36	22.32 ^a	2.39
Time to return to baseline (min)									
Total‡	35	93.16	6.97	37	63.22	4.44	38	41.92	2.77
Females	17	112.63 ^a	9.96	19	64.63 ^b	6.26	20	42.46 ^c	3.99
Males	18	73.68 ^{a*}	9.90	18	61.81 ^a	6.43	18	41.39 ^b	3.99

VHGL, very high glycaemic load; HGL, high glycaemic load; LGL, low glycaemic load; iAUC, incremental AUC.

^{a,b,c} Mean values with unlike letters were significantly different ($P < 0.05$).

* Mean value was significantly different for boys and girls ($P = 0.009$).

† Numbers vary due to missing data points or technical difficulties with the operation of the continuous glucose monitoring system monitor.

‡ Significant main effects were modified by an interaction with participant sex.

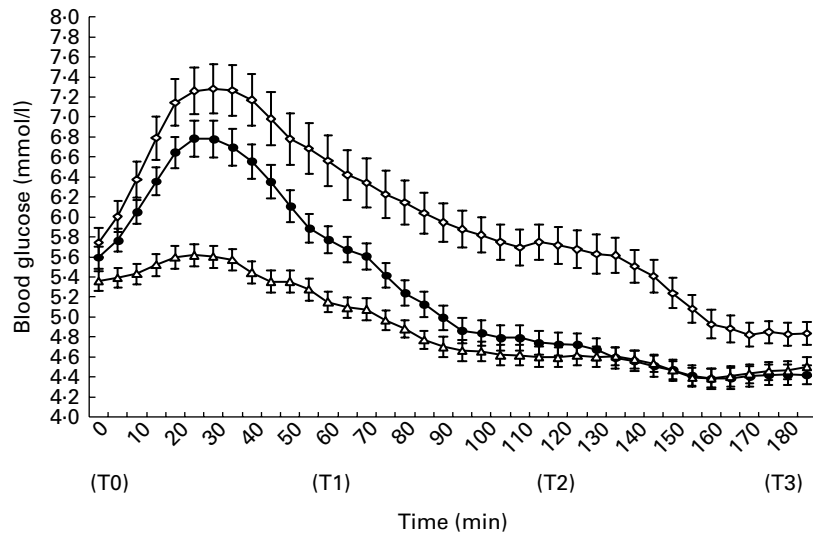


Fig. 2. Mean raw blood glucose responses (mmol) across the testing period for all children by test drink (treatment). \diamond , Very high glycaemic load; \bullet , high glycaemic load; \triangle , low glycaemic load. T0, baseline; T1, 60 min post-drink; T2, 120 min post-drink; T3, 180 min post-drink.

There were no significant main effects for test drink on any of the cognitive domains assessed (speed of processing, working memory, short-term memory, attention switching, perceptual speed and inspection time) (Supplementary Appendix B, available online). The interaction between drink condition and testing session also failed to reach significance for any of the assessments.

There was a significant interaction between participant sex and drink condition for change in short-term memory ($P < 0.001$) (see Fig. 4). *Post hoc* contrasts revealed an effect of drink condition in girls; the change in words recalled from baseline was different between the VHGL drink and the LGL (mean difference 1.15 (SE 0.40), $P = 0.014$) and HGL conditions (mean difference 1.27 (SE 0.38), $P = 0.003$). There was no difference between drinks in boys ($P > 0.09$). Finally, there were sex differences for the LGL and the HGL drinks (mean difference 1.66 (SE 0.43), $P < 0.001$ and mean difference

-1.75 (SE 0.42), $P < 0.001$, respectively), with girls showing an overall increase in words recalled from baseline and boys showing a decrease throughout testing. Further exploration of this sex effect revealed that girls (6.16 (SE 0.45)) and boys (5.58 (SE 0.38)) did not differ significantly in the words recalled at baseline on their first visit ($t(36) = -1.0$, $P = 0.33$).

There was a borderline-significant interaction between participant sex and drink ($P = 0.054$) for working memory, although *post hoc* testing failed to reveal significant differences between groups.

Despite several other significant effects of covariates on changes in cognitive function, there were no other effects associated with the test drink condition.

