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Lifestyle, glucose regulation and the cognitive effects of glucose load in middle-aged adults

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Interventions aimed at improving glucose regulatory mechanisms have been suggested as a possible source of cognitive enhancement in the elderly. In particular, previous research has identified episodic memory as a target for facilitation after either moderate increases in glycaemia (after a glucose drink) or after improvements in glucose regulation. The present study aimed to extend this research by examining the joint effects of glucose ingestion and glucose regulation on cognition. In addition, risk factors associated with the development of poor glucose regulation in middle-aged adults were considered. In a repeated measures design, thirty-three middle-aged adults (aged 35–55 years) performed a battery of memory and non-memory tasks after either 25 g or 50 g glucose or a sweetness matched placebo drink. To assess the impact of individual differences in glucose regulation, blood glucose measurements were taken on four occasions during testing. A lifestyle and diet questionnaire was also administered. Consistent with previous research, episodic memory ability benefited from glucose ingestion when task demands were high. Blood glucose concentration was also found to predict performance across a number of cognitive domains. Interestingly, the risk factors associated with poor glucose regulation were linked to dietary impacts traditionally associated with poor health, e.g. the consumption of high-sugar sweets and drinks. The research replicates earlier work suggesting that task demands are critical to the glucose facilitation effect. Importantly, the data demonstrate clear associations between elevated glycaemia and relatively poor cognitive performance, which may be partly due to the effect of dietary and lifestyle factors.

Lifestyle: Diet: Glucose: Glucose regulation: Cognition: Memory

Recent work has focused on the role of glucose and improvements in glucose regulation as potential sources of memory facilitation[1–3]. Glucose is a simple monosaccharide and is one of the most important sources of energy for both plants and animals[4]. Importantly, glucose is the main source of fuel for the brain[5]. The critical function of glucose and its memory-enhancing properties have been demonstrated in rodents[6], as well as in elderly human subjects and individuals with 'deficits' such as mild cognitive impairment[7], Alzheimer's disease[8,9], Down's syndrome[10] or schizophrenia[11]. In a similar vein, the ingestion of meals with different macronutrient compositions (i.e. carbohydrate, protein and fat) has suggested that glucose plays a key role in cognitive facilitation[12]. Considering the ingestion of glucose in an everyday meal routine, research has shown that skipping breakfast impacts on later memory performance, but the provision of a glucose supplement shortly before testing nullifies the negative effect of skipping a meal[13].

One important consideration for the utility of glucose as a memory enhancer is the role of individual differences in glucose regulation. After a carbohydrate meal or the ingestion of a glucose-containing drink, there is a significant rise in blood glucose level, with a return to baseline occurring after approximately 1 h. With increased age, the rate at which blood glucose rises and returns to baseline becomes more prolonged[14]. Crucially, the inability to efficiently regulate glucose is the key factor in disorders such as diabetes, and associated cognitive impairment within such groups can be considered one of the chronic complications[15]. However, it should be noted that in such populations other mediating factors (e.g. depression[16], cerebrovascular disease[17]) as well as glucose regulation abnormalities may contribute to cognitive and memory decline[18]. Particularly relevant to the present investigation is the fact that poor glucose regulation is more prevalent than diabetes and the milder deficits of impaired fasting and impaired glucose tolerance have proved to be useful classifications[19].

Research has shown that cognitive performance can be predicted from individual differences in glucose regulation[7,8,20]. This is an important point, as being able to identify an effective yet simple biomarker for possible subsequent memory decline would allow intervention at an earlier stage. Where glucose abnormalities are more severe, pharmacological interventions using anti-diabetic medication may be appropriate. One such anti-diabetic drug (Glipizide) was particularly effective in reducing elevated blood glucose and promoting

Abbreviations: GRI, glucose regulation index; MSE, mean squared error.

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enhanced learning of verbal material[21]. However, lifestyle interventions (e.g. diet and exercise) are particularly beneficial at an early stage when glucose abnormalities or less efficient regulation are beginning to emerge. In fact, it has been suggested that such interventions can be more effective than pharmacological treatment[22].

