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ORIGINAL INVESTIGATION

Glucose and memory: The influence of drink, expectancy, and beliefs

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Abstract
Rationale An increasing number of studies suggest that glucose can enhance aspects of memory and the central methodology is the use of the glucose–placebo design. One critical issue therefore is separating the pharmacological effects of glucose from the expectancies created by consuming a drink that might contain glucose.
Objective A modified balanced placebo design examined the role that expectancy and belief about the drink consumed has on the pharmacological changes observed following glucose consumption.
Method Ninety-three participants, allocated according to a drink (glucose, placebo) × message (told glucose, told nothing, told placebo) unrelated design, were administered tasks assessing immediate and delayed verbal free recall, spatial recognition and semantic verification. Each task has some evidence for hippocampus involvement, and variations in task difficulty were used to assess the idea that glucose effects are sensitive to task difficulty.
Results While the messages biased drink judgements in the expected direction, judgements of drink content were at chance and glucose only enhanced delayed free recall. The subtle effects of the messages did not modify the glucose enhancement. However, believing glucose had been consumed showed an independent improvement in delayed free recall. There was no evidence that task complexity enhanced the glucose effect.
Conclusions The findings indicate that expectancy effects are unlikely to be confused with glucose enhancements, but beliefs about consuming glucose can augment performance on delayed free recall. The discussion considers the hippocampus and complexity hypotheses of glucose's mode of action and proposes the routine collection of drink beliefs in future studies.

Keywords Glucose · Episodic memory · Semantic memory · Spatial memory · Expectancy · Beliefs · Balanced placebo design

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Introduction

The consumption of a drink containing glucose is typically associated with relatively selective improvements on tasks of learning and memory (Smith et al. 2011). One feature common to human research exploring this influence of glucose on cognition is the placebo design. In this design, participants are administered a glucose drink or a placebo drink that has been equated for sweetness (e.g. using aspartame or saccharine).

With the establishment of informed consent, it is usually necessary for participants to be made aware that the drink they will be asked to consume might contain glucose (but see Foster et al. 1998; Sünram-Lea et al. 2002b). As the participant's expectancies or beliefs about the drink might create its own effects or modify those of glucose, one critical issue raised is separating the effects arising from the anticipated consequence of ingesting glucose from the pharmacological effects under investigation. The standard placebo design examines the pharmacological effects of glucose by contrasting the placebo and glucose drink. However, this does not assess the impact of glucose uncontaminated by expectancies or the nature of these expectancies. Despite the care taken to equate glucose and placebo drinks on a range of relevant characteristics (e.g. volume, colour, and sweetness), the expectancy effect is uncontrolled in the sense that participants will form their own beliefs about the nature of the drink they have consumed. As formal assessments of whether participants were blind to the glucose manipulation are rare (but see Benton and Owens 1993; Winder and

Borrill 1998), the influence of beliefs about the nature of the drink consumed is not evaluated.

One effective way to examine expectancy is to administer a drink and manipulate the information given to participants about that drink (e.g. correctly or incorrectly informing them of the drink contents), and balanced placebo designs manipulate both the participant's expectancies and the active agent. The somewhat complex role that expectations play in the self-report and behavioural effects of a range of substances is acknowledged (Fillmore et al. 1994, 2002; Flaten et al. 2003; Mikalsen et al. 2001; Oei and Hartley 2005; Swartzman and Burkell 1990), although expectancy effects are more pervasive in the social cognition literature (see Stangor and McMillan 1992). Of most relevance to the effects of glucose are the expectancy effects observed in studies of caffeine and alcohol—caffeine is usually expected to improve, and alcohol to impair, performance. Using only placebo drinks, Fillmore et al. (1994) found those expecting caffeine improvements performed better on a pursuit rotor task than those expecting impairments but, for alcohol, those expecting impairments performed better than those expecting improvements. In a similar vein, Oei and Hartley (2005) found those expecting caffeine improvements had higher signal detection rates than those without this expectancy and this was independent of caffeine-related improvements. These expectancy effects are not pervasive because neither caffeine nor expectancy influences memory scanning or delayed free recall. Similarly, when given an inactive novel drug (Kvavilashvili and Ellis 1999), those told the drug impaired memory showed impaired free recall, but those told the drug enhanced memory did not show better memory. However, the self-reported changes in memory and the claimed action of the drug were consistent indicating a discrepancy between subjective reports and objective changes. Thus, the drug expected, its expected effect and the type of drug interact to determine placebo expectancy effects.

While the balanced placebo design provides a useful approach for evaluating the effects of a drug, expectancy and their interaction, only one study has utilised it to examine glucose effects (Green et al. 2001). Using a related samples design, they accurately informed participants of the drink content (50 g glucose vs. aspartame) on two occasions and misinformed them on the other two. Glucose produced faster, but equally accurate, access to words in an immediate recognition task, with improvements in a vigilance task only observed when given with a drink congruent message. There were no glucose or expectancy effects on immediate word recall or finger tapping. As the authors note, these results are inconsistent with the bulk of the glucose literature, and Bellisle (2001), commenting on this study, observes that glucose expectancy effects remain understudied. Nevertheless, since the initial work by Green et al. (2001), no additional studies have been conducted on this important topic. Given the uncertain impact of expectancy on the pharmacological action of glucose there remains a strong need to understand its influence in a substance expected to enhance cognition.

The present study employed a modified version of the balanced placebo design to investigate the role of drink content, expectancy and beliefs in four memory tasks. In addition to correctly or incorrectly informing participants of their drink content, the design also includes the condition where participants are left uninformed of the drink content—the normal situation in glucose–placebo studies. Unlike the study by Green et al. (2001), the present study used an unrelated, rather than related, samples design to circumvent issues related to mistrust buildup across multiple deception sessions.

The current debate about the processes that underlie glucose improvements suggests that one plausible mechanism is that the peripherally administered glucose functions to maintain an optimal glucose supply to the brain when local reserves are being depleted by demanding cognitive activities (for reviews, see Messier 2004; Riby 2004). The memory tasks selected for this study therefore draw on current knowledge of glucose facilitation effects as being predominantly on tasks dependent on the hippocampus and sensitive to task complexity (see Smith et al. 2011). First, a classic episodic memory task associated with glucose enhancements, delayed verbal free recall, is used. Here, nouns of varying memorability allowed the study of task difficulty in this verbal domain. As hippocampal function is also associated with spatial memory (Burgess et al. 2002; Moscovitch et al. 2005), a location recognition task with varying memory loads is used to explore this spatial domain. In addition, as there is some evidence of hippocampal involvement in semantic memory tasks (Manns et al. 2003; Moscovitch et al. 2005), a category verification task is included in which the to-be-classified nouns must be processed to varying amounts to support their verification. This semantic classification task also served as the encoding phase for an immediate verbal free recall task. This is to ascertain whether more elaborative semantic processing has an impact on immediate episodic retrieval following glucose ingestion. As indicated above, all memory tasks include complexity manipulations to ascertain whether higher levels of cognitive demand are associated with larger glucose-related improvements.