Appetite

There was no main effect of drink condition ($F(2,137.7) = 1.89$, $P = 0.16$) or interaction effect between

Table 4. Adjusted change from baseline in appetite rating and cognitive function scores by time and drink condition (treatment) (Mean values with their standard errors)

Time	Drink	Appetite rating (VAS 0–400 mm)*		Speed of processing (z-score)†		Attention switching (ms)†		Inspection time (ms)†		Working memory (percentage digits correct)‡		Short-term memory (words recalled)‡		Perceptual speed ('A' words found)‡	
		Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
T1	VHGL	-106.13	11.73	0.00	0.09	-84.76	35.39	-1.88	2.81	-0.98	1.68	-0.33	0.33	0.14	0.47
	HGL	-92.56	11.84	-0.14	0.09	-49.45	35.86	-5.78	2.72	-2.46	1.68	-0.07	0.33	0.31	0.47
	LGL	-70.20	11.85	-0.02	0.09	30.10	36.44	-0.84	2.76	-2.06	1.70	-0.01	0.34	0.61	0.48
T2	VHGL	-20.99	11.85	-0.03	0.09	-102.32	35.87	0.60	2.72	-0.95	1.68	0.17	0.33	0.14	0.47
	HGL	-37.36	11.72	-0.08	0.09	-73.24	35.80	-3.13	2.72	-3.83	1.68	-0.22	0.34	0.33	0.48
	LGL	-16.36	11.87	-0.10	0.09	-91.57	36.44	0.22	2.80	-3.86	1.70	0.21	0.34	0.30	0.48
T3	VHGL	1.37	11.73	-0.02	0.09	-119.28	36.50	-2.52	2.72	-3.06	1.71	-0.65	0.33	1.20	0.47
	HGL	-8.39	11.72	-0.22	0.09	-103.00	35.26	-0.58	2.79	-0.75	1.68	0.07	0.33	0.34	0.47
	LGL	11.90	11.88	-0.18	0.09	-111.03	36.42	-2.56	2.76	-2.69	1.70	-0.55	0.34	1.45	0.48

VAS, visual analogue scale; T1, 60 min post-drink; VHGL, very high glycaemic load; HGL, high glycaemic load; LGL, low glycaemic load; T2, 120 min post-drink; T3, 180 min post-drink.

* Negative changes indicate less appetite relative to baseline.

† Negative changes indicate faster reaction times (improvement) relative to baseline.

‡ Negative changes indicate less words/digits (decline) relative to baseline.

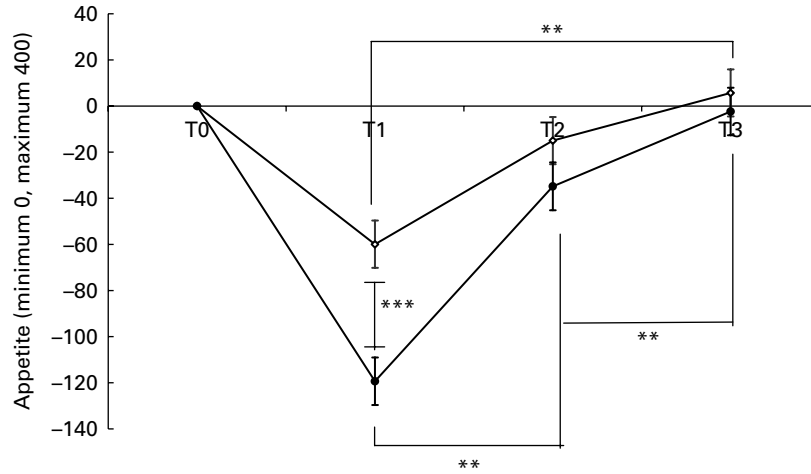


Fig. 3. Adjusted means for change in appetite by time and sex for treatments combined for males and females. T0, baseline; T1, 60 min post-drink; T2, 120 min post-drink; T3, 180 min post-drink. ** $P < 0.01$, *** $P < 0.001$. \diamond , Boys; \bullet , girls.

drink and time on change from baseline in self-reported appetite throughout the testing ($F(4,221.39) = 0.97, P = 0.43$).