Much of the research in the area of glucose and cognition has been conducted with young healthy adults or with an elderly population. The current study concentrates on a middle-aged (35–55 years) population in order to expand on previous research in this area[23] and to further investigate the effects of glucose across the adult lifespan. Therefore, this paper aims to examine the relationship between memory, glucose intake and glucose regulation as well as consider the role of diet and lifestyle in moderating these factors (see Orisaka *et al.* [24] for discussion of risk factors). The main contribution of this study is to illustrate an opportunity for early intervention where individuals are prime candidates for subsequent cognitive impairment.

Method

Participants

Thirty-three middle-aged adults (nineteen females; age 35–55 years) participated in the present study. The participants came from a volunteer sample, gained from students and staff of the Glasgow Caledonian University. None of the participants was diabetic. The present study was approved by the Department of Psychology Ethics Committee. All participants provided informed consent prior to participating in the research.

Design

Each participant attended three sessions in a counterbalanced order (placebo *v.* 25 g glucose *v.* 50 g glucose). Three versions of the test battery were also administered in a counterbalanced order (see Table 1). There was a gap of 7 d between testing sessions. The participants were not informed of the contents of the drink they had consumed until the end of the study. Each participant was administered:

i. Placebo – 200 ml water flavoured with five saccharin tablets and 45 ml 'no added sugar' whole orange squash.
ii. Glucose – 25 g glucose dissolved in 200 ml water flavoured with 30 ml 'no added sugar' whole orange squash.
iii. Glucose – 50 g glucose dissolved in 200 ml water flavoured with 30 ml 'no added sugar' whole orange squash and 20 ml 'no added sugar' whole lemon squash. The lemon was used to reduce the sweetness of the drink to a level comparable with the smaller glucose dose condition, giving a similar 'mouthfeel' and reducing sweetness reinforcement effects.

Blood glucose measurement

In order to calculate a reliable blood glucose recovery index, participants were required to give four pinprick samples of blood during each test session. These samples were taken pre-treatment (0 min), pre-test (15 min), mid-test (38 min) and post-test (55 min). The blood glucose measures were taken using a Medisense blood glucose sensor (MediSense UK, Ltd). Each time a blood sample was taken, the participant was asked to complete a subjective stress and arousal questionnaire[25] to assess changes in stress or arousal related to glucose effects.

Procedure

Participants completed three sessions, each lasting approximately 1 h. All testing was carried out between 09.00 and 18.00 hours in a laboratory at Glasgow Caledonian University. Testing was carried out at the same time of day across sessions for each participant. Before attending the first session,

Table 1. Procedural timetable – three versions administered in a counterbalanced order*

	Activity		
Time (min)	Version A	Version B	Version C
0	Pre-treatment blood sample	Pre-treatment blood sample	Pre-treatment blood sample
	Consumption of drink	Consumption of drink	Consumption of drink
	Stress & arousal questionnaire	Stress & arousal questionnaire	Stress & arousal questionnaire
	NART	NART	NART
15	Pre-test blood sample	Pre-test blood sample	Pre-test blood sample
	Stress & arousal questionnaire	Stress & arousal questionnaire	Stress & arousal questionnaire
	Story recall	Story recall	Story recall
	Concrete & Abstract Word Recall	Concrete & Abstract Word Recall	Concrete & Abstract Word Recall
	Digit symbols task	Letter cancellation task	Digit Span Forward & Backward
	Letter cancellation task	Digit symbols task	Word recall
	Trails A & B	Word recall	Letter cancellation task
	Digit Span Forward & Backward	Trails A & B	Digit Symbols task
38	Mid-test blood samples	Mid-test blood samples	Mid-test blood samples
	Stress & arousal questionnaire	Stress & arousal questionnaire	Stress & arousal questionnaire
	Word recall	Digit Span Forward & Backward	Trails A & B
	Delayed story recall	Delayed story recall	Delayed Story Recall
	Delayed Concrete & Abstract Word Recall	Delayed Concrete & Abstract Word Recall	Delayed Concrete & Abstract Word Recall
55	Post-test blood samples	Post-test blood samples	Post-test blood samples
	Stress & arousal questionnaire	Stress & arousal questionnaire	Stress & arousal questionnaire
60	Session end	Session end	Session end

NART, National Adult Reading Test.
* For details of subjects and procedures, see Method.