Method

Participants

Ninety-three participants (35 males) aged 18–35 years (mean=20.7 years) signed up for the study in exchange for

experimental hours credits. No participants were diabetic and had phenylketonuria, and all were fluent English speakers. Participants were required to fast from midnight the previous night and only drink water prior to attending the experimental session to ensure their blood glucose was at fasting levels. The University Research Ethics Committee approved the study and all participants gave written informed consent.

Design

Each participant attended one session lasting about 35 min and was assigned to one of six conditions defined by two independent factors: drink (50 g glucose, placebo) and message (told glucose, told placebo, told nothing). Between two and four participants were tested on each session. On arrival, participants were assigned to their allocated condition according to a predetermined randomisation schedule. The experimenter prepared the drinks before participants arrived, and the drinks comprised 300 ml of water mixed with 30 ml of "no added sugar" orange and lemon squash to which was added 50 g glucose (190 kcal or 795 kJ) or 75 mg saccharin (3 kcal or 13 kJ). A preliminary pilot study indicated that this resulted in the drinks having a similar "mouth feel" and sweetness.

Procedure

Participants arrived for testing in the morning at 09:30 (n=35) or 10:15 (n=58) and re-read the recruitment information sheet that included the following two critical pieces of information: "Glucose is thought to facilitate cognitive process, particularly memory" and "In this study, you will be asked to consume a drink that might contain glucose". Following consent, the experimenter gave each participant their drink and told them its contents (e.g. "You have been allocated to the placebo condition") or said nothing—this is the message manipulation. Participants consumed their drink and completed a demographic questionnaire (e.g. age, sex, fasting compliance, etc.) and a pre-session stress–arousal checklist (Mackay et al. 1978) to assess whether mood changes might mediate the influence of glucose on memory (see Meikle et al. 2004; Smith et al. 2011). After 10 min, by which time glucose levels should be raised (Meikle et al. 2004), they began the series of memory tasks. First, they saw the words for a delayed free recall task (1 min), followed by the spatial location recognition task (5 min), and then given 3 min to free recall the words seen earlier. They then undertook the category verification task (1 min) and immediately attempted to free recall as many of the nouns from that task as they could (3 min). Finally, they completed a post-session stress–arousal checklist followed by a forced-choice drink judgement (glucose–placebo) of the contents of their drink. The test session finished after about 35 min when glucose levels would be expected to begin falling (Meikle et al. 2004). Participants then received debriefing information about the study.

Memory tasks

Four computer-controlled tasks were administered from the ACT system (Stollery 1996): delayed verbal free recall, spatial location recognition, category verification and immediate verbal free recall. All words appeared in the centre of a black screen in white uppercase letters. Participants made all responses with their dominant hand using two labelled keys: "yes" (B) and "no" (N).

Delayed free recall Each participant viewed a new random sequence of 20 nouns with instructions to remember them for later recall. Each noun was shown for 2 s (1 s blank internoun interval). Immediately after the location recognition task (about 5 min, see below), participants had 3 min to write down as many of these nouns as possible. The number of nouns correctly recalled and the number of recall errors made were used as outcome measures.

Noun selection conformed to a two-factor independent design with the factors of Thorndike–Lorge written frequency (high vs. low) and imagability (high vs. low): five nouns in each condition. All nouns were six letters long and selected from the MRC database (Fearnley 1997). ANOVAs confirmed the independence of the frequency and imagability manipulations. For imagability, there was a main effect of imagability (389 vs. 598, p<0.001), but not frequency (498 vs. 489, p=0.780) or an interaction (p=0.257). For frequency, there was a main effect of frequency (26 vs. 432, p=0.001), but not imagability (290 vs. 168, p=0.538) or an interaction (p=0.522). The four sets of nouns were also matched on the number of syllables (mean=2.15, p=0.274).

Spatial location recognition Participants viewed a white rectangle (165×130 mm) shown centrally on a black background. On each trial, two, four or six white circles (memory load) are shown simultaneously within the rectangle with instructions to remember the locations. After 500 ms, a question mark probe is presented and participants decide, as quickly and accurately as possible, whether this probe is at one of the target locations: "yes" (target present) or "no" (target absent). As all stimuli are identical, recognition depends solely on the ability to discriminate the probe's location. Presentation times for the three memory loads were set at 2, 3 and 4 s, respectively (i.e. 1.0+0.5 s per memory item) and the probe remained on the screen until the participant responds. The speed and accuracy of correct decisions, together with signal detection measures (d' and β), were used as outcome measures.

On each trial, target positions are randomly selected from 81 possible locations (9×9). For target present trials, the probe is at one randomly selected valid location. For target absent trials, the probe occupies a non-valid location adjacent to a randomly selected valid location. After a brief familiarisation, participants complete seven replications of the basic truth (target present vs. absent) × memory load (two, four and six) design (i.e. 42 trials). Replications are sequential with a new random order of trials within a replication. Participants receive accuracy feedback on the familiarisation trials, but not the main trials.

Category verification and immediate free recall Participants saw a sequence of 40 nouns and decided, as quickly and accurately as possible, whether the noun (e.g. canary) named a kind of "bird". Each noun remained on the screen until answered. There were equal numbers of category (bird) and distracter (non-bird) nouns and a new random order of the nouns shown to each participant. Immediately following verification, participants had 3 min to write down as many of the 40 words as they could remember. For the verification phase, the speed and accuracy of correct decisions were used as the outcome measure. For immediate recall, the number of nouns correctly recalled and the number of recall errors made were used as the outcome measures.