Interpretation of significant main effects of testing session ($F(2,192.1) = 77.47, P < 0.001$) and participant sex ($F(1,51.2) = 5.67, P = 0.021$) was modified by a significant interaction between the two variables ($F(2,191.5) = 6.46, P = 0.002$). At 1 h after the drink (T1), girls had a significantly lower appetite than boys (mean difference 59.41 (SE 14.76), $P < 0.001$). The difference in the change at 2 (T2) and 3 h (T3) after drink consumption in boys was not significant, but at all other time points, the appetite differed significantly for boys and girls ($P \leq 0.004$) (Fig. 3).

Energy intake at lunch

The adjusted mean energy intake at lunch was 3445 (SE 202.5), 3408 (SE 199) and 3287 (SE 226.2) kJ for VHGL, HGL and LGL test drinks, respectively; these values were non-significantly different ($F(2,28.66) = 0.44, P = 0.65$). There was a borderline effect of participant sex on energy intake ($F(1,27.08) = 4.23, P = 0.05$), with boys consuming more at the buffet lunch than girls (mean difference 818 (SE 397.8) kJ). However, there was no significant interaction between participant sex and test drink for energy intake at lunch ($F(2,28.95) = 1.6, P = 0.30$). None of the other covariates, including testing day, BMI z -score and age, had a significant effect on energy intake (all $P > 0.15$).

Discussion

The present study aimed to assess differential effects of beverages varying in GL on appetite, energy intake and cognitive function in children in a clinical trial. GL was varied through reductions in glycaemic carbohydrate and increases in protein and fat from milk. Despite verifiable changes in the glycaemic response of the beverages, we saw no differences in perceived appetite or *ad libitum* energy intake of children. We observed differential effects of the GL manipulations on short-term memory in boys and girls. However, this

was the only cognitive domain in which we witnessed any significant affects.

Previous clinical trials exploring the effects of GI on children's cognitive performance have hypothesised that the differences are a result of glucoregulation, which alters glucose metabolism in the brain^(4,21). Much of the evidence in adults has been based on a glucose condition relative to a placebo; however, some studies have shown that low-GI/GL breakfasts are protective against the decline in cognitive performance that occurs throughout the morning^(6,8,9). Significant effects have generally been seen 2 h after the consumption of breakfast, when the children have most likely returned to or below their fasting blood glucose levels. Even after consuming the VHGL beverage, we observed that most children had returned to and below their fasting levels by 120 min. This suggests that it is unlikely that any effects of manipulations of GI of breakfast that have been observed are related to absolute blood glucose values. This may also explain inconsistent effects of skipping breakfast on cognitive performance, with some studies indicating enhanced performance after breakfast⁽²²⁾ and others suggesting limited effects of fasting on cognitive performance⁽²³⁾.

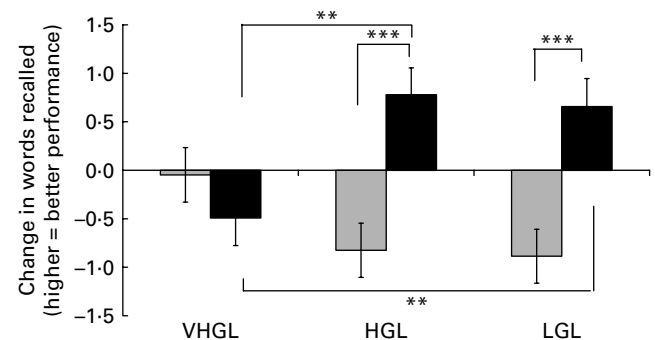


Fig. 4. Adjusted means for change in the number of words recalled in the short-term memory task for drink condition by participant sex. VHGL, very high glycaemic load; HGL, medium glycaemic load; LGL, low glycaemic load. ** $P \leq 0.01$; *** $P < 0.001$. \square , Boys; \blacksquare , girls.

Micha *et al.*⁽²⁴⁾ recently evaluated the effects of GI and GL manipulations on cognitive function and mood. They suggest that the effects of GI and GL need to be considered separately because the former is more closely related to the rate of absorption of glucose, while the latter relates to the amount absorbed. As well as collecting blood glucose, they assessed cortisol levels, as they potentially mediate the effects of glucose on memory⁽²⁵⁾. Results of the present study suggested that the GI of meals affected the cognitive performance of children (aged 11–14 years), with GL having limited effect. The high-GI meals had contrasting effects on different cognitive domains, being potentially beneficial for vigilance tasks and detrimental for memory. The authors suggest that differences in glucose and cortisol levels witnessed according to GI may trigger these differences. Unfortunately, the researchers' failure to use isoenergetic manipulations makes it difficult to ascertain whether GI/GL has effects independent of energy intake. Nevertheless, it suggests that GI or GL manipulations alone may not be reliable modulators of cognition.

