PRELIMINARY EVIDENCE THAT GLUCOSE INGESTION FACILITATES PROSPECTIVE MEMORY PERFORMANCE

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Abbreviations

PM; Prospective Memory
SD; Standard Deviation
NART; National Adult Reading Test
SART; Sustained Attention to Response Task
RT; Reaction Time

Abstract

Previous research has found that the ingestion of glucose boosts task performance in the memory domain (including tasks tapping episodic, semantic and working memory). The present pilot study tested the hypothesis that glucose ingestion would enhance performance on a test of prospective memory. In a between subjects design, 56 adults ranging from 17-80 years of age performed a computerized prospective memory task and an attention (filler) task after 25g of glucose or a sweetness matched placebo. Blood glucose measurements were also taken to assess the impact of individual differences on glucose regulation. After the drink containing glucose, cognitive facilitation was observed on the prospective memory task after excluding subjects with impaired fasting glucose level. Specifically, subjects receiving glucose were 19% more accurate than subjects receiving a placebo, a trend that was marginally non-significant, $F(1,41)=3.4$, $p=0.07$ but that had a medium effect size, $d=0.58$. Subjects receiving glucose were also significantly faster on the prospective memory task, $F(1,35) = 4.8$, $p<0.05$, $d = 0.6$. In addition, elevated baseline blood glucose (indicative of poor glucose regulation) was associated with slower prospective memory responding, $F(1, 35) = 4.4$, $p<0.05$, $d = 0.57$. These data add to the growing body of evidence suggesting that both memory and executive functioning can benefit from the increased provision of glucose to the brain.

KEYWORDS: Carbohydrates, Glucose, Glucose Regulation, Cognition, Mental Performance, Prospective Memory

1. Introduction

Recent research has addressed the value of glucose ingestion and/or improvements in glucose regulation as possible sources of memory enhancement. Memory facilitation after moderate increases in glycaemia, through the ingestion of a glucose-containing drink, has been shown in younger adults [1,2], middle aged adults [3,4], the elderly [5,6], older adults with Mild Cognitive Impairment [7] and patients with Dementia [8]. This work is mirrored by evidence showing that older adults with non-insulin dependent diabetes mellitus can boost memory functioning with improvement in glycaemic control [9]. Moreover, work on rodents has found extracellular glucose levels to be depleted during memory tasks, and that glucose administration was beneficial as a memory enhancer [10; see also [11] for similar work on humans]. The current study aimed to extend previous research to examine prospective memory. Prospective memory (PM) is a term used to describe the ability to recall and act upon future intentions [13]. It plays an important role in everyday activities such as shopping, cooking, household chores, and making social arrangements. Medium to large effect sizes have been found for other memory domains [14], therefore it is not unreasonable to predict an effect of similar size for PM. More recent papers have highlighted the need to consider the ability to regulate glucose [4,15,16], therefore a secondary aim of the current investigation is to examine the role of glucose regulation (indexed here by fasting baseline blood glucose levels) on PM performance.

Glucose is the most abundant simple sugar and the key energy source of the central nervous system. The high rate of blood flow to the brain and subsequent delivery of glucose is due to the brain's high metabolic rate (See [17] for comprehensive account of glucose

delivery to the brain). As stores of glucose in the brain are limited [18,19] it is not surprising that increasing its supply impacts on cognition. However, explaining the widely reported specificity of the glucose facilitation effect to memory tasks (particularly episodic memory) is more problematic. The dominant position is that those tasks that result in high levels of hippocampal brain activity benefit from the administration of glucose [20,21], but an alternative view is that glucose has a more global effect. For example, cognitive enhancement effects have been demonstrated on simple reaction time [22], working memory [2], implicit memory [23], attention [24] and tracking tasks [25]. This has led researchers to propose that the overall difficulty of the task is critical (e.g. [26]; see also 23 for discussion of the relationship between task difficulty and the optimal dose to be administered to observe cognitive facilitation). Kennedy and Scholey [2] reported an association between performance level and the subjects' subjective assessments of task difficulty. Sunram Lea *et al.* [27] observed greater glucose-enhanced performance for episodic memory tasks performed under dual (demanding) rather than single (less demanding) task conditions. This provides support for the "condition-based hypothesis" that only demanding tasks may be susceptible to glucose facilitation, providing that they also have a memory component [28]. Prospective memory tasks fit this description.

