# Glucose Intake Improves Executive Attention

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***Abstract*—Glucose is the essential energy source for brain, and glucose consumption is reported to be beneficial in multiple cognitive brain functions. However, it was unclear that if oral glucose intake has any effect on improving executive attention in human subjects. In this study, we firstly investigated the effect of one-shot intake of 29 g glucose on executive attention in human subjects using an internet-based Stroop color and word test (SCWT). The time interference score, defined by the reaction times in the SCWT under three different rules, was significantly lower in the glucose intake group than in the control group. The error rate in the color patch condition of the SCWT was also significantly lower in the glucose group. These results suggest that glucose enhances executive attention.**

***Index Terms*— glucose, Stroop color and word test, attention, neuropsychological assessment**

## I. Introduction

Glucose is the direct energy source for neurons and is essential for the maintenance of brain function. Previous studies have shown that glucose consumption is effective in improving several cognitive functions in humans, including verbal memory [1] and long-term episodic memory [2], and sustaining attention [3]. Glucose intake can also alleviate frustration in children [3]. Based on the effect of glucose on brain function reported thus far, we reasoned that planned and adequate glucose intake would increase the effectiveness of work and study. Here, we focused on the effect on executive attention, the ability to manage our attention in a conflicting situation where potentially distracting information also exists.

In this study, we employed the Stroop color and word test (SCWT) to evaluate the effect of glucose intake on human executive attention. The SCWT is a neuropsychological test that has been widely used to assess the ability to inhibit cognitive interference in the presence of both congruent and incongruent stimulations [4]. We modified the conventional SCWT and conducted the SCWT online for the first time.

## II. Methods

*SCWT*: The experimental protocol was approved by the Human Research Ethics Committee of the University of Tokyo (approval number: 24-3) and the Center for Information and Neural Networks (approval number: 1312260010). All participants provided informed consent, and they signed consent forms prior to each experiment. The SCWT was executed on a custom-made application, which was distributed to the participants through the file-sharing system in Google Drive. There were three rules in the test. The first rule was the color patches (rule C) condition. A circle with a color of either red, blue, green, or yellow was displayed on a screen. Then, the participants answered the color of the patch by entering arrow keys with their keyboards (here, up arrow: red, down arrow: green, left arrow: yellow, right arrow: blue). If the participant answered correctly, the next trial started immediately; that is, the next colored patch was presented on the screen. The participants were required to answer the colors for as many trials as possible in 45 s. After completing the trial under rule C, the rule switched to the second condition, the word condition (rule W). Under rule W, a word representing a color name was displayed in black font. The participants were required to answer the meaning of the word for as many trials as possible in 45 s. The third rule was the color-word rule (rule CW). Under rule CW, the words were displayed in incongruent color (for instance, the word “red” was displayed in green font). The participants were required to answer the color of the font but not the meaning of the word (in this instance, the correct answer was green). The rule CW also lasted for 45 s. During the test, the choice that the participants made and the time until input (reaction time) were recorded and used in the data analysis.

*Glucose intake*: Among a total of 89 participants who took part in the SCWT, 45 were instructed to consume 29 g of glucose 15 min before the start of the test at AM10:30. We used Ramune Soda Candy produced by Morinaga & Co., Ltd., as the source of glucose. The remaining 44 participants started the test without glucose consumption as a control group. Each group participated in the SCWT three times.

*Data analysis*: The statistical analysis was performed using a custom-written Python script. $P$ < 0.05 was considered statistically significant. For each participant, the average reaction time, the error rate, and the number of trials correctly answered in 45 s under each rule were calculated. Note that the outliers were eliminated with the quartile method. The time interference (TI) score and the number interference (NI) score were calculated using the following equations [5], [6]:

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$$TI = CWT - \frac{(WT + CT)}{2} \quad (1)$$

(CT: average reaction time under rule C; WT: average reaction time under rule W; CWT: average reaction time under rule CW),

$$NI = CWN - \frac{WN \times CN}{WN + CN} \quad (2)$$

(CN: number of correct answers in 45 s under rule C; WN: number of correct answers in 45 s under rule W; CWN: number of correct answers in 45 s under rule CW).