Without a better understanding of physiological mechanisms that may alter cognitive function after eating, it is difficult to reconcile the potential effects of different breakfasts on cognitive performance. On the one hand, it is proposed that high-GI manipulations improve memory (the glucose enhancement effect) in the short term, with studies using whole foods supporting this effect⁽²⁶⁾. On the other hand, it is suggested that low GI sustains performance, the focus of the present study. Benton *et al.*⁽²⁷⁾ speculated that prolonged availability of glucose was able to improve verbal memory at 150–210 min after a low- *v.* high-GI breakfast, despite reporting weak associations between cognitive performance and blood glucose values. In a review of studies on GL and cognitive performance, Gilshan *et al.*⁽¹⁰⁾ concluded that there is insufficient evidence to support cognitive benefits of GL manipulations. The authors suggest that physiological processes other than glycaemia, such as insulinaemia, may be more closely related to changes in cognitive performance. Higher metabolic activation and modulation in neurotransmitter synthesis have also been used to explain better cognitive performance in young men after a lower-carbohydrate, higher-protein 'foam' meal⁽²⁸⁾. A myriad of other neurochemicals as well as gut hormones may also be implicated in any benefits of different breakfasts on cognitive function⁽¹⁰⁾. Further, biological data are needed to understand how glucoregulation may moderate the effects of GL on cognitive performance in children.

Despite not witnessing any changes in cognition throughout the morning, we did find an interaction between the GL of the beverages and participant sex for the pooled change in short-term memory performance across the day. This indicated that consuming glucose had a net effect of decreasing girls' short-term memory performance, relative to either milk-containing condition. Differences between the dietary conditions failed to reach significance in boys. These findings are consistent with Mahoney *et al.*⁽²⁹⁾, who reported that girls performed better in short-term memory tasks after a low- relative to a high-GI breakfast cereal. The magnitude of the improvement that we observed on milk-containing beverage relative to glucose may be of practical relevance, as data from Australian

children show that 14-year-olds recall, on average, 0.4 words more than 9-year-olds after a single exposure to a word list⁽³⁰⁾.

The milk-containing beverages appeared to have an opposite effect on boys compared with girls, with boys demonstrating a negative net change in words recalled. Although sex differences may exist for some forms of memory⁽³¹⁾, we did not see effects of sex in word recall at baseline. Energy requirements vary by sex, and provision of the same-sized preload may account for some of the differences observed. Alternatively, sex differences in glucose tolerance have been detected in as early as 5-year-old children, even when adjusted for anthropometric measures⁽³²⁾. Although we did not see many sex differences in blood glucose levels, insulin sensitivity may be an important consideration for future research. The potentially detrimental effect of lower GL beverages on boys' short-term memory requires further investigation, and future studies should consider the potential interaction between sex and glycaemic manipulations when exploring cognitive performance.

It was interesting that memory was the only cognitive domain that showed any effects. It seems to be one of the most sensitive cognitive domains to breakfast manipulations in children⁽¹¹⁾. However, our cognitive test battery was designed to encompass cognitive domains that would be expected to be, and have been shown to be, sensitive to treatments, including dietary ones. Furthermore, the focus of the battery was on speed tasks that are optimally sensitive to subtle changes due to their measurement properties⁽³³⁾, and the cognitive tests that we used have all demonstrated sensitivity to various treatment effects in previous studies^(34–37). Hence, we consider that the present results reflect a lack of an effect (of magnitude that we were able to detect) on these constructs, as opposed to lack of sensitivity of the tasks to detect effects.