A typical laboratory paradigm for assessing PM was employed in the current study. It employed an ongoing "cover" task, where subjects had to respond to a series of stimuli. Embedded within this series were particular items that required an extra response (PM cues). Upon encountering these cues, subjects had to remember to act on their previously formed intention to respond in a different way than to the majority of the stimuli. The main hypothesis was that subjects who consumed a glucose drink would out-perform subjects receiving a placebo. This finding could be seen as evidence against the hippocampal account

of glucose facilitation because PM processes are thought to be mainly sub-served by the rostral pre-frontal cortex (see [29], for a recent review). A secondary hypothesis was that subjects who attended the lab with low fasting glucose levels ("good" glucose regulators) would out-perform those with high blood glucose levels ("poor" regulators) since such individuals would be able to efficiently utilize glucose to aid task performance.

2. Method

2.1 Subjects

Subjects were students at Glasgow Caledonian University and members of the local community selected from the Department of Psychology Participant Panel, ranging in age from 17 to 80 years (mean = 34.4; standard deviation, SD =17.0). We chose to test a wide range of ages so as to enable a more comprehensive assessment of glucose regulation, which is known to decline in ageing. The present study was approved by the Department of Psychology ethics committee. All subjects provided informed consent prior to participating. Sixty-six subjects were recruited and randomly assigned to either the placebo or glucose conditions prior to the study day. Ten of the subjects were excluded because of non-compliance of the fasting regime or failure to pass the initial health screening procedure. In order to take part, people had to confirm that they did not have diabetes, an active infection, hepatitis, haemophilia or phenylketonuria and were not pregnant or HIV positive. They were also asked to confirm that they had not suffered from an illness known to affect their brain or memory performance. Among the remaining subjects there were 25 men and 31 women. Subjects were assigned to either the placebo condition (N=29; 18 females) or the glucose condition (N=27; 13 females). Although subjects were randomly assigned to the treatment and placebo conditions potential covariates were investigated (see Table 1 for subject characteristics). Independent samples t-tests revealed no differences (all $p>0.05$) for age of the subject, total score on the National Adult Reading Test (NART; [30]), baseline arousal

and baseline stress. In addition, Chi-Squared comparisons revealed no differences across treatments for gender and time of day of testing session (early vs. late morning vs. early vs. late afternoon). Importantly, the potential covariates were not correlated with prospective memory performance (all $p>0.05$) and therefore are not included in the analyses below. An initial ANCOVA was carried out with these covariates but did not alter the pattern of results described.

2.2 Design

The experiment had a 2 x 2 independent samples design with two levels of treatment (glucose vs. placebo) and two levels of group (good glucose regulator vs. poor glucose regulator).

2.3 Measures

Pleasantness rating/prospective memory task.— The cover task (in which the prospective memory cues were embedded) involved rating a series of words for "pleasantness". This task was adapted from Marsh et al. [31] and is typical of the kind of task often employed in lab-based PM research [32]. Following Marsh et al.'s [31] procedure, 12 prospective cues (animal names) were embedded in a list of 288 other words. These words were concrete nouns obtained from the MRC Psycholinguistic Database hosted by the University of Western Australia (http://www.psy.uwa.edu.au/mrcdatabase/uwa_mrc.htm) and had between 4 and 7 letters. Two different lists were created, which were matched (all $p>0.05$) for word length (list 1 mean = 5.5; list 2 mean = 5.5), concreteness (list 1 mean = 529.6; list 2

mean = 530.8), imageability (list 1 mean = 529.7; list 2 mean = 533.0) and frequency (list 1 mean = 50.4; list 2 mean = 45.3) according to Kucera and Francis norms [33]. Two lists of 12 animal names were also created, matched (all $p>0.05$) on the same criteria (word length - list 1 mean = 5.2; list 2 mean = 5.0, concreteness - list 1 mean = 611.0; list 2 mean = 605.2, imageability - list 1 mean = 592.1; list 2 mean = 600.8 and frequency - list 1 mean = 10.8; list 2 mean = 10.5). These lists were used to create 2 versions of the pleasantness rating task. Half of the subjects received version 1 and half received version 2. Task version was randomly assigned prior to the study day. E-prime experiment-generator software was used to present the words and collect the responses. The words appeared in a different random order for each subject but prospective cues (animals) always appeared at intervals of 25 trials, with the first one occurring on trial number 22.

