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The "sweet" effect: Comparative assessments of dietary sugars on cognitive performance

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ABSTRACT

In recent years there has been increasing interest in studying cognitive effects associated with sugar consumption. Neuro-cognitive research has confirmed that glucose, as a main energy substrate for the brain, can momentarily benefit cognitive performances, particularly for memory functioning. However, there is still limited understanding of relative effects of other common sugars (e.g., fructose and sucrose) on cognitive performance. The present study tested in 49 people the effects of three common dietary sugars against a placebo sweetener (i.e., sucralose), on performance of three well-studied cognitive tasks – simple response time, arithmetic, and Stroop interference, all of which are suggested to rely on the prefrontal lobe. A double-blind, placebo-controlled, cross-over experimental design was used. Results revealed that ingestion of glucose and sucrose led to poorer performances on the assessed tasks as opposed to fructose and the placebo ($p < 0.05$); these effects were particularly pronounced under the fasting condition in comparison to the non-fasting condition ($p < 0.001$). Overall, these results indicate that cognitive effects of sugar are unlikely to be mediated by the perception of sweetness. Rather, the effects are mediated by glucose. Further research should systematically assess effects of dietary sugars on other cognitive domains, such as memory, to give further insights on general cognitive effects of sugar consumption.

1. Introduction

Sugar, associated with a positive taste quality – sweetness, has become a major component in the modern human diet. While there is increasing interest in studying effects of sugar consumption on cognitive performance [1–3], relatively little attention has been given to evaluation of the effect profiles of different sugars.

In the existing literature, the relationship between sugar consumption and cognitive effects is primarily studied through assessing acute effects of glucose ingestion [4–6], with most studies focusing on glucose effects on memory performance [7]. Glucose ingestion has been found to have a facilitating effect on memory tasks known to depend on the hippocampal region [8] in both young and elderly groups, including individuals with neurological diseases or metabolism conditions [7]. In contrast, studies that assessed glucose effects on other cognitive domains have produced somewhat mixed results. Specifically, previous studies have examined glucose effects on reaction time [10], attention [11], face recognition [12], working memory [3], and related types of tasks. Of these, a few studies observed small facilitative effects on information processing speed and attention, when measured using the

trail-making test, letter symbol digit test, or the Stroop test [13,14]. By contrast, other studies found either no difference [15–18] or deteriorative effects [10]. These inconsistent findings may be attributed to choices of cognitive tasks and domains of interest [7]. Baumeister and colleagues [19,20] in particular, stressed the importance of uncovering the link between cerebral glucose availability and prefrontal processes, due to the relevance of glucose on self-regulation. Clearly, more research is required in this area.

In comparison to glucose, cognitive effects of other dietary sugars such as fructose or sucrose have received much less attention [7,9]. Indeed, the metabolism of fructose and sucrose undergoes a very different pathway as compared to glucose. Fructose does not traverse the blood-brain barrier and is instead metabolised through the liver [21], resulting in a much slower increase in blood glucose levels. Sucrose, as a disaccharide, is first hydrolysed into glucose and fructose, and then metabolised via separate pathways. Such metabolic differences across the key sugar sources might be assumed to lead to potentially different impacts on cognitive performance, yet there exists no study demonstrating whether that is the case. More research in this area is clearly important, particularly given the increasing trend of substituting sugar

sources of a high glycaemic index with ones of a lower index (e.g., fructose or artificial sweeteners [22,23]).

In addition to the issues raised above, the exclusive role of sweetness perception on cognition presents a fascinating research topic in its own right. The question – whether sweetness perception moderates cognitive performances – has received little direct attention. Neuroimaging data have demonstrated that sensory inputs from the gustatory system are initially represented in both the primary taste cortex and the orbitofrontal cortex [24,25]. In addition, emerging data imply that the brain processing to the physical taste substance and its sensory quality may be dissociated, although the specific neural circuitry has not been defined [24]. It is therefore interesting to understand the relative cognitive effects across different types of sweeteners when their sensory characteristics are the same. An answer to this question will not only add understanding to the neural processing of various sweetness substances, but also will provide pertinent insights into the effectiveness of sugar substitutes from a cognitive perspective.

