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SUSCEPTIBILITY OF PERCEPTION OF VERTICAL TO BLOOD GLUCOSE FLUCTUATIONS IN HEALTHY YOUNG ADULTS

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Abstract

Most studies on the relationship between glucose levels and cognitive function have focused on investigating the effects of exogenous glucose administration on cognitive abilities, with results pointing to inconsistencies in glucose-related effects on cognitive tasks. Disadvantages of such an experimental manipulation include discrepancy among studies in the timing of administration of tests, namely the timing between food intake and cognitive assessment, ranging from 15 min to 4 hours from the glucose drink, and cognitive testing occurring mainly during the postprandial state, leaving the later postabsorptive and possibly fasting states void of cognitive evaluation. It is preferable to evaluate how cognitive tasks can be affected by natural variations in blood glucose levels throughout the day. Perception of subjective visual vertical (SVV), which is essential for spatial orientation and daily activities may be susceptible to glucose fluctuations since it is continuously constructed and updated by brain regions essential for human perception for verticality. SVV perception was assessed with a computerized rod and frame test (CRFT), a clinical exam that evaluates a subject's ability to align a rod to vertical position, with the recorded alignment errors providing information on the accuracy of spatial orientation. The test is carried out without a vertical reference in which the rod is displayed on a blank background and measures the subject's internal representation of vertical. Rod alignment deviation errors from gravitational vertical and time for alignment were compared between the postprandial (within 6 hours after last meal) and postabsorptive / fasting (more than 8 hours from last meal) states in 31 and 33 healthy young males respectively. The mean duration of food omission was shorter ($P < 0.0001$) and mean glucose level was significantly greater ($P = 0.0008$) in the postprandial phase. Significantly greater SVV deviation error was observed during the postprandial phase (Postprandial SVV: 0.88˚ ± 0.45˚, Postabsorptive / Fasting SVV: 0.58˚ ± 0.35˚; $P = 0.007$), while the mean time for rod alignment was significantly shorter (Postprandial SVV time: 7.44 ± 2.65 s, Postabsorptive / Fasting SVV time: 9.09 ± 3.44 s; $P = 0.04$).
Verticality perception is susceptible to blood glucose fluctuations throughout the day, with more accurate but slower response time during the postabsorptive/fasting phase. Activities that rely on verticality perception/spatial orientation may be performed more efficiently outside the postprandial phase.

Keywords: *Verticality perception, CRFT, postprandial glucose, postabsorptive/fasting glucose.*

1. Introduction

A large body of evidence suggests that cognitive functioning is susceptible to the level of blood glucose, its basic fuel. Most previous studies on the relationship between glucose levels and cognitive function have focused on investigating the effects of exogenous glucose administration on cognitive abilities. However, the beneficial effect attributed to exogenous glucose ingestion is not consistent. This may be as result of the many different factors that potentially affect cognitive abilities, such as the differential sensitivity of cognitive processes to glucose enrichment, the degree of cognitive demand for a certain task and variations in normal glucose regulation capacity.

Glucose enrichment usually involves experimental elevation of blood glucose concentrations levels in the euglycemic range (72–126 mg/dl) by a pure glucose drink before initiating the cognitive tasks after an overnight fast. Such an experimental manipulation has a few disadvantages, one of which is the inconsistency among studies in the timing of administration of tests, namely the timing between food intake and cognitive assessment, ranging from 15 min to 4 hours from the glucose drink. Because assimilation of a pure carbohydrate load is complete within 4 hours (McMahon et al, 1989), the postabsorptive and possibly fasting states are exempt of cognitive evaluation in this case, since with glucose enrichment, cognitive testing occurs mainly during the postprandial state. Moreover, as most of the cognitive testing occurs in the morning after an overnight fast, this does not necessarily reflect similar responses to glucose manipulations at lunch or dinner.