Subjects were instructed to rate each word in terms of how pleasant they found the concept it represented; using a scale of 1 to 5 where 1 was “highly unpleasant” and 5 “highly pleasant”, using the number keys at the top left of the keyboard. They were asked to respond according to their first instinct, in order to encourage them to answer reasonably quickly. They were also instructed that the experimenter was interested in their ability to remember to perform an action later, and that they should press the “m” key whenever an animal name appeared in the sequence, before making their pleasantness rating. Responses to these animal words generated prospective memory accuracy and reaction time measures.

Naturalistic prospective memory task.—The naturalistic PM task consisted of a questionnaire that subjects were told about at the beginning of the session, but were asked to delay filling in until the end of the session. The questionnaire asked them about their

experience of participating in the experiment, specifically whether they found the pleasantness rating task easy (on a scale of 1 to 7), whether they noticed that some words had more than one meaning, whether they tried to respond using their first instinct and whether they remembered to respond to the prospective memory cues. However, these questions were not actually relevant; the point of this exercise was to see how many subjects successfully remembered to go back to the questionnaire and fill it in without being prompted to do so.

Sustained Attention to Response Task (SART).—This study used a version of the Sustained Attention to Response Task as a filler task [34]. In variants of this task subjects must respond to a frequently occurring stimulus by pressing a button, but withhold this response on the infrequent occasions when a different stimulus appears. In the version used here, subjects pressed the space bar every time an X appeared, but withheld it when a Y appeared. On each trial a fixation cross appeared for 900ms, followed by the letter (X or Y) for 300ms and then an inter-trial interval of 200ms. Subjects were instructed to give equal weight to responding quickly to the X and minimizing errors (responding incorrectly to the Y). They were given a practice block of 10 trials (including 1 Y trial), followed by a block of 260 experimental trials (including 52 Y trials). These trials were presented in a pseudorandom order such that 4 Y trials appeared within every 20 trials, but at randomly determined intervals. E-prime experiment generator software was used to present stimuli and record responses.

Stress and arousal questionnaire.—Differences in arousal across glucose and placebo conditions could account for patterns of prospective memory enhancement effects. Therefore,

the Stress-Arousal Inventory [35] was administered at four intervals throughout the experiment.

2.4 Procedures

Subjects attended the lab on one occasion between 9am and 4pm (see figure 1 for summary of procedure) and after giving informed consent, were asked to complete a compliance questionnaire to ensure they had not eaten or drunk anything except water within the previous 2 hours. Two hour fasting has been demonstrated elsewhere to give rise to the glucose facilitation effect (see [36] for discussion of fasting regimes). Subsequently they were informed of the need to complete a "participant questionnaire" at the end of the session (the naturalistic PM task) and the sheet was placed to one side and out of view. Capillary blood glucose monitoring was achieved by firstly taking a small blood sample from the subject's fingertip in order to measure baseline glucose level. The blood glucose measures were taken using a Medisense blood glucose sensor (MediSense UK, Ltd). Subjects then filled in the Stress and Arousal Questionnaire for the first time, and completed the National Adult Reading Test (NART).

At this point they were given an instruction sheet describing how to complete the pleasantness rating task including instructions for the PM part of the task and had the opportunity to ask questions. Following this instruction phase, subjects were given either - 1) Placebo – 200ml water flavored with five saccharin tablets and 45ml of 'no added sugar'

