Biological Psychology 79 (2008) 209–215

Contents lists available at ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

Glucoregulatory and order effects on verbal episodic memory in healthy adolescents after oral glucose administration

Michael A. Smith [a,*], Jonathan K. Foster [b,a]

[a] School of Paediatrics and Child Health, University of Western Australia, Princess Margaret Hospital for Children, GPO Box D 184, Perth, Western Australia 6840, Australia
[b] School of Exercise, Biomedical and Health Sciences, Edith Cowan University, Australia

ARTICLE INFO

Article history:
Received 29 October 2007
Accepted 2 May 2008
Available online 13 May 2008

Keywords:
Glucose
Glucoregulation
Memory
Cognition
Order effects
Adolescents

ABSTRACT

The ingestion of oral glucose has been observed to facilitate memory performance in both elderly individuals and in young adults. However, fewer studies have investigated the effect of glucose on memory in children or adolescents. In the present study, the ingestion of a glucose laden drink was observed to enhance verbal episodic memory performance in healthy adolescents under conditions of divided attention, relative to a placebo drink. Further analyses found that this glucose memory facilitation effect was observed only in adolescents exhibiting better glucoregulatory efficiency. These findings demonstrate that the glucose memory facilitation effect can be generalised to younger individuals. The importance of controlling for treatment order in within-subjects designs investigating the glucose memory enhancement effect is also discussed.

The brain relies upon glucose as its primary fuel (Sieber and Traystman, 1992). In recent years, a rich literature has developed from both human and animal studies indicating that increases in circulating blood glucose can facilitate cognitive functioning (for a review see Messier, 2004). This phenomenon has been termed the 'glucose memory facilitation effect' (Foster et al., 1998). It has been suggested that older individuals may benefit to a greater degree from glucose administration, as healthy young individuals are close to their 'cognitive peak' (Foster et al., 1998). However, glucose has also been observed to facilitate memory in healthy young adults (e.g. Benton et al., 1994; Foster et al., 1998; Sünram-Lea et al., 2001; Meikle et al., 2005). A meta-analytic review of the glucose memory facilitation effect has supported the view that verbal episodic memory is the cognitive domain that is most amenable to improvement subsequent to glucose ingestion (Riby, 2004).

While an abundant literature now exists suggesting that glucose ingestion can facilitate verbal episodic memory in healthy young adults, it has also been suggested that glucose only reliably facilitates memory in this group of individuals under conditions of divided attention at encoding (Sünram-Lea et al., 2002). Sünram-Lea et al. (2002) administered either a glucose or a placebo drink to healthy young adult participants, before presenting them with a list of to-be-remembered words under one of four 'divided attention' conditions. Glucose was observed to facilitate memory recall, relative to placebo, when participants performed a secondary motor task or key tapping task concurrently with word list encoding. However, the authors failed to observe the glucose memory facilitation effect when participants were not required to perform a secondary task, or when cognitive demand was increased by asking participants to recall a longer word list, with target items differentiated by the speaker's gender.

By contrast, other researchers have observed that manipulating cognitive load, but not divided attention can induce a glucose memory facilitation effect in healthy young adults. For example, glucose has been demonstrated to enhance performance in these individuals on a difficult serial subtraction task, but not on a serial subtraction task associated with a relatively lower cognitive load (Kennedy and Scholey, 2000; Scholey et al., 2001). In addition, Meikle et al. (2005) have reported that glucose facilitation of verbal episodic memory for serial position is more reliably observed in younger adults when target lists are longer.

It has been further suggested that individual differences in peripheral glucose regulation may alter an individual's sensitivity to glucose enhancement of memory. Glucose regulation is reflected by the phenomenon whereby blood glucose concentration rises for approximately 30 min subsequent to a glucose load, followed by a return to baseline blood glucose concentration—typically within approximately 2 h (Donohoe and Benton, 2000). A link between glucoregulatory efficiency and cognitive functioning has now been

* Corresponding author. Tel.: +61 8 9340 7906; fax: +61 8 9388 2097.
E-mail address: msmith@meddent.uwa.edu.au (M.A. Smith).

0301-0511/$ – see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.biopsycho.2008.05.001

well established (Wenk, 1989; Awad et al., 2002; Messier, 2005). More specifically, it has been reported that glucose cognitive enhancement effects are most profound in older adults with poorer glucose regulation (Hall et al., 1989; Kaplan et al., 2000; Messier et al., 2003). These findings have also been replicated in younger individuals: young adult males with poor glucose regulation have also been observed to demonstrate superior paragraph recall subsequent to glucose ingestion, relative to ingestion of a saccharin control drink (Craft et al., 1994). In addition, younger individuals with poor glucose regulation have been shown to exhibit inferior performance on a verbal episodic memory task relative to better glucoregulators—an effect that is ameliorated if glucose is consumed prior to memory encoding (Messier et al., 1999). It has been theorised that glucose ingestion is most likely to facilitate memory in younger individuals exhibiting poor glucose regulation, as only in such individuals does blood glucose concentration remain elevated for a sufficient time period to exert a memory enhancing effect (Craft et al., 1994). By contrast, it has been reported that, in older adults, the glucose memory facilitation effect is more pronounced in those individuals exhibiting relatively better glucose regulation (Craft et al., 1994; Messier et al., 1997; Meikle et al., 2004; Riby et al., 2004).