Overall, the present study aims to test the effects of different sugars on selected cognitive tasks, using a double-blind, cross-over experimental design. Rather than focusing exclusively on a particular cognitive domain, the study is designed to include a variety of tasks that implicate prefrontal lobe functioning. According to Gailliot and Baumeister [19], processes that rely heavily on the prefrontal cortex possibly require more glucose than processes associated with other brain regions, given the critical role of prefrontal function in tasks depending on effortful, controlled and executive processes. Specifically, this study assesses effects of sugar intake on information processing, executive functioning and attention. In light of previous findings regarding the role of fasting [8], the present study incorporates a comparison between fasting and non-fasting participants.

2. Methods

2.1. Participants

A total of 49 individuals participated. They were randomly assigned into an overnight 10-h fasting group (N = 26; 15 females; 22.6 ± 4.2 years of age) or a non-fasting group (N = 23; 13 females; 24.3 ± 4.9 years of age). All participants were recruited from the university of Otago community. Prior to their participation, all underwent a screening session to ensure they were free from chronic or major diseases, type 1 or 2 diabetes, or psychiatric disorders. Participants fell within a BMI range of 17.6–32.7 kg/m [2] (fasting: 23.2 ± 3.56; non-fasting: 24.1 ± 3.87). A set of univariate analyses confirmed that neither age [$t_{(47)}$ = 0.89, p = 0.38] nor BMI [$t_{(47)}$ = 0.984, p = 0.17] differed significantly across the fasting and non-fasting groups. Participants in the fasting group undertook a 10-hour fasting period prior to each testing session. Participants in the non-fasting group were required to report the content of their most recent meal. On average, the caloric intake was 271 kcal (SD = 49.1) with ≤ 55 g of carbohydrates. Each participant attended each testing session at the same time of the day. They were instructed specifically not to vary their consumption patterns across test sessions.

The experiment was approved by the Human Participation Ethics Committee at the University of Otago (16/063). A written informed consent was completed by each participant before their participation. Each participant received a total of 100 New Zealand Dollars as reimbursements for their travel.

2.2. Samples

Across the four experimental sessions, each participant consumed sweetened drinks (250 mL) containing one type of the following sweeteners – glucose (26.0 g), sucrose (14.5 g), fructose (13.0 g), or sucralose (0.025 g). The energy content of these four drinks was 25, 14, 12 and 0 cal. All solutions were flavoured by a non-caloric lemon

flavouring agent (100 μL/L; Sigma-Aldrich) to mask possible differential tastes across solutions. These drinks were served at 4 °C. In order to minimise practice effects across sessions, the testing order of the four types of samples was counterbalanced across participants in the fasting and non-fasting groups separately, using Williams Latin Square design.[1] Concentrations were determined in a preliminary study by testing 60 participants on a series of duo-trio sensory difference tests [26], to yield an equal sweetness intensity.

2.3. Procedures

Data collection took place over 16 consecutive weeks. Each participant was assigned to a testing session and asked to attend the same session every week for 4 weeks. In order to minimise biases due to differences in testing time, effort was made to counterbalance testing times between the two experimental groups. For the fasting group, the 26 participants were randomly assigned to the 7.00 h and 10.00 h sessions. For the non-fasting group, eight participants were assigned to the 7.00 h, ten participants were in the 10.00 h, and the remaining five participants attended the session at 15.00 h.

Upon arrival to each testing session, the participants were asked to complete a pre-check list either to confirm their compliance to the fasting requirement (fasting group), or to report their food consumption within 10 h prior to the test (non-fasting group).