whole orange squash or 2) Glucose – 25g of glucose dissolved in 200ml water flavored with 30ml of 'no added sugar' whole orange squash. A dose of 25g glucose was chosen since this has previously been shown to be the optimal dose to enhance memory performance in healthy individuals compared to doses of over 25g (See [14] for meta-analysis; [37] for dose-response investigation into memory facilitation). Subjects (who were blind to the drink) were asked to rate the drink for sweetness on a scale of 1 to 5. There was no difference in sweetness ratings across drinks and therefore is not discussed further. After 10 minutes, subjects completed the filler task (SART). Another capillary blood sample was drawn to measure glucose levels before the main PM task. Subjects also filled in the stress and arousal questionnaire for the second time. The pleasantness rating/prospective memory task took 20-25 minutes and subjects were given a copy of the rating scale to keep in front of them. However, they were given no reinforcement of the PM instructions before task commencement. A third capillary blood sample was taken after the pleasantness rating/prospective memory task, and subjects filled in the stress and arousal questionnaire for the final time. Finally, if subjects did not spontaneously remember to fill in "participant questionnaire" (Naturalistic PM task) they were prompted to do so. Subjects were assumed to have forgotten the questionnaire if they attempted to leave the room without completing the form.

2. 5 Statistical Analyses

In order to determine the effectiveness of the glucose manipulations we begin by reporting the analysis of blood glucose changes. The primary analyses are concerned with

mean accuracy and response times for the prospective memory task. Since individual differences in glucose regulation (baseline blood glucose here) may impact on the enhancing properties of glucose, the influence of glucose regulation (and the interaction with treatment) on prospective memory performance was examined. In order capture 'healthy' individuals only and to exclude those subjects who might be categorized as pre-diabetes/diabetic a cut off of equal to or above 6.1 mmol/l was chosen (impaired fasting; [38]). Five subjects in the placebo and 5 subjects in the glucose condition were excluded on this basis. Subjects were assigned as 'good' or 'poor' regulators of glucose based on the baseline blood glucose measurement. A median split was performed and all subjects above the median were classed as poor regulators, whereas all subjects below the median were classed as good regulators (See Riby, Meikle and Glover [39] and Meikle et al [40] for similar procedure for examining blood glucose levels and performance). Finally, we consider the naturalistic task performance, the filler task and the impact of stress and arousal on the glucose facilitation effect.

3. Results

3.1 Analysis of Blood Glucose Changes

Blood glucose level was measured at 3 time points during the study – a baseline measure taken just after subjects arrived, before they attempted the PM task (15 minutes after arrival) and at the end of the session 45 minutes after arrival (but before they attempted the naturalistic task). These data are displayed in Figure 2. In order to determine the effectiveness of the glucose manipulation, an initial analysis was conducted on the blood glucose data. A 3 (time point: baseline, midpoint, endpoint) x 2 (treatment - placebo, glucose) ANOVA was conducted on the blood glucose measures. There were main effects of treatment ($F(1, 44) = 33.8$, $p < 0.001$) and time point ($F(2,88) = 22.5$, $p < 0.001$). There was also a treatment by time point interaction ($F(2,88) = 19.4$, $p<0.001$). Planned comparisons of the interaction showed that glucose levels remained constant across time in the placebo condition (all $p>0.05$), increased from baseline to the midpoint following glucose consumption ($p<0.001$) and remained stable between the midpoint and the endpoint measurement ($p>0.05$).

3.2 Prospective memory performance

The percentage of PM trials for which subjects responded correctly by pressing the "m" key was calculated (see Table 2). A 2 (treatment: glucose, placebo) x 2 (regulation group: poor, good) ANOVA revealed a non-significant trend towards a main effect of treatment, i.e.,

more accurate responding after the glucose solution ($F(1,41)=3.4$, $p=0.07$, $d=0.58$). Neither the main effect of glucose regulation group nor the interaction between regulation group and treatment were significant. The median reaction time on all correct PM trials was calculated for each subject. Group means of these median RTs are shown in Table 2. Subjects who did not respond correctly to the prospective memory trials (N = 7) were excluded from this analysis. A 2 (treatment: glucose, placebo) x 2 (regulation group: poor, good) ANOVA revealed a significant main effect of treatment in that subjects responded more quickly after the glucose solution ($F(1,35) = 4.8$, $p<0.05$, $d = 0.6$). The interaction between treatment and glucose regulation group was not significant, but there was a significant main effect of regulation group, revealing quicker responding for 'good' compared to 'poor' regulators ($F(1, 35) = 4.4$, $p<0.05$, $d = 0.57$).