In healthy young adults, research on the effect of meals on cognitive function has yielded few conclusions about the effects of specific macronutrients on cognitive performance (Bellisle et al, 1998; Kenarek, 1997). More importantly, there are indications that blood glucose levels can affect cognitive function independent of any glucose enrichment, with higher level of baseline blood glucose being associated with better performance. This is especially true for memory (Parker and Benton, 1995), performance on a vigilance task (Benton et al, 1994) and on the Water Jars task (Donohoe & Benton, 1999). If we accept that higher glucose levels facilitate cognitive function, then our hypothesis is that cognitive function may be enhanced during the postprandial state, in which there is an increase in blood glucose levels after food consumption, in comparison to performance in the postabsorptive state.

2. Design

To test our hypothesis, we selected the cognitive aspect of human vertical perception and orientation, known as subjective visual vertical (SVV). SVV is a psychophysical measure of the angle between perceptual vertical and gravitational vertical, and represents a fundamental spatial reference for maintaining an erect bipedal posture, for balance on Earth (Mazibrada et al, 2008; Van Pelt et al, 2005) and for judging visual orientations in space. The importance of investigating susceptibility of SVV glucose is that it is continuously constructed and updated (Barra, 2010) by brain regions, which play a pivotal role in human perception for verticality, and thus may be impacted due to natural variations in blood glucose levels throughout the day. SVV is typically assessed by the rod-and-frame task (RFT) (Asch & Witkin, 1948; Baccini et al, 2014; Docherty & Bagust, 2010), a clinical exam that evaluates a subject’s ability to align a line to vertical position, with the recorded alignment errors providing information on the accuracy of spatial orientation. The test is carried out without a vertical reference in which the rod is displayed on a blank background and measures the subject’s internal representation of vertical. The capacity to do so requires a complex integrative mechanism of visual, vestibular, and proprioceptive information relative to gravity (Vingerhoets et al, 2009). The design of the study included the independent variable of glucose level and the dependent variables were average rod alignment errors and alignment times.

3. Objectives

The aim of this study was to evaluate verticality perception through assessing subjective visual vertical (SVV) at different blood glucose levels that are more representative of real-life daily conditions, and not only falling within the postprandial state, but also within the longer postabsorptive state. Results may have implications to the adequacy of daily timing for performing some activities that heavily rely on spatial orientation.

4. Methods

Since restoration of the postabsorptive state takes at least 6 hours after a meal (McMahon et al, 1989), we evaluated SVV during the postprandial (within 6 hours after last meal) and postabsorptive/fasting (more than 8 hours from last meal) phases in 31 and 33 healthy young males respectively. Participants did not receive any incentives for their participation, and they all gave written informed consent.

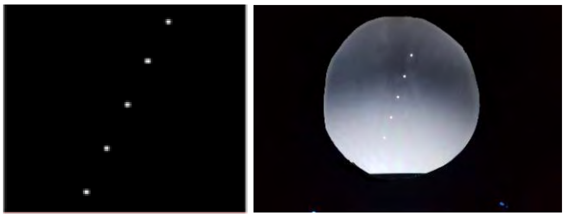
4.1. The computerized rod and frame test (CRFT)

We have utilized a computerized version (Bagust, 2005) of the Rod and Frame Test (RFT) to assess the spatial measures of verticality perception. This test is a modified version of the CRFT (Dochety & Bagust, 2010) in which the rod displayed in the center of the screen consisted of five white dots and had two starting positions, tilted 20 degrees in either a clockwise (CW) or counter clockwise (CCW) direction from vertical. The CRFT comprised 6 presentations and consisted of four replicates of SVV presentation (Figure 1a). A round black paper ring was stuck on the laptop screen to conceal its edges and reduce clues to verticality, while exposing the rod presentation in the center of the screen (Figure 1b). The test was performed in a dark room minimizing further any vertical cues within the room.

4.2. Procedure

Information on the times of the last meal and the blood collection just before cognitive testing were recorded., Prior to beginning the test, random blood glucose levels were measured with the ACCU-CHEK ACTIVE (Roche, Germany) glucometer. Participants were then shown two instructional presentations that allowed them to familiarize themselves with the process but were not included in the analysis. During testing, participants were seated in front of the laptop screen and asked keep their head in a fixed position without tilting or turning. They were instructed to rotate the dots using the right and left mouse buttons to a position perceived to be vertical. The dots rotated around their virtual midpoint in 0.5 degrees increments. When the participant was satisfied with the alignment of the dots, the program was advanced using the space bar of the computer keyboard. Positioning errors were recorded by the computer in degrees from gravitational vertical. The time for each rod alignment was also recorded.