We found that our manipulations of GL had little effect on appetite and energy intake at a buffet lunch. This is in contrast to observations made by Warren *et al.*⁽¹⁵⁾, indicating favourable effects of low-GI breakfasts for pre-lunch hunger in children. Lomenick *et al.*⁽³⁸⁾ also reported that overweight children experienced significantly lower appetite and prolonged satiety on a high-protein, low-carbohydrate meal (approximately 1806 kJ, 41 g carbohydrate, 49 g protein) compared with a higher-carbohydrate meal (approximately 1848 kJ, 99 g carbohydrate, 2 g protein) for over 4 h. In normal-weight children, differences were similar, but only trended towards significance. Trends for the effect of a low-GI breakfast on reduced intake at a buffet lunch in primary school children have also been reported⁽³⁹⁾. Ball *et al.*⁽⁴⁰⁾ reported that there were no differences in satiety or energy intake between high- and low-GI meal replacements (shake and bar), but that food was requested sooner after a high-GI meal in a sample of overweight adolescents. In the present study, the buffet was provided at a fixed time. An interval of 3 h may have been too long to detect different influences of the drinks, as all children had returned to baseline levels of appetite and blood glucose by this stage. Yet, Ball *et al.*⁽⁴⁰⁾ also found that blood glucose levels were below baseline for over half of the morning. The lunches that we presented

included limited variety and foods typical of an Australian lunch to avoid increases in consumption driven by novelty and variety. Although this may have led to some boredom, which could have influenced energy intake, testing day did not have a significant effect, suggesting that children did not tire of the limited options made available.

There has been a suggestion that insulin, but not glucose, is associated with short-term appetite regulation in healthy adult participants⁽⁴¹⁾ and, therefore, the net effect on appetite may not be simply a function of carbohydrate composition. Ball *et al.*⁽⁴⁰⁾ reported a larger than expected difference in insulin levels between a whole food and a liquid low-GI meal, regardless of similar effects on blood glucose, and suggested that gastric emptying influenced these results. Other studies have supported their findings, indicating that liquid meals evoke a 50% greater insulin response than solid meals of the same macronutrient composition⁽⁴²⁾. Therefore, the liquid form of our dietary manipulations may have hindered our ability to witness differences in appetite and energy intake. The osmolar load of beverages may also have contributed to a small delay in gastric emptying⁽⁴³⁾. However, carbohydrates may have a more pronounced effect than osmolar load, with a delay in gastric emptying by more than 1 h witnessed for low (40 g/l) and high carbohydrate (188 g/l) concentrations⁽⁴³⁾. This could partially explain the finding that the glucose drink resulted in the most prolonged elevation of blood glucose.

Despite suggestion in adult samples that dairy protein in a liquid pre-load can result in improved satiety⁽¹⁶⁾, no prolonged satiety effects were shown in our sample of children. The level of protein may not have been enough to evoke an effect. Our pure milk condition had a higher protein content (13 g) relative to the other drink conditions; however, it was less than that used in previous studies (approximately 50 g)^(16,38). The smaller amount of protein was partly due to the fact that, overall, our energy load was also smaller than has been previously used (by 30–80%)^(15,16). However, the energy content of the drink conditions was similar to the size of breakfasts consumed by 7–11-year-old children in other samples⁽⁴⁴⁾. Another consideration of our dietary manipulations was the size of the glucose load (65 g), which was greater than those that have been used previously. Finally, we chose to vary GL using a recommended beverage for children – dairy milk – and sequentially replaced 50% of the volume with a glucose beverage. Although we altered the macronutrient profile in doing so, we believe that this provides external validity, and furthermore, we were able to verify that the GL was modified. We argue that if the glycaemic response is truly the mediator of changes in appetite and cognition, we would observe this effect even if GL is modified by reducing the carbohydrate load.

The present findings suggest that girls may respond more favourably to lower-GL dairy beverages in terms of short-term memory; however, further research investigating solid meals with higher preloads may assist in assessing the consistency of these findings.

Supplementary material

To view supplementary material for this article, please visit <http://dx.doi.org/10.1017/S0007114512005296>

Acknowledgements

The trial was partially funded by the Dairy Health and Nutrition Consortium (DHNC). Data collection, study implementation and statistical procedures were performed without input from the DHNC. The final manuscript was approved by the DHNC. E. B. performed the statistical analysis and interpretation, wrote the paper and along with M. N. is responsible for the final content of the paper. D. B. contributed to the paper and statistical analysis and interpretation. A. S. conducted data collection. J. B., V. D. and C. W. contributed to the design of the study. M. N. conceived the research and oversaw the study. All authors reviewed and contributed to the final manuscript. The authors declare no conflict of interest. The authors wish to thank Kylie Lange for her statistical direction and input, Kathryn Bastiaans and Julie Syrette for their data management, the CSIRO Clinical Research Unit for assistance with data collection, Nadia Corsini, who contributed to the design of the cognitive component of the study, Sean Fitzgibbon, who assisted in the programming of software for cognitive testing and all other staff involved in data collection.