3.2 Naturalistic PM task performance

A comparison was made across treatment groups in terms of the frequency with which subjects remembered to fill in the questionnaire at the end of the session without prompting. With the placebo drink, 46% succeeded compared to 55% of subjects in the glucose group. These figures would be consistent with a model where treatment has a positive effect on the likelihood of remembering the questionnaire. However, Chi-square analysis revealed a non-significant effect for treatment ($p>0.59$) and glucose regulation group ($p>0.77$).

3.3 SART Filler Task Performance

Accuracy (hits minus false alarms) and reaction times for hits during the SART task were analyzed by 2 (treatment: glucose, placebo) x 2 (regulation group: poor, good) ANOVAs. No effects of treatment or glucose regulation group were observed in either case (see table 2).

3.4 Stress and Arousal Questionnaire

In order to consider physiological or psychological changes in state [3] we administered a stress and arousal questionnaire throughout the testing session. In order to firstly determine the influence of stress a 2 (glucose vs. placebo) x 3 (time of measurement - baseline, 15 minutes later, 45 minutes later) ANOVA was conducted. There were main effects of time only ($F(2, 108) = 4.97$, $p < 0.01$; means = 4.1, 3.9, 3.0 for time point 1,2,3 respectively). The same analysis was repeated on the arousal component of the questionnaire. There were main effects of time only ($F(2, 108) = 5.5$, $p < 0.01$; means = 9.4, 9.0, 8.0 for time point 1,2,3 respectively). Both stress and arousal decreased significantly over time. There was no evidence of stress or arousal effects across treatment so this is not discussed further.

4. Discussion

The current study set out to investigate the conditions whereby glucose facilitates cognitive performance and to examine the significance of glucose regulation. While reliable cognitive enhancing effects of glucose have been reported for memory tasks (particularly episodic memory), the impact on prospective memory has previously been neglected. Prospective memory is critical to everyday cognitive activities (e.g. remembering to take medicine) and has been reported to be particularly problematic in a number of populations (e.g. older adults and individuals with dementia; [41]).

Consider first the correct responses during the prospective memory task. After a glucose containing drink, the beneficial effects were evident for memory regarding future intentions; showing a 19% boost in prospective memory performance (d=0.58; non-significant trend p=0.07). The further finding was of facilitation for response times (d = 0.6, p <0.05). These medium effect sizes (cohen's d effects of 0.3, 0.5 and 0.8 are typically regarded as small, medium and large respectively) provide persuasive evidence in support of our hypothesis, that the glucose action can be extended to prospective memory. Episodic memory is the cognitive domain that has consistently shown enhanced performance following the administration of glucose (d = 0.91; [14]). The retrieval of episodic information has much in common with prospective memory retrieval; prospective memory tasks are characterized by the requirement to remember and act upon a previously learned intention, in the current study triggered by a specific event. These task requirements are similar to those often used in episodic memory tasks, and it is widely acknowledged that prospective memory

has a retrospective component (see for example [42,43] for discussion). As well as remembering that something has to be done, one also has to remember *what that something is*. It is therefore possible that the glucose facilitation effect in this task is linked to the retrieval of the details of the intention (e.g., recalling which key to press). Indeed it has been argued that glucose facilitates general retrieval from memory ([44]), and Riby [14] found that the magnitude of the glucose effect varied across tasks requiring retrieval of item and contextual information (e.g. episodic memory), the retrieval of item only information (e.g. semantic memory) and the retrieval of short term working memories. This interpretation could be applied to the results of the present experiment where subjects in the glucose condition might have been better able to recall the content of the intention.

However, this account may not tell the full story. In addition to retrieving the relevant information from episodic memory, subjects in an event-based PM task also have to notice the target event when it occurs and associate it with the intention. It is thought that subjects typically accomplish this task by effortful monitoring the environment for the target cue (e.g., [45]), although McDaniel and Einstein (e.g., [46]) have argued that in some circumstances the PM cue can trigger spontaneous retrieval of the intention. Strategic monitoring is likely to rely on executive control processes (e.g., [47,48); consequently experimental manipulations which decrease the availability of these resources have a disruptive impact on PM performance (e.g., [49]). We propose that the availability of glucose in the brain may increase a subject's capacity to use executive resources to engage in strategic monitoring of the environment for PM cues.