The 40 nouns selected conformed to a truth (category vs. distracter) × relatedness (strong vs. weak) design—with 10 nouns in each condition. The category nouns comprised equal numbers of typical (e.g. robin) and atypical (e.g. puffin) members. Typicality refers to the degree that the instance is representative of the category, with typical instances strongly related, and atypical instances weakly related, to the target category (e.g. Smith et al. 1974). The distracter nouns comprised equal numbers of related and unrelated non-bird nouns. The related distracters relate to the search category through the common super-ordinate "animals". The unrelated distracters weakly relate to the search category by sharing the unrelated category of "plants". The related distracters comprised five fish (e.g. sardine) and five insects (e.g. spider) and the unrelated distracters comprised five vegetables (e.g. pea) and five flowers (e.g. lily). The length of the nouns varied between three and nine letters and the four noun groups were matched (Fearnley 1997) on the number of letters (p=0.317), number of syllables (p=0.165) and Thorndike–Lorge written frequency (p=0.218).

Statistical analysis

The basic design was a two-factor independent samples ANOVA: drink (50 g glucose vs. placebo) × message (told glucose, told nothing, told placebo). All other factors are related samples and are identified at the start of each analysis. A measure of effect size (partial eta-squared, η_p^2) for significant glucose or message effects is cited (0.01 ≅ small, 0.06 ≅ medium, 0.15 ≅ large) with the F-ratio. For all related sample analyses, when sphericity is violated, the Huynh–Feldt corrected p values are given, but for readability, the original degrees of freedom are cited. Post hoc analysis used the Tukey (HSD) test.

Results

Manipulation check

The ability to detect the drink consumed and its relationship to the message condition were assessed using a three-way loglinear analysis (see Table 1): drink (glucose, placebo), belief (glucose, placebo) and message (glucose, nothing, placebo). Using backward elimination, the only significant effect was the message × belief interaction (χ^2 (2, N=93)= 8.7, p=0.013) with this model producing an excellent fit (likelihood ratio: χ^2 (6)=0.647, p=0.996). Of particular importance, participants were unable to detect the drink they consumed (p=0.550), and this did not vary with the message condition (p=0.880). Exploration of the message × belief interaction indicates that participant's beliefs reflect the instructional set. Odds ratios using the "told nothing" group as baseline, where participants are twice as likely to say they had glucose, show those "told glucose" are only slightly more likely to believe they had glucose (OR=1.22), whereas those "told placebo" are three times more likely to believe they had placebo (OR=3.33). Thus, participants are unable detect the content of their drink and the message biases drink judgements in the expected direction, primarily due to those told they were getting placebo. Finally, the six groups did not differ in age (F<1) or in the distribution of males and females (χ^2 (5)=3.62, p=0.606).

Self-reported stress and arousal

Stress and arousal ratings were analysed using a three-factor mixed ANOVA, with time (pre-session vs. post-session) as the related sample factor (see Table 1). Stress scores were not influenced by drink (p=0.999) and message (p=0.160) and did not change with time (p=0.551), and none of the interactions were significant (all F<1). Arousal ratings were not influenced by drink (p=0.307) and message (p=0.826) and did not change with time (p=0.157), and none of the interactions were significant (all F<1). Thus, stress and arousal scores are not influenced by drink or message and remained constant during the session.

Table 1 Post-drink belief, stress, arousal, delayed free recall (±SD) as a function of drink given and drink message

		Drink consumed					
		Glucose			Placebo		
Drink message		Glucose	None	Placebo	Glucose	None	Placebo
Sample size (males)		15 (6)	15 (5)	16 (7)	16 (7)	15 (7)	16 (3)
Age (years)		20.9 (2.3)	21.3 (4.0)	21.3 (4.4)	20.3 (2.4)	20.9 (2.8)	19.4 (1.2)
Believed had "glucose"		11	10	7	11	10	5
Stress and arousal							
Pre-session stress		3.2 (4.0)	3.8 (4.4)	2.1 (3.8)	3.6 (5.0)	4.1 (3.4)	2.0 (2.3)
Post-session stress		3.9 (4.5)	3.5 (3.7)	2.9 (4.1)	3.2 (3.7)	4.3 (4.2)	2.3 (3.4)
Pre-session arousal		5.4 (3.5)	6.9 (3.9)	6.3 (3.7)	5.1 (3.0)	5.1 (3.0)	5.6 (4.1)
Post-session arousal		6.1 (3.4)	6.7 (2.8)	6.6 (3.7)	6.3 (4.3)	5.9 (4.0)	6.1 (3.8)
Delayed free recall[a]							
Frequency	Imagability						
High	High	2.80 (1.01)	2.53 (1.06)	2.81 (0.83)	2.88 (1.09)	2.33 (1.05)	2.63 (0.96)
	Low	2.07 (1.10)	2.00 (1.00)	1.94 (1.18)	1.63 (0.81)	1.67 (0.98)	2.00 (1.10)
Low	High	2.27 (1.10)	2.07 (1.39)	1.44 (1.32)	1.81 (1.64)	1.20 (1.15)	1.56 (1.15)
	Low	1.47 (1.06)	1.80 (1.32)	2.00 (0.97)	1.25 (1.00)	1.20 (1.15)	1.63 (1.03)
Recall errors		0.80 (1.15)	0.47 (0.64)	0.19 (0.40)	0.88 (1.15)	0.73 (0.70)	0.56 (0.81)

[a] Main effect of glucose

Delayed verbal free recall

Free recall was examined using a four-factor mixed ANOVA, with word frequency (high vs. low) and word imagability (high vs. low) as the related factors. About 5 min after encoding, participants correctly recalled an average of 7.8 nouns and made 0.6 errors (see Table 1).

Those receiving glucose tended to recall more words (total recall, 8.40 vs. 7.26, $F(1, 87)=3.75$, $p=0.056$, $\eta_p^2=0.041$) with a medium effect size (Cohen's $d=0.39$). Free recall was not influenced by the message ($p=0.593$) nor the drink × message interaction ($p=0.529$). There were strong effects of task difficulty on recall, with generally better recall of high frequency ($F(1, 87)=41.7$, $p<0.001$) and high imagability ($F(1, 87)=21.3$, $p<0.001$) words. The word frequency × imagability interaction ($F(1, 87)=8.0$, $p=0.006$, MSE=1.092) simply showed higher recall for high frequency–high imagability nouns compared to all other noun types ($p<0.01$), which did not differ among themselves. Of particular interest, the glucose effect did not interact with either frequency ($p=0.249$), imagability ($p=0.749$) or the frequency × imagability interaction ($p=0.757$), indicating that the improvement due to glucose was independent of the ease of recall.