Figure 1. a) Presentations of the rod during testing. The order of presentation was randomly assigned by the computer. b) Set up showing the concealment of the vertical edges of the laptop to obscure any cues of verticality from the subject.



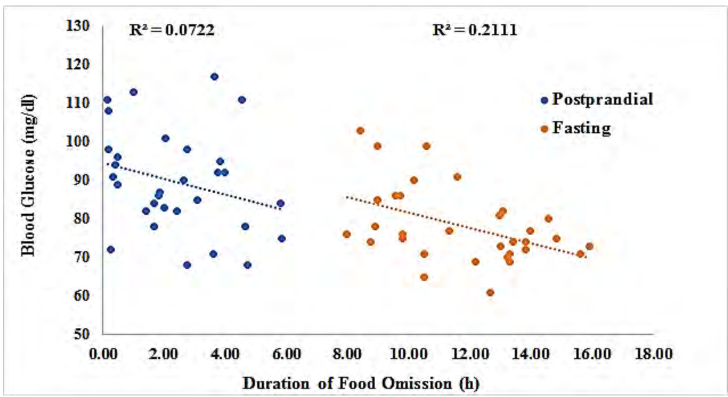
4.3. Spatial error calculations & statistical analysis

Deviations from vertical were recorded in degrees as positive values if the deviation was in a CW direction, and negative values for CCW deviations. These values were used to calculate the mean signed errors and the mean absolute (unsigned) errors for the four SVV presentations for each participant. The reported alignment errors in this study are the absolute (unsigned) values. The SVV alignment errors of the two glucose criteria were then compared. All statistical analyses were carried out using INSTAT (Graph Pad Inc.). Data were tested for normality using the Kolmogorov-Smirnoff method. Differences between the two groups were determined by unpaired t-test. Data were reported as mean ± SD, and level of significance was set at $p < 0.05$.

5. Results

All data passed the normality test. Figure 2 reveals negative correlation between food omission and glucose levels, but the association was significant only for the fasting state (Postprandial: r = - 0.27, P = 0.14; Fasting: r = - 0.46, P = 0.008). Table 1 illustrates the differences in glycemic and verticality perception parameters between the postprandial and fasting states. Mean glucose level was significantly greater during the postprandial phase. Significantly greater SVV deviation error was observed during the postprandial phase, while the mean time for rod alignment was significantly shorter. In figure 3, the mode of deviation errors for both groups was in the same error bin, however, the mode was greater for the fasting group. Almost all subjects falling within the larger error bins were in the postprandial phase.

Figure 2. Relationship between food omission and glucose levels during the postprandial and postabsorptive state.



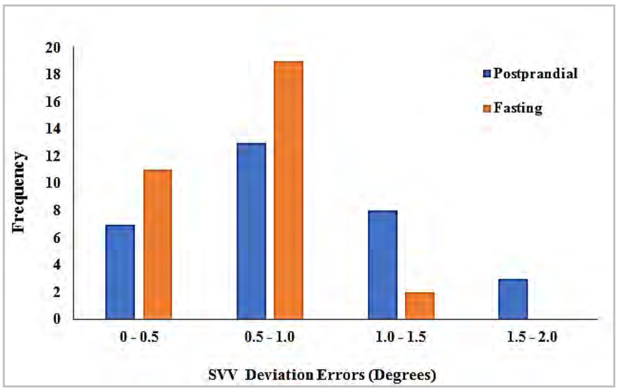
6. Discussion

This is the first study to examine the effects of glucose on verticality perception as measured by SVV. Our knowledge of SVV perception as a cognitive task that is mediated by complex integration of sensory inputs led us to hypothesize it may be cognitively demanding enough to influence brain glucose consumption. As it is constructed and updated continuously, it may be susceptible to actual changes in blood glucose concentrations throughout the day. We examined cognitive perceptual function without manipulating participants' levels of blood glucose. It is true that majority of the day is spent in the postprandial state because people usually eat at least three times a day, but this is not applicable to those who skip meals or those who are observing religious fasting.