A typical testing session lasted 55 min. It involved asking the participants to consume the tested beverage and then perform three cognitive tasks, with three blood glucose measures taken throughout the testing. Fig. 1 illustrates a schematic of sequence of events in a testing session. The experiment used a 20-minute latency between consumption of the drink and commencement of the task, following the typical protocol used in previous studies of glucose effects [3,10]. Blood glucose measures were obtained by a finger prick method (HemoCue® Glucose 201 Microcuvette). Finger pricking was performed on participants' fingers that were not required for the cognitive task.

2.4. Cognitive tasks

Three computerised cognitive tasks (Inquisit 5, Millisecond software, USA) – the simple response time task, arithmetic processing, and the Stroop task – were administered at 20-minute post-ingestion of the testing drink, and required 20 ± 2 min for completion, following the protocol outlined in previous studies [10]. Broadly, these three tasks tested information processing, executive function, and selective attention, all of which are suggested to be associated with the prefrontal lobe. All participants undertook the tasks in the same order as a precaution against bias due to testing orders. The tasks were spaced 1-minute apart. Instructions for each task were given both verbally and in writing at the beginning of each task. Further details of each task are described below, in order of occurrence.

2.4.1. Simple response time task

Each participant received two blocks of 42 trials in the simple response time task. The first 12 trials in each block were practice trials and were omitted in data analyses. The participant was asked to fixate attention on a cross located in the middle of the computer screen, and then press the response key using the index finger of the dominant hand as quickly as possible when the target stimulus (red circle) appeared. The time interval between the start of a trial and the appearance of the target stimulus varied between 500 ms and 8000 ms. Any trials with response time < 100 ms were replaced with new trials in order to mitigate biases caused by error of expectation or habituation. Similarly,

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[1] Note: One participant assigned into the non-fasting group withdrew from the study causing an incomplete permutation of testing orders for the non-fasting group. This minor change is unlikely to affect results obtained from the study.
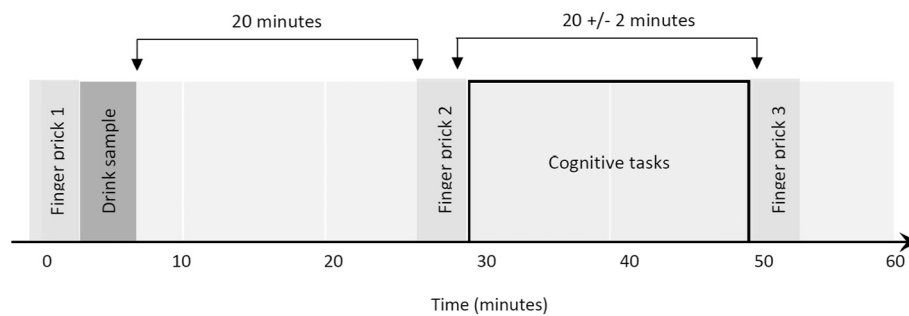
trials with response times ≥ 1000 ms were considered as indicative of attention deficiency and were replaced with new trials. This task is typically used to assess speeded responses with no decision-making other than deciding to respond [27].

2.4.2. Arithmetic task

The second cognitive task was an arithmetic task [28]. The task comprised two blocks of 55 trials. The first 10 trials in each block were warm-up trials. Each trial consisted of presentation of a subtraction problem presented for 3000 ms duration, followed by an 'equal' sign (for 1500 ms), and a proposed solution to the problem (for up to 3000 ms). The participant was required to respond as to whether the proposed answer was correct by pressing one of two response keys ("F" and "J") using the index fingers. In order to maintain relatively equal attentional engagement across participants on the task, mathematical problems were altered adaptively across five difficulty levels. A 10-second inter-trial-interval was presented between each problem. This task was used to assess speed of processing in a task requiring a relatively simple problem (in this case, arithmetic, which follows a simple learned rule) that people must attend to and solve quickly.