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participants were asked to complete the Rapid Eating and Activity Assessment for Patients[26], which is designed to give an assessment of an individual's diet and physical activity and which has been used successfully as a dietary assessment for individuals at risk of diabetes and related disorders[27]. The questionnaire contained items related to: (1) skipping breakfast; (2) meals with grain; (3) vegetables and fruits; (4) dairy; (5) meats; (6) fried foods; (7) snacks; (8) fats and oils; (9) sweets; (10) soft drinks; (11) Na; (12) alcohol consumption; (13) physical activity.

Participants were asked to fast (eating and drinking nothing other than water) for at least 2 h before each session (see Sünram-Lea *et al.* [28] for discussion of appropriate fasting regimens and time of day effects). A compliance questionnaire was issued at the start of each session to ensure that participants had conformed to these instructions. A pre-treatment blood sample was taken from the participant before they were administered one of the sweetened drinks. All drinks were administered using a double-blind system. Participants then used a 5-point Likert scale to assess level of sweetness of the drink they had been administered. No differences in sweetness were reported and therefore these data are not discussed further. Three versions of the testing schedule were counterbalanced across participants and sessions (see Table 1). After completion of all three sessions, participants completed a questionnaire rating the level of difficulty of each task (7-point scale; 1 = easy; 7 = hard). The perceived levels of task difficulty are shown in Table 2 (see Kennedy & Scholey[29]).

Episodic memory

Episodic memory was examined using tests of story and word-list recall. During the story recall task, a short passage was read aloud by the experimenter and the participant then retold as much as possible, with one point awarded for each detail correctly remembered and a half-point awarded for partially recalled information. Delayed story recall was subsequently assessed after the mid-point blood glucose assessment, 38 min into the session (see Table 1). For word-list recall, two lists of words (concrete and abstract) were read aloud at a rate of one word every 2 s. After the list was presented (30 s), the participant freely recalled as many words as possible. Again, a delayed recall task was administered following the mid-point blood glucose assessment.

Cognitive battery

To test the specificity of glucose facilitation on episodic memory, a battery of non-episodic memory tasks was administered.

National adult reading test (verbal intelligence quotient)[30]. Participants were required to read aloud fifty words that do not follow the typical rules of pronunciation (e.g. topiary, campanile). The total correct pronunciations are recorded as an estimate of verbal intelligence quotient.

Digit symbols (speed of cognitive processing)[31]. Participants were provided with a key to a selection of nine symbols and their corresponding numbers and were required to replace as many numbers with their appropriate symbols as possible within a 60 s time period. The number of correct replacements was recorded for each participant (maximum 100).

Letter cancellation (attention)[32]. During a 60 s period, participants were required to systematically work through rows of lower- and upper-case letters, striking through as many upper-case letters as possible and ignoring the lower-case letters. The score recorded was the number of correct

Table 2. Cognitive performance across treatment (placebo *v.* 25 g glucose *v.* 50 g glucose) and regulatory group (poor *v.* good)*
(Mean values and standard deviations)

	Treatment across regulation group													
	Placebo				25 g Glucose				50 g Glucose				Difficulty rating	
	Poor		Good		Poor		Good		Poor		Good			
Task type	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Story Recall Immediate	11·4	2·6	10·7	2·7	12·1	2·8	10·8	3·4	12·0	2·2	11·3	2·6	3·9	0·87
Story Recall Delayed	10·5	2·6	9·4	2·8	10·8	2·7	10·0	3·6	11·3	2·5	10·3	3·2	4·3	0·98
Concrete Words Immediate†	8·1	2·1	7·8	1·4	7·8	1·5	7·8	1·6	8·8	1·6	8·0	2·0	4·2	0·99
Concrete Words Delayed†	4·7	1·8	5·3	2·6	4·9	1·7	4·9	1·9	5·2	1·4	5·7	3·0	5·0	0·95
Abstract Words Immediate†	5·3	1·7	5·3	1·7	5·8	1·9	4·9	1·6	6·8	1·6	6·6	1·5	5·2	0·93
Abstract Words Delayed†	3·1	2·0	2·8	1·7	3·0	1·7	3·1	2·1	3·6	1·9	3·6	2·4	6·0	1·05
Word Generation Easy	18·2	3·2	18·5	4·6	19·9	3·7	19·8	4·1	20·5	3·4	17·4	4·1	3·5	0·83
Word Generation Difficult	16·4	3·9	13·9	3·8	15·9	3·8	15·7	5·1	17·4	5·4	16·8	3·6	3·6	0·87
Cancellation Task Hits	50·0	8·7	51·5	10·5	49·7	6·9	50·8	8·5	50·1	8·6	51·7	11·5	3·1	0·65
Cancellation Task Errors	0·6	1·9	1·2	2·2	1·1	2·9	0·5	0·9	1·1	3·0	0·8	1·2		
Cancellation Task Omissions	4·6	4·1	4·1	4·2	6·2	5·8	4·7	4·6	6·1	4·9	3·7	4·0		
Trail-Making A	24·8	6·9	21·5	6·4	23·2	5·9	23·4	8·5	24·6	7·9	21·4	6·6	3·1	0·88
Trail-Making B‡	50·2	15·7	57·0	21·6	52·3	18·4	53·3	15·2	55·4	17·0	48·4	19·0	3·7	0·98
Digit Span Forward	11·9	2·4	11·6	2·4	11·3	2·0	11·4	2·0	11·3	2·5	11·5	1·9	3·6	1·00
Digit Span Backward	8·6	2·9	9·3	3·0	8·6	2·6	8·8	2·7	9·0	3·5	10·1	2·5	4·4	1·39
Digit Symbols Substitution	45·9	8·3	47·1	7·4	47·1	7·4	46·7	7·0	46·8	7·0	47·2	7·1	3·2	0·76