The only other effect to achieve significance was the imagability × message interaction ($F(2, 87)=3.31$, $p=0.041$, $\eta_p^2=0.071$, MSE=0.981). Post hoc analysis showed better recall of high imagability words for those "told glucose" ($p<0.01$) and "told nothing" ($p=0.05$), but those "told placebo" recalled an equivalent number of high and low imagability words. Analysis of recall errors showed no effects of drink ($p=0.180$), message ($p=0.105$) or a drink × message interaction ($p=0.780$).

In summary, participants recalled about 39 % of the words encoded 5 min earlier. Those receiving glucose tended to recall more words, and word frequency and imagability both influence recall in the expected manner. The improved recall in those given glucose was independent of the difficulty of recalling words. In comparison to the "told nothing" group, the imagability effect was enhanced in those "told glucose" and reduced in those "told placebo".

Spatial location recognition

Correct recognition times and accuracy were analysed using a four-factor mixed ANOVA with truth (target present/absent) and memory load (two, four and six) as the related factors. On average, participants correctly detected the location of the probe in 1.109 s with 74 % accuracy (see Table 2).

For recognition times, there were no main effects of drink ($p=0.451$), message ($p=0.162$) or a drink × message interaction ($p=0.269$). Target present and absent decision times did not differ ($p=0.706$), and the only effect to achieve significance was that of memory load ($F(2, 174)=36.15$, $p<0.001$, MSE=0.074). Post hoc analysis simply shows slower reaction times with increasing memory load (0.873,

Table 2 Correct reaction time and accuracy (±SD) in the location recognition task as a function of drink and message

		Drink consumed					
		Glucose			Placebo		
Drink message		Glucose	None	Placebo	Glucose	None	Placebo
RT (s)	Load						
Target present	Two	0.915 (0.238)	0.887 (0.352)	0.882 (0.205)	0.847 (0.192)	0.885 (0.288)	0.934 (0.342)
	Four	0.934 (0.221)	0.966 (0.326)	0.840 (0.150)	0.918 (0.188)	0.996 (0.330)	1.042 (0.469)
	Six	1.079 (0.406)	1.060 (0.375)	1.027 (0.305)	1.094 (0.210)	1.178 (0.457)	1.048 (0.293)
Target absent	Two	0.880 (0.372)	0.897 (0.261)	0.815 (0.153)	0.841 (0.218)	0.884 (0.394)	0.808 (0.175)
	Four	1.021 (0.340)	0.966 (0.299)	0.941 (0.172)	0.992 (0.253)	0.990 (0.399)	1.101 (0.254)
	Six	1.016 (0.280)	1.182 (0.447)	0.996 (0.293)	1.206 (0.459)	1.069 (0.361)	1.183 (0.944)
Accuracy (%)[a]							
Target present	Two	80.0 (16)	81.9 (18)	84.9 (14)	85.7 (19)	90.5 (12)	79.5 (20)
	Four	76.2 (19)	81.0 (19)	77.7 (19)	81.3 (21)	76.2 (18)	74.1 (18)
	Six	61.0 18)	69.5 (19)	70.5 (17)	63.4 (24)	73.3 (26)	67.0 (21)
Target absent	Two	77.1 (21)	87.6 (11)	87.5 (16)	83.0 (11)	75.2 (21)	81.3 (19)
	Four	64.8 (19)	73.3 (19)	59.8 (25)	68.8 (22)	67.6 (23)	73.2 (13)
	Six	71.4 (22)	60.0 (16)	61.6 (29)	55.4 (23)	68.6 (18)	66.1 (16)

[a] Load × drink interaction for those given the "glucose" message

0.968 and 1.095, all $p<0.01$). Importantly, memory load did not interact with drink ($p=0.270$) or message ($p=0.981$).

For recognition accuracy, there were no main effects of drink ($p=0.904$), message ($p=0.441$) or a drink × message interaction ($p=0.943$). Accuracy declined with increasing memory load (83, 73 and 66 %; $F(2, 174)=55.0$, $p<0.001$), with target present accuracy being higher than target absent accuracy (76 vs. 71 %, $F(1, 87)=5.88$, $p=0.017$). The borderline memory load × truth interaction ($F(2, 174)=2.74$, $p=0.067$, MSE=300.9) simply indicated as memory load increased accuracy declined faster for target absent decisions.

While memory load did not interact with drink ($p=0.817$) or message ($p=0.749$), the memory load × drink × message interaction ($F(4, 174)=3.31$, $p=0.012$, $\eta_p^2=0.071$) was significant. Follow-up analyses showed that the basic memory load × drink interaction was localised to the "told glucose" message group ($F(2, 58)=3.30$, $p=0.044$, $\eta_p^2=0.102$): "told placebo" ($p=0.183$) and "told nothing" ($p=0.149$). Post hoc analysis for the "told glucose" group (MSE=226.5; see Table 2) showed that accuracy declined faster under placebo (84 vs. 74 vs. 59 %; $p<0.01$) than glucose (79 vs. 76 vs. 66 %; $p<0.05$), although none of the comparisons between glucose and placebo were significant.

Given this effect of message on recognition accuracy, the data were reanalysed with signal detection measures using the two high threshold model with corrected hit and false alarm rates (see Snodgrass and Corwin 1988). The discrimination index (P_r) reflects the participant's ability to discriminate old and new items and the response bias index (B_r) reflects the probability of saying "yes" to an item when in an uncertain state, with 0.5 indicating a neutral bias.

Participants had a relatively neutral bias (0.539) and bias did not vary as a function of drink ($p=0.258$), message ($p=0.552$) or memory load ($p=0.157$), and no interactions were significant. The discrimination index showed no effects of drink ($p=904$) or message ($p=0.441$), but declined with increasing memory load (0.575, 0.399 and 0.274, $F(2, 174)=55.0$, $p<0.001$). Again, while memory load did not interact with drink ($p=0.817$) or message ($p=0.749$), the memory load × drink × message interaction ($F(4, 174)=3.31$, $p=0.012$, $\eta_p^2=0.071$) was significant. In common with the accuracy analysis, the basic memory load × drink interaction was localised to the "told glucose" message group ($F(2, 58)=3.30$, $p=0.044$, $\eta_p^2=0.102$, MSE=0.035): "told nothing" ($p=0.183$) and "told placebo" ($p=0.149$). Similar to the accuracy findings, discrimination declined faster under placebo (0.602 vs. 0.437 vs.0.164; $p<0.01$) than glucose (0.500 vs. 0.358 vs. 0.283; $p<0.05$), but none of the differences between glucose and placebo were significant.