Given that the improvement in accuracy marginally failed to reach conventional levels of statistical significance in our data, further research clearly needs to be carried out in order to assess the validity of this proposal. However, it would be in line with recent brain imaging evidence that suggests that glucose ingestion can facilitate frontal lobe - executive functioning [50, 51]. For example, Riby et al. [51] showed that glucose boosted the P3a event-related potential component during a visual oddball task. This component is thought to reflect frontal lobe – executive functioning and the orienting of attention [52]. Also, it has been shown that nicotine can improve PM performance in both smokers and non-smokers [53,54]. This effect has been interpreted by Rusted and colleagues as showing that nicotine can increase the resources available to devote to the strategic monitoring process. We would argue that glucose is likely to have a similarly beneficial effect, and the enhancement for the glucose group in both PM accuracy and reaction time would seem to be consistent with this interpretation. From a neuropsychological perspective, it would be reasonable to suggest that during complex task performance glucose can benefit brain areas other than the hippocampus, including the rostral pre-frontal areas thought to "play a super-ordinate role during many stages of creating, maintaining and enacting delayed intentions"[29, abstract]. The 'hippocampal hypothesis' has dominated previous research on the glucose memory facilitation effect. Selective insulin stimulated uptake of glucose in the hippocampus may facilitate memory function (as the hippocampus is an area that is densely populated with insulin receptors [55, 56; see 12 for other candidate mechanism responsible for the glucose facilitation effect). However, this might be an over-simplification, since insulin receptors are highly concentrated elsewhere. Indeed, Park [57] noted that not only are insulin receptors high in concentration in the hippocampus, but also in areas of the olfactory bulb, cerebral cortex and cerebellum.

A secondary aim of the current study was to examine the relationship between glucose regulation and prospective memory performance. Earlier studies suggest a complex relationship between glycaemia, glucose load and memory enhancing effects. It is evident from Figure 2 that glucose administration gave rise to the desired glycaemic response. Although our study was not directly investigating the clinical realms of glucose abnormalities (e.g. diabetes status) there was a difference between glucose regulation groups in relation to response times (d= 0.57), partially supporting our secondary hypothesis. This finding is compatible with a number of studies demonstrating a relationship between gluco-regulatory status and cognitive performance. Indeed, ageing studies on humans (e.g. [4], work on diabetes e.g. [9]) and earlier rodent studies (e.g. [58]) have shown poor glucose control leads to cognitive deficits. The pattern of means (see Table 2) and the effects size (d=0.52) for PM accuracy is also consistent with this suggestion. Interestingly, from a diagnostic viewpoint, elevated blood glucose could be a useful biomarker of cognitive decline. Indeed, one study comparing older adults and adults with Mild Cognitive impairment (MCI) found elevated blood glucose associated with poor memory abilities. In that study, the key finding was that elevated baseline glycaemia predicted MCI status compared to 'normal' ageing [7]). Although in the present study we used a broad age range it was not possible to investigate this issue due to too few older adults in the sample (over 65 years of age). However, further work is clearly warranted given that older adults find prospective memory skills problematic [41] and glucose regulatory mechanisms are more susceptible to the ageing process [e.g. 16]. Another caveat related to the blood glucose data is that a 2-hour fast was employed. Although research investigating the glucose facilitation effect favours such an approach, a more traditional overnight fast may have produced different results. For instance, research has demonstrated that even after an overnight fast, differences in meals consumed prior to test

impacts on the glycaemic response after glucose load (see for instance [59]). However, our approach favors examining glucose mediated cognitive facilitation under more naturalistic conditions. Previous research indicates that differences in baseline blood glucose resulting from differences in fasting regime (i.e. overnight vs. 2-hr) do not impact on observed cognitive enhancement effects [36].

Although the difference did not reach statistical significance, it is interesting to note that more subjects remembered to fill in the questionnaire at the end of the session without prompting after glucose. The naturalistic task was only a side issue in the current investigation, but this could be one avenue for future research into the benefits of glucose on PM performance. Regarding the filler task (SART) there was no evidence of glucose facilitation in the present study possibly due to insufficient time after treatment (10 mins) to promote cognitive facilitation. This finding is also consistent with previous research showing no effects on simple attention tasks (d=0.12; [14]).