References

1. Riby LM (2004) The impact of age and task domain on cognitive performance: a meta-analytic review of the glucose facilitation effect. *Brain Impairment* **5**, 145–165.
2. Owens DS & Benton D (1994) The impact of raising blood glucose on reaction times. *Neuropsychobiology* **30**, 106–113.
3. Donohoe RT & Benton D (1999) Cognitive functioning is susceptible to the level of blood glucose. *Psychopharmacology* **145**, 378–385.
4. Benton D & Nabb S (2003) Carbohydrate, memory, and mood. *Nutr Rev* **61**, S61–S67.
5. Chugani HT, Phelps ME & Mazziotta JC (1987) Positron emission tomography study of human brain functional development. *Ann Neurol* **22**, 487–497.
6. Wesnes KA, Pincock C, Richardson D, *et al.* (2003) Breakfast reduces declines in attention and memory over the morning in schoolchildren. *Appetite* **41**, 329–331.
7. Mahoney C (2005) Effect of breakfast composition on cognitive processes in elementary school children. *Physiol Behav* **85**, 635–645.
8. Benton D, Maconie A & Williams C (2007) The influence of the glycaemic load of breakfast on the behaviour of children in school. *Physiol Behav* **92**, 717–724.
9. Ingwersen J, Defeyter MA, Kennedy DO, *et al.* (2007) A low glycaemic index breakfast cereal preferentially prevents children's cognitive performance from declining throughout the morning. *Appetite* **49**, 240–244.
10. Gilsenan MB, de Bruin EA & Dye L (2009) The influence of carbohydrate on cognitive performance: a critical evaluation from the perspective of glycaemic load. *Br J Nutr* **101**, 941–949.
11. Hoyland A, Dye L & Lawton CL (2009) A systematic review of the effect of breakfast on the cognitive performance of children and adolescents. *Nutr Res Rev* **22**, 220–243.