## III. Results

Lower TI scores indicate the ability to respond quickly even in a conflicting situation with other distracting information. Conversely, higher NI scores signify the ability to inhibit interfering information that leads to more answers in a limited amount of time [4]. The glucose group had significantly lower TI scores than the control group ($P = 0.024$, $t = 2.3$, $df = 87$, Student's $t$-test) (Fig. 1). On the other hand, the NI scores were not significantly different between the glucose group and the control group ($P = 0.12$, $t = -1.5$, $df = 87$, Student's $t$-test) (Fig. 1).

Regarding the error rates with each rule, only under rule C did the glucose group have a significantly lower error rate than the control group ($P = 0.0004$, $t = 3.6$, $df = 87$, Student's $t$-test) (under rule W, $P = 0.31$, $t = -1.0$, $df = 87$; under rule CW, $P = 0.15$, $t = 1.4$, $df = 87$, Student's $t$-test) (Fig. 2). For all three rules, there was no significant difference in the number of correctly answered trials between the glucose group and the control group (under rule C, $P = 0.89$, $t = 0.13$, $df = 87$; under rule W, $P = 0.89$, $t = -0.14$, $df = 87$; under rule CW, $P = 0.66$, $t = -0.44$, $df = 87$, Student's $t$-test) (Fig. 3).

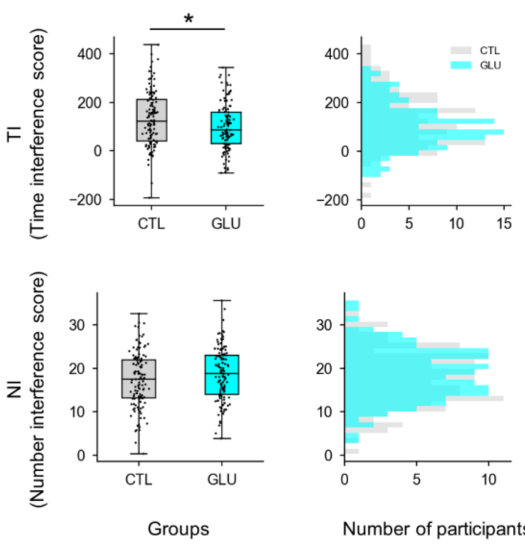


Figure 1. The glucose intake group has lower TI scores but not IN scores.
*Top*: The group that consumed glucose before the test (GLU) had significantly lower TI scores than the control group (CTL). $*P < 0.05$, Student's $t$-test. *Bottom*: There was no significant difference in the NI scores between the two groups.

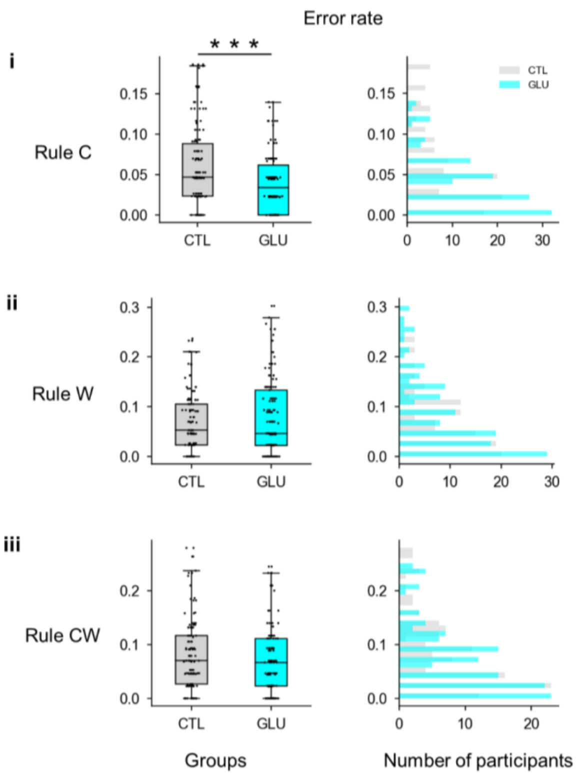


Figure 2. The glucose intake group has lower error rates under rule C. *i*, The glucose intake group (GLU) had significantly lower error rates under rule C than the control group (CTL). $***P < 0.001$, Student's $t$-test. *ii*, There was no significant difference in the error rates under rule W between the glucose group and the control group. *iii*, The same as ii but under rule CW.