Table 1. Glycemic and verticality perception parameters in the postprandial and postabsorptive states. Values represent mean ± SD and (range of values) for each parameter.

	Duration of Food Omission (h)	Blood Glucose level (mg/dl)	SVV Deviation Error °	Time for SVV Alignment (s)
Postprandial	2.40 ± 1.72 (0.17 – 5.87)	89.7 ± 13.2 (68.0 – 117.0)	0.88 ± 0.45 (0.25 – 2.00)	7.44 ± 2.65 (4.32 – 15.38)
Postabsorptive / Fasting	11.72 ± 2.24 (8.00 – 15.92)	78.6 ± 9.9 (61.0 – 103.0)	0.58 ± 0.35 (0.00 – 1.25)	9.09 ± 3.44 (3.85 – 15.83)
t (*P*-vlaue)	18.55 (< 0.0001)	3.89 (0.0002)	Welch t = 3.26 (0.002)	2.06 (0.04)

Figure 3. Distribution of SVV alignment errors in 0.5 degree bins for subjects within postprandial or postabsorptive state.



This is advantageous over glucose enrichment because the use of a single nutrient in the glucose drink is not representative of our usually mixed meals, and consuming a meal to increase blood levels may lead to different results from when the same amount of glucose is consumed in just a drink (Gold, 1986; Green et al., 2001). Because the assimilation of the constituents of a mixed meal and restoration of the postabsorptive state takes at least 6 hours, we carried our cognitive testing within 6 hours of meal ingestion, a relatively prolonged postprandial period.

Our results indicate to better verticality perception during the postabsorptive/fasting state as measured by smaller SVV mean alignment errors than during the postprandial phase. This may seem equivocal, since the glucose levels were higher in the postprandial phase in comparison the later glycemic phase. A possible explanation is that food omission for longer than 8 hours for our subjects in the postabsorptive states would induce a stable supply of glucose through glycogenolysis, while during the postprandial period, there will be post-meal glucose excursions as well. Such excursions, even if they are within the normal glucoregulation process, may negatively affect cognitive function. However, a stable supply of glucose as a result of glycogenolysis may be beneficial since stable blood glucose which avoids regular peaks and troughs in glucose is associated with better cognitive function (Sunram-Lea et al, 2016). A new hypothesis put forward by Wheeler et al (2017) states that on a daily basis there are dynamic interactions among hyperglycemia, hypoglycemia and cerebral blood flow, with brain exposure to circulating glucose excursions causing reduction in cerebral flow and early stage damage. If hyperglycemia time is long, this would result in adaptation to inhibit blood to brain glucose transport (Wheeler et al, 2017).

It is important to note the relatively small absolute values of the errors in the current study may seem within the acceptable normal range in comparison to that of the 3D mechanical RFT (Asch & Witkin, 1948), in which most people deviate within ±2° from gravitational vertical. This may render the interpretation and functional significance of the present results inconclusive. However this is expected as the CRFT has been reported to produce smaller errors (Isableu et al; 2008) in comparison to the mechanical system.

The shorter alignment times during the postprandial phase are consistent with studies reporting that blood glucose levels influence the speed of cognitive processing, such that, enriched blood glucose

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levels are associated with faster cognitive processing and shorter response times (Owens & Benton, 1994). The higher accuracy of rod alignment with low glucose levels might have been at the expense of response time which slowed with the need to concentrate.

7. Conclusions

Verticality perception over the course of the day may be impacted due to natural variations in blood glucose levels, with less accurate but shorter response time during the postprandial phase. Given the frequent use of sugary drinks or snacks in modern society, these results suggest a possible detriment of postprandial elevated glucose levels for verticality perception, and activities that rely on verticality perception/spatial orientation may be performed more efficiently outside the postprandial phase. For optimal verticality perception, it may be beneficial to adopt mechanisms that reduce blood glucose fluctuations throughout the day such as eating foods that cause a slow and steady rise in blood glucose.

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