12. Slater A, Bowen J, Corsini N, *et al.* (2010) Understanding parent concerns about children's diet, activity and weight status: an important step towards effective obesity prevention interventions. *Public Health Nutr* **13**, 1221–1228.
13. Dye L & Blundell J (2002) Functional foods: psychological and behavioural functions. *Br J Nutr* **88**, S187–S211.
14. Ludwig DS (2000) Dietary glycemic index and obesity. *J Nutr* **130**, 280s–283s.
15. Warren JM, Henry CJ & Simonite V (2003) Low glycemic index breakfasts and reduced food intake in preadolescent children. *Pediatrics* **112**, e414.
16. Bowen J, Noakes M, Trenerry C, *et al.* (2006) Energy intake, ghrelin, and cholecystokinin after different carbohydrate and protein preloads in overweight men. *J Clin Endocrinol Metab* **91**, 1477–1483.
17. Cole TJ, Bellizzi MC, Flegal KM, *et al.* (2000) Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* **320**, 1240–1243.
18. Rolls BJ, Rowe EA, Rolls ET, *et al.* (1981) Variety in a meal enhances food intake in man. *Physiol Behav* **26**, 215–221.
19. Mastrototaro J (1999) The MiniMed Continuous Glucose Monitoring System (CGMS). *J Pediatr Endocrinol Metab* **12**, Suppl. 3, 751–758.
20. Flint A, Raben A, Blundell JE, *et al.* (2000) Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. *Int J Obes* **24**, 38–48.
21. Nabb S & Benton D (2006) The influence on cognition of the interaction between the macro-nutrient content of breakfast and glucose tolerance. *Physiol Behav* **87**, 16–23.
22. Cooper SB, Bandelow S & Nevill ME (2011) Breakfast consumption and cognitive function in adolescent schoolchildren. *Physiol Behav* **103**, 431–439.
23. Green MW, Elliman NA & Rogers PJ (1995) Lack of effect of short-term fasting on cognitive function. *J Psychiatr Res* **29**, 245–253.
24. Micha R, Rogers PJ & Nelson M (2011) Glycaemic index and glycaemic load of breakfast predict cognitive function and mood in school children: a randomised controlled trial. *Br J Nutr* **106**, 1552–1561.
25. Sauro MD, Jorgensen RS & Pedlow CT (2003) Stress, glucocorticoids, and memory: a meta-analytic review. *Stress* **6**, 235–245.
26. Sünram-Lea SI, Foster JK, Durlach P, *et al.* (2004) The influence of fat co-administration on the glucose memory facilitation effect. *Nutr Neurosci* **7**, 21–32.
27. Benton D, Ruffin MP, Lassel T, *et al.* (2003) The delivery rate of dietary carbohydrates affects cognitive performance in both rats and humans. *Psychopharmacology* **166**, 86–90.
28. Fischer K, Colombani PC, Langhans W, *et al.* (2002) Carbohydrate to protein ratio in food and cognitive performance in the morning. *Physiol Behav* **75**, 411–423.
29. Mahoney CR, Taylor HA, Kanarek RB, *et al.* (2005) Effect of breakfast composition on cognitive processes in elementary school children. *Physiol Behav* **85**, 635–645.
30. Forrester G & Geffen G (1991) Performance measures of 7- to 15-year-old children on the Auditory Verbal Learning Test. *Clin Neuropsychol* **5**, 345–359.
31. Kramer JH, Yaffe K, Lengsfelder J, *et al.* (2003) Age and gender interactions on verbal memory performance. *J Int Neuropsychol Soc* **9**, 97–102.
32. Murphy MJ, Metcalf BS, Voss LD, *et al.* (2004) Girls at five are intrinsically more insulin resistant than boys: The Programming Hypotheses Revisited – The EarlyBird Study (EarlyBird 6). *Pediatrics* **113**, 82–86.
33. Danthiir V, Burns NR, Nettelbeck T, *et al.* (2011) The older people, omega-3, and cognitive health (EPOCH) trial design and methodology: a randomised, double-blind, controlled trial investigating the effect of long-chain omega-3 fatty acids on cognitive ageing and wellbeing in cognitively healthy older adults. *Nutr J* **10**, 117.
34. Frearson W, Barrett P & Eysenck HJ (1988) Intelligence, reaction time and the effects of smoking. *Person Individ Diff* **9**, 497–517.
35. Henke KG, Grady JJ & Kuna ST (2001) Effect of nasal continuous positive airway pressure on neuropsychological function in sleep apnea–hypopnea syndrome – a randomized, placebo-controlled trial. *Am J Respir Crit Care Med* **163**, 911–917.
36. Haskell CF, Kennedy DO, Milne AL, *et al.* (2008) The effects of L-theanine, caffeine and their combination on cognition and mood. *Biol Psychol* **77**, 113–122.
37. Einother SJL, Martens VEG, Rycroft JA, *et al.* (2010) L-Theanine and caffeine improve task switching but not inter-sensory attention or subjective alertness. *Appetite* **54**, 406–409.
38. Lomenick JP, Melguizo MS, Mitchell SL, *et al.* (2009) Effects of meals high in carbohydrate, protein, and fat on ghrelin and peptide YY secretion in prepubertal children. *J Clin Endocrinol Metab* **94**, 4463–4471.
39. Henry CJK, Lightowler HJ & Strik CM (2007) Effects of long-term intervention with low- and high-glycaemic-index breakfasts on food intake in children aged 8–11 years. *Br J Nutr* **98**, 636–640.
40. Ball SD, Keller KR, Moyer-Mileur LJ, *et al.* (2003) Prolongation of satiety after low versus moderately high glycemic index meals in obese adolescents. *Pediatrics* **111**, 488–494.
41. Flint A, Gregersen NT & Glud LL (2007) Associations between postprandial insulin and blood glucose responses, appetite sensations and energy intake in normal weight and overweight individuals: a meta-analysis of test meal studies. *Br J Nutr* **98**, 17–25.
42. Edes TE & Shah JH (1998) Glycemic index and insulin response to a liquid nutritional formula compared with a standard meal. *J Am Coll Nutr* **17**, 30–35.
43. Vist GE & Maughan RJ (1995) The effect of osmolality and carbohydrate content on the rate of gastric emptying of liquids in man. *J Physiol* **486**, 523–531.
44. Maffei C, Provera S, Filippi L, *et al.* (2000) Distribution of food intake as a risk factor for childhood obesity. *Int J Obes Relat Metab Disord* **24**, 75–80.