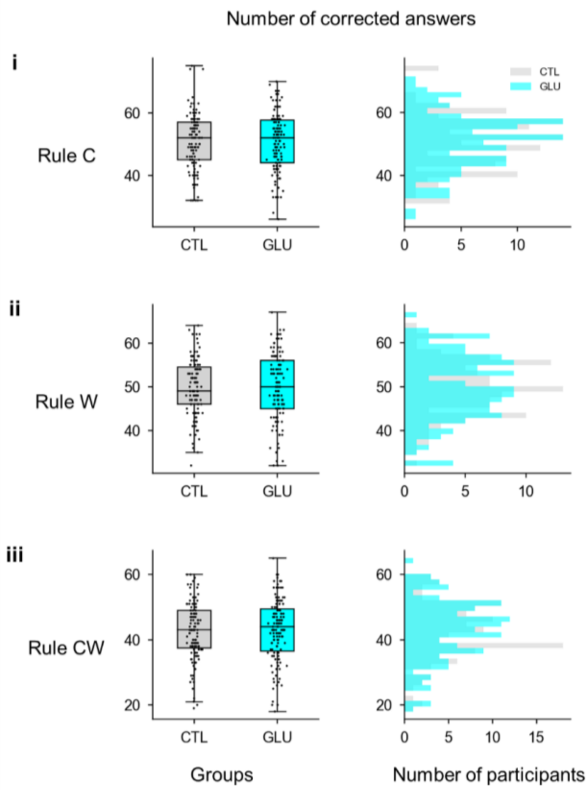


Figure 3. Glucose intake does not affect the numbers of trials correctly answered with either rule.
*i*, There were no significant differences in the numbers of correct answers under rule C between the glucose group (GLU) and the control group (CTL). *ii*, The same as i but under rule W. *iii*, The same as i but under rule CW.

## IV. Discussion

### *A. Effect of Glucose on Enhancing Cognitive Function Via the Cholinergic System*

In our research, the glucose group showed significantly lower TI scores than the control group, which suggests that oral glucose consumption before a task enhances the ability to extract necessary information from a situation where other distracting information exists.

Previous research has shown that glucose consumption before a task can contribute to improving human memory and attention [1] [7]. In animals, several studies have shown that posttraining glucose injection can improve the performance of mice on memory tasks [8], [9]. Since training in a novel behavioral task increased the activity of cholinergic neurons [10], the injection of glucose may supplement acetylcholine (ACh) in presynaptic neurons and maintain cholinergic activity [9]. Moreover, increased blood glucose levels enhance central acetylcholine synthesis and release due to the increased availability of acetyl coenzyme A (acetyl-CoA) produced in the process of glucose metabolism [9]. Glucose enters the brain from cerebral vessels by passing the blood–brain barrier through glucose transporter 1 expressed in endothelial cells and is taken up by astrocytes, oligodendrocytes, microglia, and neurons [11] [12]. Glucose taken up by cells is then converted to pyruvate through glycolysis. Pyruvate is transformed into acetyl-CoA, which is the precursor of Ach [11].

The cholinergic system has long been studied in terms of learning and memory [13], especially in the hippocampus; acetylcholine levels increase during spatial memory tasks in the rat hippocampus [14]. Similarly, glucose injection into the rodent brain enhances scopolamine-induced acetylcholine overflow from the hippocampus [15] and attenuates scopolamine-induced amnesia [9]. Another study has shown that the injection of nicotine into the hippocampus reverses the cognitive deficits caused by septal lesions [16].