2.4.3. Stroop task

The final cognitive task in this study was a modification of the classic colour-word Stroop paradigm [29]. The task consisted of two blocks of 96 trials, with the first 12 trials in each block serving as warm-up trials. On each trial, the participant was asked to indicate the colour of the presented stimulus, which could be either a coloured word or rectangle. The presented colour word was written in either a congruent colour or an incongruent colour. This design led to three experimental conditions: colour-word congruent; colour-word incongruent; neutral (coloured rectangle). The testing trials consisted of a randomized and balanced series of trials for the three experimental conditions. Unlike in the simple response task (which required no choice-decision component), or the arithmetic task (for which there was a correct or incorrect answer on each trial), the Stroop task required inhibition of prepotent responses (reading of the word/identifying the shape) in favour of eliciting a less automatic (i.e., more attention-demanding) response to the colour of the stimulus, which also requires attentional processes. Thus, together, the three behavioural tasks aimed to assess potentially different aspects of attention demands.

2.5. Data analyses

With the simple response time task and the Stroop task, the performance measure was the averaged response time (RT) for correct trials. On the arithmetic task, the resulting RT from each trial was influenced by trial difficulty. A simple RT-correction protocol was therefore applied to compensate for differences across difficulty level by multiplying the proportion correct on a given difficulty level (number of correct trials divided by number of total trials; proportion correct ranges from 0% to 100%) by the mean RT on that level. Notably, the performance measure remained as RT-dependent, meaning a higher measure corresponded to poorer performance.

The blood glucose measures were also analysed using a mixed-model ANOVA, with time-points being the within-subject factor, and experimental conditions (i.e., sugar manipulations) and fasting status being the between-subject factors. Similarly, data obtained from each cognitive task were also analysed by a mixed-model, repeated-measures univariate analysis of variance (ANOVA), with experimental conditions (glucose, fructose, sucrose, and sucralose) as the within-subjects factor and experimental group (fasting and non-fasting) as the between-subjects factor. The treatment order was also included in the model as a fixed factor, in case it biased the effects. Any dataset that violated the assumption of sphericity was corrected using the *Greeenhouse-Geisser* correction. In case of significant effects being detected, post-hoc tests with *Bonferroni* correction were applied to disentangle higher-order effects. All analyses were performed in SPSS 24 (IBM).

3. Results

3.1. Blood glucose measurements

Fig. 2 illustrates changes in the averaged glucose measures across three time-points for each of the tested sugar solutions, for the fasting (Panel A) and non-fasting group (Panel B), separately. A mixed-model ANOVA was performed to indicate changes in the glucose measures (in mmol/L) across the time-points within an experimental session, and to detect differences between four sugar conditions and fasting status. Although a three-way interaction was absent, a significant two-way interaction was observed between time-points and experimental conditions [$F_{(6,356)} = 26.59$, $p < 0.001$]. Post-hoc tests showed that blood glucose levels were elevated significantly post ingestion of glucose (1st to 2nd measure: 5.0 mmol/L to 7.1 mmol/L) and sucrose (1st to 2nd measure: 5.1 mmol/L to 6.3 mmol/L), shown by significant differences between the first and second time-points ($p < 0.05$). Nevertheless, the glucose measure at the third time-point in the sucrose condition returned to a level similar to baseline. On the other hand, no significant interaction was observed between the time-points and fasting status ($p > 0.05$), indicating comparable trajectories of blood glucose across the fasting and non-fasting groups.

Significant main effects were also observed for experimental condition [$F_{(3,177)} = 47.23$, $p < 0.001$] and fasting status ($F_{(1,177)} = 11.47$, $p = 0.001$; fasting group: 5.34 ± 0.17; non-fasting group: 5.74 ± 0.14).