* For details of subjects and procedures, see Method.
† Main effect of glucose for episodic memory word recall.
‡ Three-way interaction between glucose condition, difficulty and glucose regulation index. Note the faster responds for good glucose regulators in the 50 g condition.

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capitals that had been scored through, the number of errors and the number of omissions.

Trail-making tasks (attention, switching and executive control)[32]. Trail-making A required participants to connect consecutively numbered circles on a sheet of paper (twenty-five in total). The participant was urged to connect the circles as fast as they could without lifting the pen from the paper. Version B required subjects to connect consecutively numbered and lettered circles by alternating between the two sequences, e.g. 1-A-2-B-3-C (thirteen numbers and twelve letters in total). For each task the dependent variable was the time taken to complete the task.

Digit span forward and backward (short-term memory)[33]. In the forward span task, participants immediately recalled a sequence of numbers read to them by the experimenter, with the length of the sequence gradually increasing (two trials for each span length). In the backward task, participants were required to reverse the sequence read to them. The span task stopped when the participant was unsuccessful on two consecutive trials of the same span length.

Category fluency (semantic memory retrieval)[32]. There were three versions of the category fluency task, administered in a counterbalanced order across sessions. In each version the participant was asked to provide as many items of a given category as possible in a 1-min period with two levels of difficulty in each task version (easy: fruits, vegetables, colours; hard: tools, kitchen utensils, vehicles). The total number of words recalled and the number of repetitions were recorded.

Results

Analysis of blood glucose changes

Regulation was calculated by subtracting baseline blood glucose levels from levels obtained at the end of the experiment after 50 g treatment. A median split was then performed on the data to create groups of good (*n* 17) and poor (*n* 16) regulators. A similar strategy has been used elsewhere (e.g. Meikle *et al.* [34]). There was no difference between good and poor glucose regulators in age, BMI, fasting glucose levels or degree of physical activity (all $P>0{\cdot}05$).

In order to establish the effectiveness of the glucose manipulations, a two (glucose regulation index (GRI) – good, poor) × three (glucose condition – placebo, 25 g, 50 g) × four (time of measurement – baseline, 15 min, 38 min and 55 min) ANOVA was conducted on the blood glucose measures. There were main effects of glucose condition ($F(2, 62)$ 103·7, mean squared error (MSE) 2·03, $P<0{\cdot}001$) and time of measurement ($F(3,93)$ 105·9, MSE 1·07, $P<0{\cdot}001$). There was also a glucose condition × time interaction ($F(6,186)$ 36·2, MSE 0·90, $P<0{\cdot}001$), a GRI × time interaction ($F(3,93)$ 10·4, MSE 1·07, $P<0{\cdot}001$) and finally a glucose condition × time × GRI interaction ($F(6,186)$ 5·5, MSE 0·90, $P<0{\cdot}001$). Fig. 1 displays the blood glucose levels across time, treatment and GRI.