The current pilot study has provided preliminary evidence that glucose may have a beneficial effect on the retrieval of prior intentions in response to prospective cues. We propose that glucose may increase the capacity for strategic monitoring of the environment for the PM target event. In terms of glucose regulation abnormalities, these data add to the growing body of evidence suggesting a link between one's own ability to regulate glucose and cognitive performance.

6. Acknowledgments:

We would like to thank Alan Smith for contributions during the planning stage and Valerie Gunn, Jonathon Reay for helpful comments on an early draft of the paper. The work was carried out in the Division of Psychology, Glasgow Caledonian University and supported by internal funding.

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672

673
674 Table 1

675 Characteristics of subjects in the placebo and glucose drink treatment groups[a]

	Placebo (n=29)	Glucose (n=27)
Age (y)	35.2 ± 18.0	33.5 ± 16.1
Pre-morbid IQ NART[b]	29.4 ± 4.0	37.9 ± 4.7
Baseline Arousal Score[c]	9.7 ± 3.6	8.9 ± 3.2
Baseline Stress Score[c]	4.1 ± 3.8	4.3 ± 4.3
Baseline glucose (mmol/L)	5.5 ± 0.7	5.4 ± 0.8

676
677 [a]Values are means ± SD
678 [b]National Adult Reading Test scores
679 [c]Mackay et al. Stress and Arousal Inventory scores

Table 2.

Accuracy (hits) and reaction time for prospective memory task and Accuracy (hits minus false alarms) and reaction time for the SART filler task across treatment and glucose regulation groups[a]

	PGR- Placebo (n=13)	PGR-Glucose (n=10)	GGR-Placebo (n=11)	GGR-Glucose (n=12)
PM Accuracy (%)	52.6 ± 44.8	82.5 ± 20.2	80.3 ± 29.4	86.1 ± 27.4
PM RT (ms)	2038 ± 694	1459 ± 433	1472 ± 419	1380 ± 359
SART Accuracy (%)	47.8 ± 21.0	31.9 ± 35.9	49.9 ± 19.6	40.7 ± 23.1
SART RT (ms)	335 ± 59	321 ± 24	311 ± 58	326 ± 41

[a]Values are means ± SD

PGR, Poor glucose regulators; GGR, Good glucose regulators, PM, Prospective memory; SART, Sustain attention to response task