3.2. Simple response time task

Table 1 summarises performance measures on the cognitive tasks across the four experimental conditions. For the simple response time task, the mixed-model ANOVA showed a significant interaction between the experimental condition and the fasting status on RT [$F_{(2.21,55.43)} = 7.01$, $p = 0.002$]. The factor of treatment order did not incur any significant effect. Post hoc tests suggested that RT in the glucose condition was significantly slower than in the fructose and sucralose condition for both fasting and non-fasting groups. For the comparison between glucose and sucrose, significant difference was not
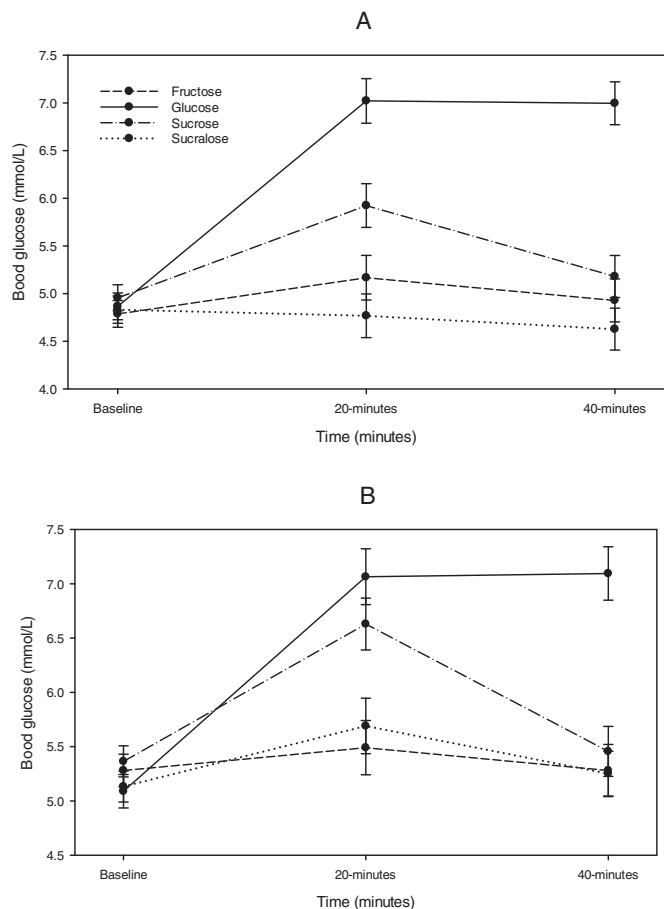
Fig. 2. Illustration of glycaemic changes (mmol/L) after consuming a sweetened drink (250 mL) across three testing time-points for the fasting group (Panel A; N = 26) and non-fasting group (Panel B; N = 23).

Table 1
Summary of means and standard errors (SE) of the performance measures in each of four experimental conditions on the three cognitive tasks.

	Sample	SRTT (ms)		Arithmetic (score)		Stroop (ms)	
		Mean	SE	Mean	SE	Mean	SE
Fasting	Glucose	358	16.1	817	39.4	921	11.1
	Fructose	321	8.5	612	35.6	734	7.5
	Sucrose	318	14.2	703	44.9	827	9.3
	Sucralose	311	8.5	679	38.6	729	7.8
Non-fasting	Glucose	349	17.8	773	43.6	783	12.9
	Fructose	298	9.5	642	39.4	723	10.9
	Sucrose	329	15.8	730	49.7	748	8.8
	Sucralose	298	9.4	624	42.8	733	9.1

Abbreviations: SRTT: Simple response time task; ms: milliseconds.

detected for the non-fasting group, but was found for the fasting group (p < 0.05; see Fig. 3 Top Panel). These differences across sugar treatment were also reflected by the significant main effects of experimental condition [$F_{(2.21, 55.43)}$ = 28.03, p < 0.001].