In summary, correctly identifying the location of circles became slower and less accurate at higher memory loads, with a tendency for accuracy to decline faster for target absent decisions. Glucose did not influence recognition speed, but those receiving glucose with a drink congruent message showed a slower decline in accuracy as memory load increased. Signal detection analysis indicates that this decline reflects changes in discrimination rather than response bias.

Category verification

The speed and accuracy of correct verifications were analysed using a four-factor mixed ANOVA with truth (category vs. distracter) and relatedness (strong vs. weak) as the related factors. Overall, participants correctly classified the nouns in 1.080 s with 93 % accuracy (see Table 3).

For verification times, there was no effect of drink (p=0.570), a borderline effect of message (F(2, 87)=2.95, p=0.057, η_p^2=0.064) and no drink × message interaction (p=0.908). Post hoc analysis of the message effect (MSE= 0.913) showed slower verification in those "told glucose" compared to those "told placebo" (1.186 vs. 0.914, p=0.068), with those "told nothing" being intermediate (1.141) and not different from the other two message conditions.

Post hoc analysis of the truth × relatedness interaction (F(1, 87)=34.02, p<0.001) showed the expected effects of task difficulty. For category members, typical instances are classified faster than atypical instances (p<0.01). For distracters, unrelated distracters are classified faster than related distracters (p<0.01), with atypical instances of the category classified at the same speed as related distracters. There were no significant interactions involving drink or message.

For accuracy, there was no effect of drink (p=0.376), message (p=0.732) or a drink × message interaction (p=0.275). Post hoc analysis of the truth × relatedness interaction (F(1, 87)=63.8, p<0.001, MSE=65.3) mirrored the pattern shown for verification times: classification accuracy was higher for typical than atypical members and higher for unrelated than related distracters (both p<0.01). There were no significant interactions involving drink or message.

In summary, typical category members are verified faster and more accurately than atypical members, and related distracters are verified slower and less accurately than unrelated distracters. There were no effects of glucose on speed and accuracy, but those "told glucose" tended to respond more slowly than those "told placebo".

Immediate verbal free recall

Immediately following the category verification task, participants had 3 min to recall as many of the 40 nouns as possible. On average, participants recalled 14.6 nouns and made 0.6 errors (see Table 3).

Immediate free recall was examined using a four-factor mixed ANOVA with truth (category vs. distracter) and relatedness (strong vs. weak) as the related factors. There were no effects of drink (p=0.861), message (p=0.766) and no drink × message interaction (p=0.111). In general, more category words were recalled than distracters (p<0.001), and the truth × relatedness interaction (F(1, 87)=19.2, p<0.001)

Table 3 Category verification speed, accuracy and immediate free recall (±SD) as a function of drink and message

	Drink consumed					
	Glucose			Placebo		
Drink message	Glucose	None	Placebo	Glucose	None	Placebo
Verification speed (s)[a]						
Typical instances	0.991 (0.517)	1.089 (0.519)	0.800 (0.281)	0.913 (0.312)	0.906 (0.498)	0.827 (0.258)
Atypical instances	1.212 (0.312)	1.237 (0.445)	0.922 (0.324)	1.187 (0.605)	1.229 (0.844)	0.930 (0.292)
Related distracters	1.477 (0.901)	1.229 (0.384)	1.062 (0.351)	1.426 (0.974)	1.217 (0.798)	1.006 (0.312)
Unrelated distracters	1.276 (0.727)	1.136 (0.449)	0.871 (0.319)	1.009 (0.347)	1.085 (0.673)	0.891 (0.220)
Verification accuracy (%)						
Typical instances	94.7 (11)	95.3 (11)	93.8 (10)	99.4 (3)	90.7 (17)	99.4 (3)
Atypical instances	86.7 (18)	90.7 (18)	87.5 (11)	88.1 (17)	87.3 (19)	92.5 (9)
Related distracters	88.0 (10)	89.3 (12)	89.4 (9)	91.3 (8)	91.3 (7)	91.9 (8)
Unrelated distracters	96.7 (8)	97.3 (5)	95.6 (13)	98.1 (4)	94.0 (12)	99.4 (3)
Immediate free recall[b]						
Typical instances	5.20 (1.21)	4.72 (1.16)	4.75 (1.65)	5.37 (1.41)	5.07 (1.22)	5.44 (1.21)
Atypical instances	3.93 (1.30)	3.40 (1.50)	3.44 (1.71)	3.69 (1.49)	2.73 (1.34)	4.25 (1.69)
Related distracters	3.07 (1.87)	3.13 (2.13)	3.63 (2.03)	2.69 (1.66)	2.60 (1.40)	3.19 (1.68)
Unrelated distracters	2.67 (1.35)	3.67 (1.72)	1.87 (1.31)	2.56 (1.26)	3.07 (1.49)	3.25 (1.77)
Recall errors	0.87 (1.06)	0.73 (0.88)	0.50 (0.73)	0.50 (0.63)	0.60 (0.74)	0.50 (1.10)

[a] Main effect of message

[b] Message × truth × relatedness interaction

showed the expected effects of task difficulty: recall levels declined numerically in the order of typical instances, atypical instances, related distracters and unrelated distracters (5.09, 3.57, 3.05 and 2.85, respectively). Post hoc analysis (MSE= 2.106) showed better recall of typical than atypical instances (5.09 vs. 3.57, $p<0.01$), but no difference in the recall of related and unrelated distracters. The higher recall of atypical instances compared to related distracters was of borderline significance (critical difference=0.56 at 5 %).

These recall difficulty effects only varied significantly with respect to the three message conditions: there was a truth × message ($p=0.052$) and a truth × relatedness × message ($F(2, 87)=3.43$, $p=0.037$, $\eta_p^2=0.073$) interaction. Post hoc analysis (MSE=2.106) showed that for all message groups, there was better recall of typical than atypical instances ($p<0.01$) and no difference in the recall of related and unrelated distracters. In contrast, there was better recall of atypical instances compared to unrelated distracters for the message groups "told glucose" ($p=0.05$) and "told placebo" ($p=0.05$), but not those "told nothing". Finally, an analysis of recall errors showed no influence of drink ($p=0.360$), message ($p=0.655$) or a drink × message interaction ($p=0.702$).