689 Figure Caption

690

691 Figure 1 Sequence of testing

692 Figure 2 Changes in blood glucose levels over time as a function of treatment (placebo, 25g)

693

Figure 1

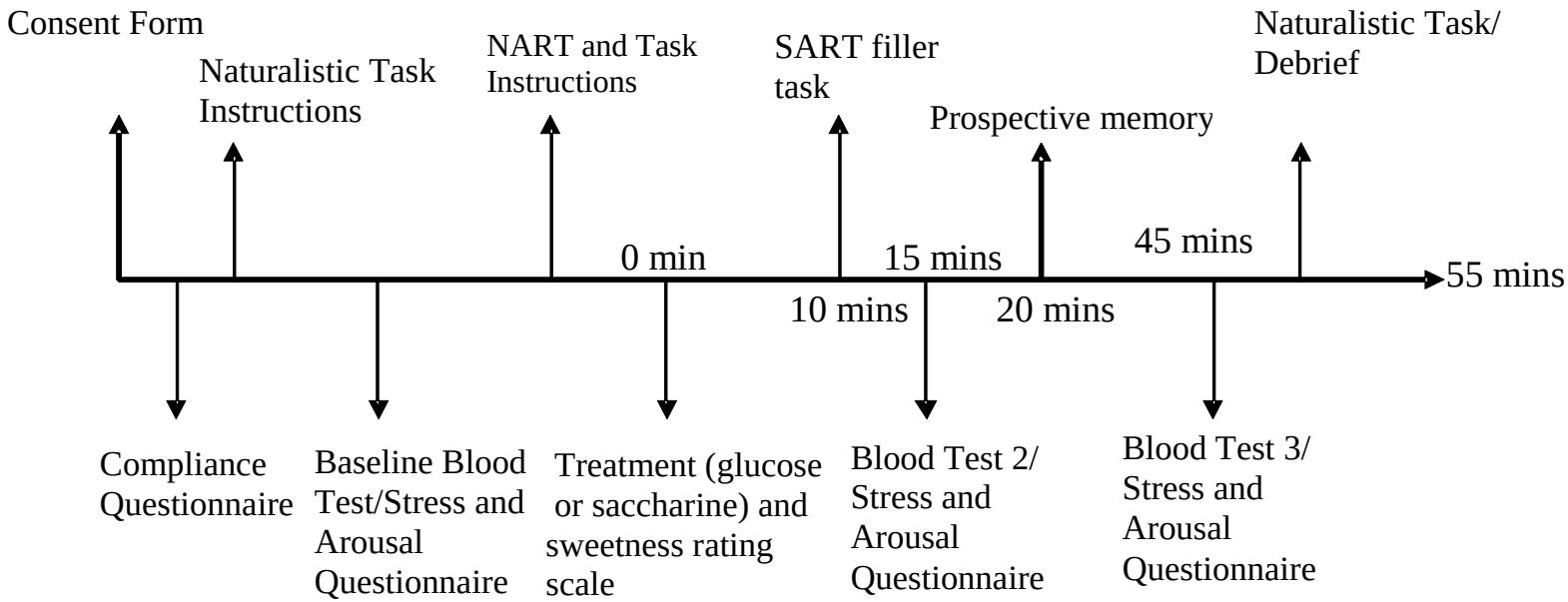
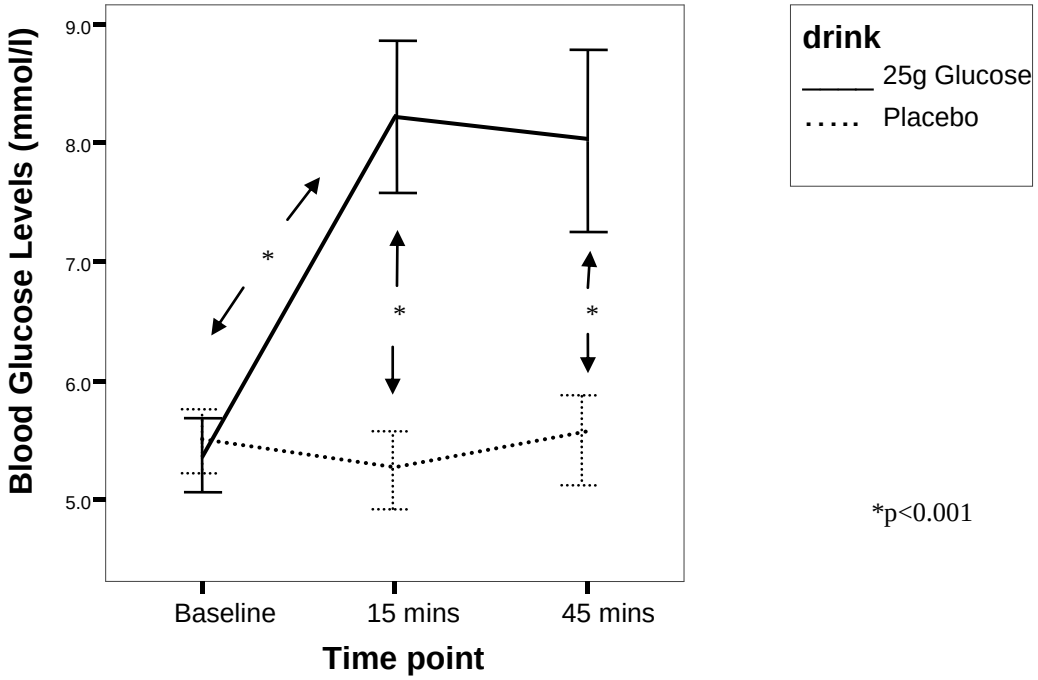

Consent Form
Naturalistic Task Instructions
NART and Task Instructions
SART filler task
Prospective memory
Naturalistic Task/ Debrief
0 min
10 mins
15 mins
20 mins
45 mins
55 mins
Compliance Questionnaire
Baseline Blood Test/Stress and Arousal Questionnaire
Treatment (glucose or saccharine) and sweetness rating scale
Blood Test 2/ Stress and Arousal Questionnaire
Blood Test 3/ Stress and Arousal Questionnaire

Figure 2



*p<0.001