3.3. Arithmetic task

Similar to the simple response time task, results from the arithmetic task suggested the participants' performances varied significantly across the experimental conditions, depending on the fasting group, $F_{(1.58, 23.73)}$ = 16.92, p < 0.001; Fig. 3, middle panel. Post hoc tests suggested that, in the fasting group, the score in the glucose condition
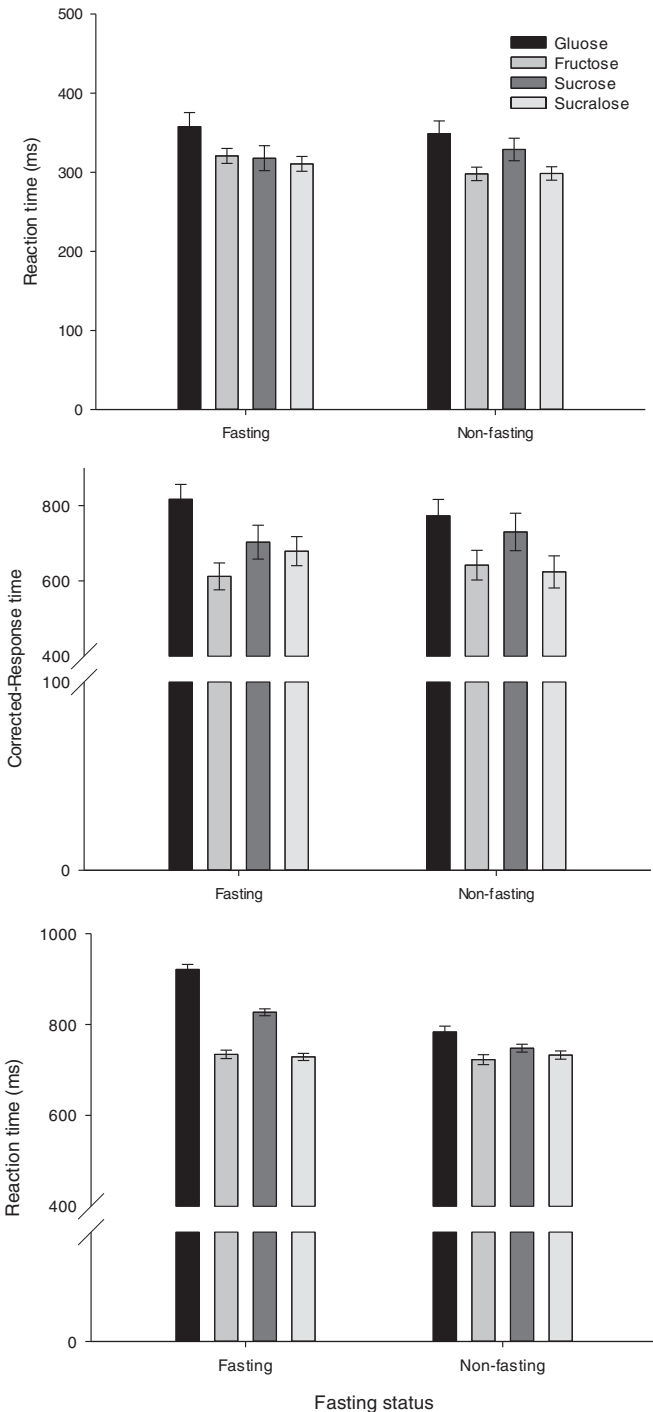

Fig. 3. Comparisons of cognitive performance after ingestion of sweeteners on the three cognitive tasks, for the fasting (N = 26) and non-fasting (N = 23) experimental groups. Cognitive performance was quantified by response time in the simple response time task (top) and Stroop task (bottom), and by corrected-response time for the arithmetic task (middle). Asterisks represent significant differences between fasting and non-fasting groups.

was significantly higher than that of other conditions, implying inferior performance associated with the former. By contrast, the non-fasting group performed similarly in the glucose and sucrose condition. On average, the corrected-RT of the glucose condition was higher than in the other conditions, suggested by the significant main effect [$F_{(1.58, 23.73)}$ = 8.89, p = 0.001].

3.4. Stroop task

Dissimilar to results from the first two tasks, analysis of the pooled RT from the Stroop task did not detect a significant interaction between experimental condition and fasting group. The results suggested sugar manipulations produced a significant main effect regardless of experimental group [$F_{(3,33)} = 25.30$, p < 0.001]. As indicated by the post hoc tests, average RT in the glucose and sucrose conditions was significantly slower than in the other two conditions in both experimental groups (Fig. 3; bottom panel).