In summary, participants recalled about 37 % of the words just seen, and the influence of the initial classification task had the expected effect on immediate free recall. There were no effects of the glucose, but the generally better recall of atypical instances compared to unrelated distracters is absent for the "told nothing" message group.

Influence of drink belief

While it is clear that the messages bias judgements of drink content in the desired manner, the belief participants formed about the drink did not always coincide with the message given. Indeed, when no message is given, the bias is to believing glucose had been consumed. Consequently, the expectancy effects reported above might simply derive from the belief the participant formed about their drink, rather than from a message-induced expectancy per se. It is therefore of particular interest to examine the joint impact of drink (glucose vs. placebo) and belief (glucose vs. placebo) on stress, arousal and memory (see Table 4).

Stress ratings showed no influence of belief, but arousal shows a time × belief interaction ($F(1, 89)=7.74$, $p=0.007$, $\eta_p^2=0.080$). Post hoc analysis (MSE=5.853) shows arousal increases over the session for those believing they had glucose ($p<0.05$), but remains constant for those believing they had placebo.

For delayed free recall, in addition to the tendency for higher recall with glucose reported earlier ($F(1, 89)=3.83$, $p=0.054$, $\eta_p^2=0.041$), recall tends to be higher when participants believe they had glucose ($F(1, 89)=3.46$, $p=0.066$, $\eta_p^2=0.037$), but the drink × belief interaction is not significant ($p=0.363$). As facilitative effects of glucose on delayed free recall are a classic glucose effect in placebo-controlled trials, and "no message" the natural situation, a separate analysis examined the impact of drink belief within those with no message-induced expectancy. Again, recall tends to be higher under glucose ($F(1, 26)=3.72$, $p=0.065$, $\eta_p^2=0.125$), higher when the drink is believed to contain glucose ($F(1, 26)=5.76$, $p=0.024$, $\eta_p^2=0.181$), with no significant interactions. Cohen's d shows both effects are in the medium-to-large range (drink=0.66 and belief=0.84). Thus, in a typical placebo trial, although participants cannot detect which drink they consumed, drinking glucose and believing you had drunk glucose independently contribute to better recall. Finally, it is worth noting that those believing they had glucose show an increase in arousal over the session. However, delayed free recall is not correlated with either pre-session ($p=0.113$), post-session ($p=0.113$) or arousal change ($p=0.962$).

Delayed free recall errors show a drink × belief interaction ($F(1, 89)=4.30$, $p=0.041$, $\eta_p^2=0.041$) that does not yield to post hoc analysis (MSE=0.704). The pattern suggests that those given placebo holding a congruent belief produce more errors than the other groups (see Table 4).

For location recognition, the participant's belief had no influence on accuracy or the two signal detection measures. For recognition times, the only influence of belief was revealed in the truth × drink × belief interaction ($F(1, 89)=4.33$, $p=0.040$, $\eta_p^2=0.046$). The critical truth × drink interaction approached significance for those believing they had placebo ($p=0.070$), but not those believing they had glucose ($p=0.248$). Unsurprisingly, the effect failed to yield to post hoc analysis (MSE=0.061), but the pattern implies faster target present decisions under glucose (1.008 vs. 0.915 s), with no impact on target absent decisions (0.969 vs. 0.940 s), for those believing they had the placebo drink.

Finally, category verification times were 202 ms slower when participants believed they had glucose ($F(1, 89)=4.0$, $p=0.049$, $\eta_p^2=0.043$, Cohen's $d=0.42$), but there are no effects of belief on verification accuracy, immediate free recall or recall errors.

Discussion

Using a modified balanced placebo design, the aim of this study was to separate the pharmacological and expectancy effects of glucose using four memory tasks. In addition to providing congruent and incongruent information about drink content, a "no message" condition was included to replicate the design used in double-blind studies. The memory tasks included one classically associated with glucose enhancement (delayed free recall) and the other three

Table 4 Mood and average memory performance (±SD) as a function of drink and drink belief

	Drink consumed			
	Glucose		Placebo	
Drink belief	Glucose	Placebo	Glucose	Placebo
Sample size (males)	28	18	26	21
Age (years)	21.6 (4.3)	20.4 (2.2)	20.3 (2.4)	20.0 (2.0)
Stress				
Pre-session stress	2.71 (3.0)	3.50 (4.9)	2.96 (3.1)	3.48 (4.6)
Post-session stress	3.04 (3.9)	4.06 (4.3)	2.88 (3.2)	3.71 (4.4)
Arousal[a]				
Pre-session arousal	6.21 (3.7)	6.22 (3.7)	4.62 (3.0)	6.10 (3.6)
Post-session arousal	7.00 (3.1)	5.67 (3.5)	6.62 (4.0)	5.43 (3.9)
Delayed free recall				
Total correct[b]	8.61 (2.4)	8.06 (3.5)	8.00 (2.5)	6.38 (2.9)
Total errors[c]	0.54 (0.9)	0.39 (0.6)	0.46 (0.6)	1.05 (1.1)
Location recognition				
Mean RT (s)[d]	0.972 (0.3)	0.942 (0.2)	1.013 (0.3)	0.974 (0.2)
Mean accuracy (%)	74.0 (11.2)	73.2 (7.8)	73.6 (7.9)	74.2 (9.4)
Category verification				
Mean RT (s)[e]	1.173 (0.6)	0.998 (0.3)	1.152 (0.6)	0.925 (0.3)
Mean accuracy (%)	91.4 (9.5)	93.1 (6.6)	92.4 (10.2)	95.2 (4.1)
Immediate free recall	14.68 (3.3)	14.17 (4.1)	14.73 (3.6)	14.57 (4.6)

[a]Belief × time interaction
[b]Main effects of drink and belief
[c]Drink × belief interaction
[d]Truth × drink interaction for those believing placebo
[e]Main effect of belief

(spatial recognition, category verification and immediate free recall) sought to establish the generality of glucose enhancements on memory processes with a presumed hippocampal involvement. All tasks incorporate task difficulty manipulations to examine the idea that more demanding cognitive activities are most effective in demonstrating glucose enhancements.