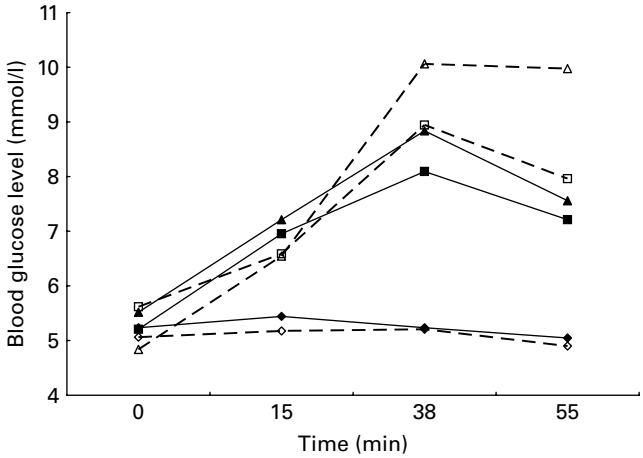

Fig. 1. Changes in blood glucose levels over time (post treatment) as a function of treatment (placebo, 25 g and 50 g) and glucose regulation index group (good, poor). –◆–, Good placebo; –■–, good 25 g; –▲–, good 50 g; –◇–, poor placebo; –□–, poor 25 g; –△–, poor 50 g.

Story recall

A two (GRI – good, poor) × three (glucose condition – placebo, 25 g glucose, 50 g glucose) × two (delay – immediate, delayed) ANOVA was carried out on story recall accuracy. The analysis revealed a main effect of delay, demonstrating relatively poorer performance during the delayed recall task ($F(1,31)$ 51·8, MSE 0·90, $P<0{\cdot}001$).

Abstract and concrete word recall

A two (GRI – good, poor) × three (glucose condition – placebo, 25 g glucose, 50 g glucose) × two (difficulty – concrete, abstract) ANOVA was carried out on the accuracy data showing a main effect of glucose condition ($F(2,62)$ 9·25, MSE 2·12, $P<0{\cdot}001$; mean placebo 6·6, mean 25 g 6·6, mean 50 g 7·5). There was also a main effect of difficulty ($F(1,31)$ 92·6, MSE 2·73, $P<0{\cdot}001$) and delay ($F(1,31)$ 249·7, $P<0{\cdot}001$). The interaction between glucose condition and difficulty approached significance ($F(2,62)$ 2·6, MSE 1·6, $P=0{\cdot}08$). Although this interaction failed to reach significance, a planned comparison was carried out across difficulty (abstract *v.* concrete words) since previous research in this area suggests both a memory component and sufficient task difficulty are necessary to observe the glucose facilitation effect (e.g. Meikle *et al.* [35]). An analysis of simple main effects demonstrated glucose facilitation for abstract words only ($P<0{\cdot}01$).

Category recall

A two (GRI – good, poor) × three (glucose condition – placebo, 25 g, 50 g) × two (difficulty – easy, hard) ANOVA was carried out on the total number of exemplars generated. The effect of glucose condition approached significance ($F(2,62)$ 2·6, MSE 11·8, $P=0{\cdot}08$) and a main effect of difficulty ($F(1,31)$ 26·7, MSE 16·9, $P<0{\cdot}001$). The number of items within each category repeated was also analysed in a separate ANOVA and a main effect of difficulty demonstrated more repeats in the difficulty category condition ($F(1,31)$ 10·5, MSE 0·15, $P<0{\cdot}01$).

Trail-making task

A two (GRI – good, poor) × three (glucose condition – placebo, 25 g, 50 g) × two (difficulty – easy, hard) ANOVA was

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carried out on the completion time data. A main effect of difficulty was observed ($F(1,31)$ 188·2, MSE 230·4, $P<0·001$). There was also a three-way interaction between glucose condition, difficulty and GRI ($F(2,62)$ 3·1, MSE 65·9, $P=0·05$). Table 2 indicates faster completion time for good regulators after 50 g glucose on the difficult trail task.

Digit span

A two (GRI – good, poor) × three (glucose condition – placebo, 25 g, 50 g) × two (difficulty – forward, backwards) ANOVA was carried out on the digit span data. A main effect of difficulty was observed ($F(1,31)$ 44·0, MSE 6·6, $P<0·001$) showing greater recall in the forward span condition.