While the effect of glucose on memory has been well investigated in younger and older adults, fewer studies have investigated glucose effects on memory in children and adolescents. Lapp (1981) reported that subsequent to ingestion of a carbohydrate rich meal (which elevated blood glucose concentration), healthy adolescents outperformed a fasted control group of adolescents on a paired-associate learning task. The findings of Lapp's (1981) study may, however, reflect the negative effects of fasting on memory, rather than the positive effects of elevated blood glucose (see Doniger et al., 2006). It has also been reported that attentional capacity benefits from ingestion of a confectionary snack in school children (Busch et al., 2002). Further, the consumption of breakfast has been associated with superior attention and memory in children (Wesnes et al., 2003), an effect that is more apparent subsequent to the ingestion of breakfast meals associated with a slower and more prolonged release of glucose into the bloodstream (Mahoney et al., 2005; Ingwersen et al., 2007). However, the macronutrient composition of the different treatments used in these studies renders it difficult to infer whether glucose, or other potentially cognitive enhancing nutritional components of these treatments (Gibson and Green, 2002) were responsible for the findings.

Therefore, the effect of pure glucose ingestion on episodic memory in healthy adolescents has not been well established. Adolescence is a unique period with regard to brain development (Giedd et al., 1999), and also a time of increased vulnerability for experiencing heightened stress (Byrne et al., 2007). This is relevant, given that stress hormones (i.e. cortisol) are known to impact upon glucose regulation (Plat et al., 1996). While the measurement of stress hormone levels is beyond the scope of the present investigation, it is nevertheless important to establish whether glucose ingestion has a similar effect on memory in this age group compared with other populations in which the glucose memory facilitation effect has been demonstrated.

The aim of the present study was therefore to investigate the influence of glucose ingestion and glucoregulatory efficiency on verbal episodic memory in healthy adolescents. In line with previous research conducted with healthy young adults, memory encoding took place under dual task conditions (Foster et al., 1998; Sünram-Lea et al., 2001, 2002). It was hypothesised that oral glucose ingestion would enhance memory for a supraspan word list in healthy adolescents, relative to a sweetness matched placebo. It was further hypothesised that the glucose memory facilitation effect would be observed only in the healthy adolescent participants with poor glucose regulation, in accordance with previous findings indicating that glucose facilitation of memory is observed only in young adults with poor glucose regulation (Craft et al., 1994; Messier et al., 1999).

1. Method

1.1. Participants

A total of 32 healthy adolescents participated in the present study (12 males, 20 females), ranging in age between 14 and 17 years (M_{age} = 15.6, S.D.$_{age}$ = 0.9). Participants were recruited from independent and government secondary schools in Perth, Western Australia. One participant withdrew from the study after becoming nauseous subsequent to consumption of the glucose drink. A further five participants attended only one testing session, and thus were not included in any of the analyses reported here. An additional participant reported being non-compliant with the fasting instructions of the study. This participant was also removed from the data set for all analyses in order to avoid any potential confounds from a 'second meal effect'. Therefore, a total of 25 participants were included in the final analyses.

Prior to testing, all participants and parents of participants were provided with a questionnaire in order to screen for the following exclusion criteria:

- Diagnosis of diabetes mellitus and/or a history of hypoglycaemic or hyperglycaemic episodes.
- Lactose intolerance.
- Allergies to foods administered as part of the experimental procedure.
- Diagnosis of phenylketonuria (PKU).
- Needle/blood phobia or objection to having blood samples taken (e.g. for religious or cultural reasons).
- Diagnosis of an eating disorder.
- Having sought medical advice for a weight control issue.

This questionnaire has been used to screen for exclusion criteria in other investigations of nutritional influences on psychological functioning in our laboratory (e.g. Foster et al., 2007). A 'yes' response by the participant or their parent to any of the exclusion criteria listed above renders that participant ineligible to participate in the study. Based on both parental and participant responses to the screening questionnaire, all remaining 25 participants were eligible to participate in the study.

Ethics approval for the present study was obtained from the Human Research Ethics Committee of the University of Western Australia.

1.2. Treatment and design

A within-subjects design was employed. There was a single within participants factor (treatment), with two levels (glucose, placebo). A subsequent mixed model design also incorporated a single between-subjects factor (treatment order), with two levels (glucose first, placebo first).

In order to analyse whether individual differences in glucose regulation impacted upon the glucose memory facilitation effect, a median split was performed on the data for the area under the glucose response curve (AUC) for each participant. The above mixed model analysis was then repeated (i) for individuals demonstrating relatively better glucose regulation and (ii) for individuals demonstrating relatively poorer glucose regulation.

The glucose treatment consisted of 25 g 'Glucodin' Glucose Powder (Boots Healthcare Australia Pty Ltd) dissolved in 300 ml water. The placebo treatment consisted of five 'Equal' tablets (10% Aspartame, The Merisant Company) dissolved in 300 ml water. This quantity of aspartame was matched for sweetness with 25 g glucose powder when dissolved in 300 ml water (Sünram-Lea et al., 2008). Participants attended two test sessions. They were administered one treatment (i.e. glucose or placebo) in the first session and the complementary treatment in the second session. Treatment order was initially counterbalanced, with 16 participants of the original 32 participants assigned to each test order. However, two thirds of the 25 participants included in the final data analysis were administered the glucose treatment in the first testing session, as six of the seven participants whom it was necessary to exclude from the final analysis were to be administered the glucose treatment in the second testing session.

1.3. Materials

1.3.1. Modified California Verbal Learning Test-II (CVLT-II)

The CVLT-II (Delis et al., 2000) is a test of immediate, short delay and long delay episodic memory for a 16-item supraspan word list. The test comprises a standard form and an alternate form, which can be used for a repeat testing session. The reliability of the alternate form has been demonstrated, with reliability coefficients for immediate, short and long delayed free recall ranging between 0.72 and 0.79 across the different recall phases of the test (Delis et al., 2000; Strauss et al., 2006).