A recent study investigated the effect of central ACh on attention [17]. The performance accuracy of rats in the five-choice serial-reaction time task was improved by the local injection of nicotine into the prefrontal cortex [18] and exacerbated by the injection of scopolamine into the medial prefrontal cortex and anterodorsal lateral frontal cortex [19]. The administration of scopolamine to the intraparietal cortex in rhesus monkeys also aggravated the performance of the Posner cueing task [20]. Thus, the enhancement of executive attention by glucose uptake may be caused by the central cholinergic system.

### *B. Detection of Brain Activities with and Without Glucose Intake During SCWT*

In this research, the effect of glucose intake was evaluated by the score of SCWT. However, it remains unclear about the neural activities during SCWT with and without glucose intake. We believe that by using noninvasive imaging methods such as functional magnetic resonance imaging (fMRI) can detect the changes of brain activities. fMRI was reported to be used in multiple studies on visualization of neural activities including the assessment of depression treatment and meta-analysis of fear extinction represents [21] [22]. Therefore, narrowing down the brain regions highly related to executive attention caused by glucose intake using fMRI may contribute to the detailed mechanism of our research at neural activity levels.

### *C. Timing of Efficient Glucose Intake*

In humans, after ingestion of 75 g of glucose, the blood glucose concentration rises within 10 min, reaches its peak 30–60 min later, and returns to normal levels within 3–4 hours [23]. In our study, the participants consumed 29 g of glucose 15 min before the start of the SCWT. Blood glucose was not monitored in our experiments because all tests were conducted online. Therefore, further enhancement of executive attention could be achieved by controlling the timing of glucose consumption.

## V. Conclusion

We conducted an online SCWT to test the effect of oral glucose consumption on executive attention in human subjects. As the result, the glucose group showed significantly lower TI score compared to the control group. The error rate in the color patch condition (rule C) was also significantly lower in the glucose group. These results suggest that oral glucose intake enhances the ability of humans to focus on necessary information from a complex environment. Since the test was conducted completely online, the results of our research have implications for improving the efficiency of online learning.

## Conflict of Interest

This work was supported by Morinaga & Co., Ltd. for funding and experimentation. Data analysis and manuscript writing were conducted by the authors only.

## Author Contributions

JL, KY and YI performed the experiments. JL and KY analyzed the data. LJ, KY and YI discussed the project and wrote the manuscript by mutual consent. All authors contributed to the article and approved the submitted version.

## References

[1] L. A. Brown and L. M. Riby, "Glucose enhancement of event-related potentials associated with episodic memory and attention," *Food & Function*, vol. 4, no. 5, pp. 770-776, 2013.

[2] A. Meikle, L. M. Riby, and B. Stollery, "The impact of glucose ingestion and gluco-regulatory control on cognitive performance: A comparison of younger and middle aged adults," *Human Psychopharmacology: Clinical and Experimental*, vol. 19, no. 8, pp. 523-535, 2004.

[3] D. Benton, V. Brett, and P. F. Brain, "Glucose improves attention and reaction to frustration in children," *Biological Psychology*, vol. 24, no. 2, pp. 95-100, 1987.

[4] F. Scarpina and S. Tagini, "The stroop color and word test," *Frontiers in psychology*, vol. 8, p. 557, 2017.