The central point to note is the effectiveness of the messages in biasing judgements of drink content. Given that twice as many participants in the "no message" group believed they had glucose, it is not surprising that of the two messages "told placebo" biases judgements more effectively than "told glucose". Of equal importance, irrespective of the message provided, none of the participants could distinguish between the two drinks. As we created our drinks using typical combinations of ingredients, our study offers reasonably good evidence that current drink matching routines for blinding participants are effective (see also Winder and Borrill 1998). This reassurance that blinding is probably successful in other studies is important because, unfortunately, even when double-blind procedures are followed, the effectiveness of this blinding is not formally reported (e.g. Meikle et al. 2004, 2005; Riby et al. 2008, 2009, 2011; Scholey et al. 2009; Sünram-Lea et al. 2011).

There are three reasons why it might seem unlikely that the lack of any formal assessment of drink belief could compromise our understanding of glucose effects. First, it is probable that in other studies, participants are only at chance when judging the contents of the drink consumed. Second, the message effects are generally restricted to the "told glucose" group and the implicit rule in glucose studies is the "no message" condition—although it is worth noting that most given "no message" believe they had glucose. Finally, the message effects observed are quite subtle and tend to involve trade-offs among the task components rather than arbitrary perturbations of performance. For example, in the delayed free recall task, those "told glucose" did not recall more words; rather, they showed a preference to recall the easier words (high imagability) at the expense of the harder words (low imagability). Together this implies that conclusions about glucose effects from studies not formally assessing drink beliefs are probably robust.

Of course, ensuring that participants are blind to the nature of their drink does not remove expectancy effects linked to the beliefs formed. Thus, it is worth considering what implications there might be for our understanding of glucose effects by not formally assessing drink beliefs. The main evidence bearing on this question comes from analyses considering drink beliefs rather than message-induced expectancies. In contrast to those subtle perturbations relating to the message, those relating to beliefs were mostly clear-cut. For example, those believing they consumed glucose recall more words on the delayed free recall task and are slower on the category verification task.

As noted earlier, the delayed free recall task is a classic task showing glucose enhancements. The idea that simply believing you consumed glucose can exhibit similar improvements to actually consuming it might create uneasiness over the effect's robustness. However, as long as participants are unable to detect their actual drink, then there should be equivalent representation of glucose beliefs, and the associated improvement, in both the placebo and glucose conditions. Crucially, the absence of interactive effects between drink content and beliefs implies that any influence of that belief is unrelated to the drink actually consumed. A similar argument is applicable to the "reverse placebo" effect where those believing they had glucose perform more slowly in the category verification task. This might arise due to expectations that glucose would enhance speed resulting in less effort or in an attempt to improve subsequent recall. Thus, it is tempting to conclude that there is minimal, if any, influence of beliefs that could have a bearing on our understanding of glucose effects.

However, the conclusion that beliefs minimally influence our understanding of glucose effects rests on two key requirements: participants are blind to the drink content and the effects of belief and drink are independent. The present findings provide some confidence that the majority of studies meet the first requirement. The second requirement has yet to be widely evaluated. Although the enhancements due to drink and belief are independent in the delayed recall task, this is not the case for the spatial recognition task. For example, those drinking glucose seem to be faster at recognising a valid location, but not at rejecting an invalid location. However, this only holds for those believing they received placebo. Thus, believing glucose had been consumed "masked" this effect—assuming of course that it is "real". While clearly one of only a few isolated findings, it does serve to remind us that the second requirement can vary with circumstances. Furthermore, depending on how beliefs and drink act together, independent, synergistic or antagonistic effects are possible.

It follows that important gains can be made from incorporating formal assessments of glucose beliefs in future studies. The most obvious is the assurance it provides that study participants are truly blind to their treatment condition. While current practices provide no reason to doubt this, empirical evidence must surely be preferable. Second, it can be determined whether beliefs influence performance since not all task measures show such an influence. More importantly, if beliefs do influence performance, it can be determined if belief operates in an additive or interactive fashion in relation to the actual drink consumed. Conceptually, additive effects are easier to understand (as in delayed free recall), but cannot be presupposed. Third, the power of any experimental study is dependent on adequate control of influential factors. To the extent that beliefs influence psychological process, their incorporation into the analysis strategy serves to improve statistical power.

As an illustrative example, consider the finding that glucose enhancements are more readily seen in unrelated, rather than related, designs (Riby 2004). This is puzzling as related designs, with their control of individual differences, should be the more powerful design. Riby (2004) notes that interpreting this is problematic as study design and task domain are often confounded, but reasonably considers it unlikely that the larger effect size for unrelated designs is linked to the usual arguments for and against each design. Could one possibility be that this discrepancy relates to drink beliefs? In the unrelated design used here, participants are twice as likely to believe they had consumed glucose. Thus, for unrelated designs involving delayed episodic memory, beliefs and drink can produce effects in the same direction—the effect size for beliefs being somewhat larger than drink in the current study. When we consider related designs, the question is what beliefs might participants form about their drink on the second occasion. Might many switch to believing the opposite? If this is the case, then the study would still be blind, but there would be a reduced influence of belief on the second session reducing the average effect size for the related design. This clearly implies order effects, with a greater treatment effect on the first session. As an extension of this, consider the idea that drink beliefs might also underlie treatment order effects, but with larger effects on the second session (Smith and Foster 2008). Here the lack of glucose effects on the first session might reflect a masking due to the initial dominance of glucose beliefs. Of course, alternative interpretations are possible (e.g. task familiarity, etc.). Nevertheless, the example serves to draw attention to how the incorporation of drink beliefs might clarify some unusual findings or at least exclude their causal or mediating role.

Turning now to the effects of glucose on the memory tasks, there are two, possibly related, modes of action to consider in the interpretation of the present findings. The first relates to the idea that glucose effects are more readily observed on hippocampal tasks. As noted earlier, all memory tasks employed here were selected on the basis that there is some evidence of hippocampal involvement, and therefore, all should be influenced by glucose. The second broader explanation relates to the role of task difficulty, with glucose enhancements being more readily detected when the cognitive demands of the task are high, irrespective of whether the tasks draw on hippocampal function (see Smith et al. 2011). However, the present study only examined this idea within tasks with suspected hippocampal involvement.

Our finding that glucose enhancement is seen on delayed verbal free recall is obviously consistent with many previous studies and the hippocampal hypothesis, although the

smaller effect size may reflect a sub-optimal glucose dose (Sünram-Lea et al. 2011). However, contrary to the predictions of the cognitive demand view, there is no evidence that the glucose enhancement is greater for the more difficult material to remember. This is consistent with Riby et al. (2006), who also report that glucose enhancement of delayed free recall is independent of item difficulty.