Digit symbol substitution

A two (GRI – good, poor) × three (glucose condition – placebo, 25 g, 50 g) ANOVA was carried out on the total correct substitutions. No main effects or interactions were significant.

Letter cancellation

A two (GRI – good, poor) × three (glucose condition – placebo, 25 g, 50 g) ANOVA was carried out on the total correct cancellations, errors and omissions. No main effects or interactions were significant.

Glucose concentration and cognitive performance

Pearson's correlation analysis was carried out on the blood glucose measurements throughout the testing session and cognitive performance. Since a large number of relationships were examined, this could lead to spurious correlations and therefore some care should be taken when interpreting these data. For this reason, only correlations reaching $P<0·001$ significance are reported here.

After 25 g glucose, elevated blood glucose level was associated with: (1) impaired concrete word recall performance at time points 3 and 4 (r −0·43; r −0·45) in the 25 g glucose testing session; (2) impaired delayed abstract recall at time point 3 (r −0·45) in the saccharin testing session; (3) impaired delayed abstract recall at time point 4 (r −0·47) in the 50 g glucose session. For non-episodic memory tasks, after 25 g glucose, elevated blood glucose was associated with: (1) greater letter cancellation omission errors at time point 2 (r 0·54) in the 25 g glucose session; (2) greater letter cancellation omission errors at time points 3 and 4 (r 0·49; r 0·47) during the saccharin testing session; (3) impaired easy word fluency performance at baseline (r −0·43) in the 50 g glucose session; (4) greater repeats in the difficult word fluency task at time point 2 (r 0·47) in the 50 g glucose session.

After 50 g glucose, elevated blood glucose was associated with: (1) impaired delayed abstract recall (r −0·54) at baseline in the 25 g glucose session; (2) impaired performance on the National Adult Reading Test task (r −0·53) at time point 3 in the 25 g glucose session; (3) impaired digit span forward performance (r −0·43) at time point 1 in the 50 g glucose session.

Glucose regulation and the nutrition and lifestyle questionnaire

A Pearson's correlation analysis was carried out on glucose regulation and the nutrition and lifestyle questionnaire data. The 'high sugar, calories, sweets and drinks' category was related to poor glucose regulation (r 0·36, $P<0·05$). This was followed up with a logistic regression (enter method). With all variables entered, 82 % of the variance was accounted for. The 'high sugar, calories, sweets and drink' category was significant ($P<0·01$) and the 'high fat, saturated fats, dairy and meats' ($P=0·07$) category approached significance. The importance of 'high sugar, calories, sweets and drink' was confirmed by carrying out a forward stepwise regression. This variable was the only factor remaining in the final model and accounted for 73 % of the variance (i.e. participants were correctly classified as good and poor regulators on 73 % of occasions).

Changes in self-reported stress and arousal

A two (GRI – good, poor) × three (glucose condition – placebo, 25 g, 50 g) × four (time – pre-treatment, pre-test, mid-test, post-test) ANOVA was carried out on the stress and arousal data. The stress and arousal scores did not vary as a function of treatment.

Discussion

The overarching aim of the current paper was to expand previous research by examining the effect of glucose ingestion on the cognitive performance of middle-aged adults by specifically focusing on the role of glucose regulation. The results highlighted a number of important features that add to this area of research, specifically emphasising the crucial role played by an individual's ability to regulate blood glucose and the subsequent effect on their cognitive performance. Importantly, possible risk factors associated with poor glucose regulation, such as lifestyle and dietary impacts, were considered.

First, the research considered the specificity of glucose ingestion on cognitive performance. Previous research has emphasised that task domain is crucial for glucose facilitation, with memory tasks showing greatest enhancement, particularly episodic remembering. The results of the current paper suggest that task domain is indeed central for the observation of glucose facilitation on task performance. The study included a variety of both episodic and non-episodic memory tasks and the greatest facilitation was found for abstract recall, a difficult episodic memory assessment. Although some degree of facilitation was also evident for category recall, a semantic memory assessment, and trail-making B, a difficult executive task, more reliable facilitation was evident within the episodic memory domain. However, task domain appears not to be the only contributing factor to glucose facilitation for middle-aged adults. The results emphasise that an episodic component and/or tasks of high demand lead to the greatest facilitation. Indeed, facilitation was greater for abstract than concrete word recall, a task rated as more difficult by participants in the research (see Table 2). The findings are therefore consistent with previous research concerning the 'cognitive demand

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hypothesis', which indicates that task difficulty is an important factor in glucose facilitation[35–38]. The fact that story recall did not show facilitation suggests an important interplay between task difficulty and task domain. In this case, the episodic task was rated less demanding compared with abstract word recall. Therefore, it appears that the results are consonant with the idea that task demand and task domain have additive effects on glucose facilitation[35].