[5] W. V. D. Elst, M. P. V. Boxtel, G. J. Van Breukelen, and J. Jolles, “The Stroop color-word test: influence of age, sex, and education; and normative data for a large sample across the adult age range,” *Assessment*, vol. 13, no. 1, pp. 62-79, 2006.
[6] R. J. Ivnik, J. F. Malec, G. E. Smith, E. G. Tangalos, and R. C. Petersen, “Neuropsychological tests' norms above age 55: COWAT, BNT, MAE token, WRAT-R reading, AMNART, STROOP, TMT, and JLO,” *The Clinical Neuropsychologist*, vol. 10, no. 3, pp. 262-278, 1996.
[7] D. Benton and D. S. Owens, “Blood glucose and human memory,” *Psychopharmacology*, vol. 113, no. 1, pp. 83-88, 1993.
[8] C. Messier and C. Destrade, “Improvement of memory for an operant response by post-training glucose in mice,” *Behavioural Brain Research*, vol. 31, no. 2, pp. 185-191, 1988.
[9] C. Messier, T. Durkin, O. Mrabet, and C. Destrade, “Memory-improving action of glucose: Indirect evidence for a facilitation of hippocampal acetylcholine synthesis,” *Behavioural Brain Research*, vol. 39, no. 2, pp. 135-143, 1990.
[10] A. Toumane, T. Durkin, A. Marighetto, D. Galey, and R. Jaffard, “Differential hippocampal and cortical cholinergic activation during the acquisition, retention, reversal and extinction of a spatial discrimination in an 8-arm radial maze by mice,” *Behavioural Brain Research*, vol. 30, no. 3, pp. 225-234, 1988.
[11] P. Mergenthaler, U. Lindauer, G. A. Dienel, and A. Meisel, “Sugar for the brain: The role of glucose in physiological and pathological brain function,” *Trends in Neurosciences*, vol. 36, no. 10, pp. 587-597, 2013.
[12] I. A. Simpson, A. Carruthers, and S. J. Vannucci, “Supply and demand in cerebral energy metabolism: The role of nutrient transporters,” *Journal of Cerebral Blood Flow & Metabolism*, vol. 27, no. 11, pp. 1766-1791, 2007.
[13] S. V. Maurer and C. L. Williams, “The cholinergic system modulates memory and hippocampal plasticity via its interactions with non-neuronal cells,” *Frontiers in Immunology*, vol. 8, p. 1489, 2017.
[14] R. Stancampiano, S. Cocco, C. Cugusi, L. Sarais, and F. Fadda, “Serotonin and acetylcholine release response in the rat hippocampus during a spatial memory task,” *Neuroscience*, vol. 89, no. 4, pp. 1135-1143, 1999.
[15] T. P. Durkin, C. Messier, P. de Boer, and B. H. C. Westerink, “Raised glucose levels enhance scopolamine-induced acetylcholine overflow from the hippocampus: An in vivo microdialysis study in the rat,” *Behavioural Brain Research*, vol. 49, no. 2, pp. 181-188, 1992.
[16] M. W. Decker, M. J. Majchrzak, and D. J. Anderson, “Effects of nicotine on spatial memory deficits in rats with septal lesions,” *Brain Research*, vol. 572, no. 1-2, pp. 281-285, 1992.
[17] I. Klinkenberg, A. Sambeth, and A. Blokland, “Acetylcholine and attention,” *Behavioural Brain Research*, vol. 221, no. 2, pp. 430-442, 2011.
[18] B. Hahn, M. Shoaib, and I. P. Stolerman, “Involvement of the prefrontal cortex but not the dorsal hippocampus in the attention-enhancing effects of nicotine in rats,” *Psychopharmacology*, vol. 168, no. 3, pp. 271-279, 2003.
[19] T. W. Robbins, S. Granon, J. L. Muir, F. Durantou, A. Harrison, and B. J. Everitt, “Neural systems underlying arousal and attention: Implications for drug abuse a,” *Annals of the New York Academy of Sciences*, vol. 846, no. 1, pp. 222-237, 1998.
[20] M. C. Davidson and R. T. Marrocco, “Local infusion of scopolamine into intraparietal cortex slows covert orienting in rhesus monkeys,” *Journal of Neurophysiology*, vol. 83, no. 3, pp. 1536-1549, 2000.
[21] R. L. Carhart-Harris and L. Roseman, *et al*., “Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms,” *Scientific Reports*, vol. 7, no. 1, pp. 1-11, 2017.
[22] M. A. Fullana, A. Albajes-Eizagirre, C. Soriano-Mas, B. Vervliet, N. Cardoner, O. Benet, R. Radua, and B. J. Harrison, “Fear extinction in the human brain: A meta-analysis of fMRI studies in healthy participants,” *Neuroscience & Biobehavioral Reviews*, vol. 88, pp. 16-25.
[23] E. Georga, D. Fotiadis, and S. Tigas, *Personalized Predictive Modeling in Type 1 Diabetes*, 2.1.3, 2018.



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