The absence of effects of glucose on location recognition, uncontaminated by drink beliefs, seems at odds with the long established role of the hippocampus in spatial cognition (O'Keefe and Nadel 1978), especially memory for locations (Burgess et al. 2002), and might indicate that not all hippocampal functions are sensitive to enhancement. Furthermore, despite the detrimental impact of increasing memory load on both speed and accuracy, the increase in spatial memory demands does not assist in promoting any enhancement. Indeed, earlier studies examining spatial memory in young adults have shown mixed evidence for an influence of glucose, with some showing facilitation (Metzger 2000; Sünram-Lea et al. 2001, 2002a, b; Sünram-Lea et al. 2011) and some no facilitation (Benton and Owens 1993; Donohoe and Benton 1999; Foster et al. 1998). It can only be concluded that the kinds of spatial memory tasks that are sensitive to facilitation by glucose remain evasive.

In the current study, the speed of access to semantic memory also fails to show enhancement following glucose. The distinction between semantic and episodic memory has a long history (Tulving 1972) and the contribution of the hippocampus, and underlying structures, to both kinds of memory has been the focus of much discussion (Moscovitch et al. 2006). While the single system unitary model implicates the hippocampus and associated structures with both forms of memory, the hierarchical model sees two interrelated systems with only episodic memory being primarily dependent on the hippocampus (see de Haan et al. 2006). Given the close linkage between the two memory systems, it is unsurprising that neuroimaging studies have yet to clarify the role of the hippocampus in semantic memory tasks (see Binder and Desai 2011; Binder et al. 2009). The current findings are therefore equivocal in relation to the hippocampal hypothesis because it depends on whether the hippocampus is actually active during our semantic classification task. However, as our study shows that the difficulty of making semantic decisions (either within or between semantic categories) fails to promote a glucose effect (see also Riby et al. 2006), it is inconsistent with a general cognitive demand view.

Of course, while category verification involves rapid access to semantic memory, the immediate free recall of the classified items must necessarily be episodic in nature. Here, the manipulations of semantic difficulty had the anticipated effects on memory as it is well know that this positively impacts on recall through encoding distinctiveness (e.g. Jacoby et al. 1979). Thus, despite clear differences in the memorability of the nouns, induced by their relationship to the search category, there are no effects of glucose on overall recall levels or preferentially promoting the recall of the more difficult items. Given that the hippocampus is crucial for episodic memory as long as working memory capacity is exceeded (Jeneson et al. 2011; Jeneson and Squire 2012), and our 40-item list exceeds this span, hippocampal involvement should be assured. Indeed, glucose enhancements have been observed on both immediate and delayed episodic memory tasks (see Riby 2004). Thus, there is no evidence for the hippocampal or cognitive demand hypotheses in this task.

In summary, based on the findings reported here, there is mixed evidence for glucose enhancing hippocampal tasks and no support for the idea that increasing task difficulty results in greater susceptibility to glucose enhancement. Of course, the message-induced expectancy effects might mask glucose effects by increasing performance variability. This is because while the messages are generally effective in biasing drink beliefs, the messages do not convince all participants and some form beliefs that conflict with their message. A consideration of the influence of message-induced expectancy and drink beliefs, however, suggests that insensitivity to the pharmacological effects of glucose is unlikely. First, typical patterns of performance coupled with robust effects of task difficulty are evident in all four memory tasks. Second, the expectancy effects observed are modest and relatively isolated. Indeed, when they are present, they only weakly modulate performance mainly by inducing within-task trade-offs and their presence does not produce disruptive or widespread effects on performance. Finally, in the delayed free recall task, the influence of both glucose and drink belief is equivalent in the "no message" condition and the overall analysis. However, it is acknowledged that the inconsistency of the current findings with the hippocampal hypothesis is governed by the extent of hippocampal involvement in our spatial recognition, category verification and immediate free recall tasks. Thus, their insensitivity to glucose facilitation should not be taken as compelling evidence against the hippocampal hypothesis, particularly given potential dose–response effects (Sünram-Lea et al. 2011). More generally, the hippocampal system is known to be involved in the acquisition, retention and retrieval of episodic memories (Olsen et al. 2012), and there is good evidence that glucose impacts on at least some of these processes (Smith et al. 2011). The broader question of whether glucose has a preferential impact on hippocampal activity or has a more pervasive influence dependent on cognitive demands will require further systematic evaluation.

In view of the above, and given the lack of support for the cognitive demand hypothesis, it is worth considering what boundaries this may indicate for the idea that glucose effects are more apparent with increasing task difficulty—albeit in memory tasks with an alleged hippocampal involvement.

We provisionally propose that sources of difficulty determined by properties intrinsic to the stimuli that determine memorability (e.g. frequency, imagability, typicality, relatedness) are insensitive to glucose facilitation. This idea is consistent with other studies failing to find task difficulty effects when difficulty is intrinsic to the stimuli (e.g. Meikle et al. 2005; Messier et al. 1999; Riby et al. 2006). Reducing general processing resources by having participants engage in a secondary task during encoding has sometimes shown glucose enhancements only under dual-task conditions (e.g. Sünram-Lea et al. 2002b) and sometimes only under single task conditions (e.g. Riby et al. 2006). In one of the tasks used by Meikle et al. (2005), the strong phonological similarity effect is not sensitive to glucose, but memory demands relating to list length is. Similarly, in broad range of working memory style tasks, the more demanding tasks show enhancement (for reviews, see Messier 2004; Riby 2004). Thus, intrinsic properties of the material that determine memorability seem insensitive to glucose, but general demands on memory do seem to promote enhancement. However, the failure of increasing spatial memory load to induce enhancement in this study is evidence inconsistent with this suggestion. Further work is clearly necessary to establish whether such memory demands relate to the process of encoding, consolidation, retrieval or capacity limits. Identifying the constraints on the nature of the difficulty manipulations that lead to glucose enhancement remains a fertile area for research.

In conclusion, the findings from the current study suggest that expectancy effects are probably minimal in glucose studies and, when present, are unlikely to be confused with those arising from the pharmacological action of glucose. Despite the likelihood that participants are blind to their drink in most glucose studies, the belief they form about the drink content, and the expectancy effects that derive from this, can influence performance. We recommend that future studies routinely collect information on drink beliefs because it has two major advantages. It allows a straightforward determination of the efficacy of the drink blinding and it permits the separation of the belief-related expectancy effects from the pharmacological action of glucose.

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