In general, the error rates were low for all experimental conditions (3.5%), with no detected significant differences [$F_{(3,33)} = 1.59$, p = 0.21]. As expected, the averaged error rate for the incongruent trials (6.1%) was slightly higher than for the control (3.1%) and congruent trials (3.6%), albeit non-significantly.

These findings taken together indicate that glucose and sucrose ingestions yielded negative effects on the assessed cognitive performances, compared to the fructose and placebo drinks. These effects appeared to be more pronounced in the fasting group compared to the non-fasting group.

4. Discussion

The present study, based on a repeated-measures design, assessed cognitive effects of three dietary sugars – sucrose, glucose and fructose—against a non-caloric sweetener. Overall, the findings showed that glucose and sucrose had relatively negative effects on the assessed cognitive tasks. In contrast, no apparent effect on task performances was found with fructose ingestion compared to the placebo.

Indirectly, these results imply that the observed differences were not moderated by the perception of sweetness. This deduction is in line with recent neuroimaging data, which suggest that caloric and noncaloric sweeteners could activate different brain regions, despite having equip-sweetness [30,31]. There has been little data providing direct comparison of cognitive effects across sugars. A number of early studies have tested effects of sucrose consumption on children's behaviour and cognition, primarily using behavioural observational data [32,33]. Despite some inconsistencies in the findings, it has been generally believed that sucrose has no direct impact on behaviour or cognition. On the other hand, fructose has been suggested by a previous study to have a similar enhancing effect on memory as does glucose [34], casting doubt on the role of glucose in moderating the cognitive effect. In the future, more research is required to assess cognitive effects across various sweeteners, particularly given that these effects could have important impact on the choice and intake of sweeteners.

In the present study, given that the main contrasting cognitive effects were present between the glucose-containing and glucose-free sweeteners, it is tempting to speculate that glucose is the mediator of the obtained effects. Of course, this deduction rests on the assumption that blood glucose is proportional to extracellular glucose [35]. The observation of poorer cognitive performances after ingestion of glucose-containing drinks contradicts some previous studies [13,14,36]. Previous research has recognised that aging and individual differences in gluco-regulatory efficiency could contribute to inconsistent effects on the relation between glucose and cognitive effects [8,37]. The present study recruited participants from a relatively narrow and young age band with assumed similar gluco-regulatory control, which may partially explain the contrasting findings.

In addition, the present study found that the contrasting effect due to glucose ingestion appeared to be more pronounced in the fasting group compared to the non-fasting group. Another line of research that has discussed the role of fasting on cognitive effects is related to the cognitive impact of breakfast omission. For instance, Benton and Parker ascertained that consuming a glucose drink could reverse the negative effects of breakfast omission on some (but not all) cognitive tasks [24]. Furthermore, Veasey and others found using an attention task that breakfast omission actually led to faster response times than did the consumption trial, in line with the current findings [38]. Additional assessments of glucose effects under fasting conditions are much-needed.

As a *caveat* of the present study, the testing samples varied in energy content. Thus, the glycaemic responses were expectedly variable, and effects of levels of sweetness therefore do not give the whole story without concurrent or convergent studies on energy levels of the different sugar substances. It is recommended that future studies incorporate designs that standardise both the energy level and sweetness to gain more accurate insights into cognitive effects across different sugar sources. The present study adopted a rigorous protocol to ensure equivalent sweetness across the tested samples, which should be recommended for future research in this area. This method is particularly useful given that exclusive activation of taste receptors by non-caloric sweeteners can predict some insulin changes [39].

Overall, the present study adds to the growing body of literature concerning sugar effects on behavioural and cognitive performances. Contrasting effects of the different sugar types indicate that the cognitive effects of sugar are unlikely moderated by the perception of sweetness. Rather, the effects are mediated by glucose. Further research should systematically assess effects of dietary sugars on other cognitive domains including memory (to make direct comparisons with previous work), to provide a more complete picture of the effects of sugar consumption on brain and cognitive activity.

Acknowledgements

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