The second area of investigation for the current paper was the examination of the relationship between blood glucose level and cognitive performance. For the trail-making B task (an executive function task), good glucose regulators appeared to benefit from the additional glucose resource provided by the ingestion of a 50 g glucose drink (Table 2). This finding suggests a possible relationship between glucose regulatory status, glucose load and executive abilities (known to decline in ageing). Indeed, research has suggested that glucose regulatory status is a useful predictor of cognitive decline as indexed by executive abilities as well as episodic memory performance[20]. Interestingly, recent work using functional imaging techniques with younger adults[39] and individuals with schizophrenia[40] has pointed to executive-frontal lobe functions benefiting from glucose load. More informative, however, were the data demonstrating relationships between elevated blood glucose concentration (and thus poor glucose regulation) and relatively poorer performance on the cognitive tasks, particularly episodic memory tasks. With a decline in episodic memory prevalent during old age, the current research points to an important role for glucose regulation in episodic memory decline during ageing. The link between episodic memory ability and glucose regulation emphasised here is consistent with previous suggestions that regulatory ability impacts on facilitation[20].

Assessments of the nature utilised here may provide the opportunity to predict susceptibility to subsequent poor memory performance in adults during middle age, prior to the onset of age-related memory decline. However, it may be that the assessment of glucose regulation utilised (blood glucose level at time 4 minus baseline) may need some adjustment for a clear and reliable measure to be used. This new assessment may take the form of an additional testing session rather than being analysed during task performance since depletion of glucose will occur during the session. A separate glucose tolerance test is proposed for future work in this area and may provide a more sensitive and reliable measure of the relationship between glucose 'abnormalities' and cognition. This development would allow early interventions to be designed and implemented to minimise cognitive decline, for example, the implementation of a low-fat diet and encouraging the use of regular exercise. Lifestyle interventions of this nature could help prevent any further decrease in memory performance throughout old age and link directly to the lifestyle assessments utilised in the current research. As the current results were observed during middle age, this opens the way for interventions aimed at improving glucose regulation without pharmacological treatment.

Finally, the current study explicitly investigated the relationship between diet, lifestyle and glucose regulation. The results demonstrated that the quantity of high-sugar sweets and drinks consumed during an individual's everyday diet predicted their ability to self regulate glucose. Although a less robust finding, the study also emphasised that scoring high on the consumption of 'high fat, saturated fats, dairy and meats' may exacerbate an already lessened ability to regulate blood glucose. Clearly, the macronutrient components of diet play a functional role, interacting with one another in order to regulate cellular functioning; in this case, impacting on cognitive performance. Therefore, the Rapid Eating and Activity Assessment for Patients is a useful dietary assessment tool for identifying possible risks associated with glucose regulation. The self-report method quickly identifies which items on the food pyramid are consumed regularly, highlighting any behaviours that may indicate a pattern of risk, e.g. not eating breakfast or excessive consumption of saturated fats. This type of FFQ can be considered a useful addition to research in this area as it demonstrates links between an individual's diet and their ability to adequately regulate blood glucose levels, again substantiating the possibility of predicting cognitive decline as a consequence of lifestyle in later years. Together, these data are in line with WHO recommendations, which suggest the intake of a balance of macronutrient components in a daily diet for optimal physical and, importantly, mental performance.

One *caveat* of the current investigation is that the results may be underpowered because of the number of comparisons made. However, we attempted to integrate experimental studies of the glucose facilitation effect and work on lifestyle and nutrition. Indeed, the investigation emphasised that further research is warranted to consider glucose regulation, cognitive performance and lifestyle factors when identifying possible interventions for individuals who may be more susceptible to memory decline during old age. The practical applications of the current results, with further detailed investigations and the development of more robust blood glucose assessments, is crucial in today's society, where healthy eating is encouraged and the size of the aged population is increasing exponentially.

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