Functional MRI of the responses of the human hypothalamus to sweet taste and calories

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Introduction

Evidence exists that caloric beverages do not trigger appropriate anticipatory physiologic responses. The hypothalamus is important in energy homeostasis, integrating multiple neural and hormonal signals [1,2]. Previously, we found a prolonged dose-dependent decrease in the fMRI signal in the hypothalamus after ingestion of a glucose solution [3]. We suggested that this response is triggered by the sweet taste and energy content of glucose and is associated with changes in the blood insulin concentration. Here, we elaborated on this work and investigated the effects of sweet taste and energy content on the hypothalamic response to glucose ingestion and concomitant changes in blood glucose and insulin concentrations.

Subjects and methods

Five healthy normal-weight men participated in a randomized cross-over design. Subjects were scanned 4 times for 37 min on separate days after fasting overnight. After 7 min, they ingested one of 4 stimuli (300 mL): water, a glucose, an aspartame (sweet taste) or a maltodextrin (non-sweet carbohydrate) solution. For the functional scan a 10 mm midsagittal slice was scanned with a T_2^*-weighted gradient-echo segmented EPI sequence (TR/TE = 120/40ms, flip = 30º, FOV = 208 × 208 mm, 12 signal averages per scan). Every subject's hypothalamus was manually segmented and 2 regions of interest (ROI) were delineated using a T_1-weighted image of the same slice [4]. Also, a square reference area (10 × 10 pixels) in the frontal cortex was delineated. After registration of the functional scans, the mean gray value in each ROI was calculated at every time point. Next, the percentage signal change from the mean baseline was calculated. To correct for global signal changes the signal in the reference area was subtracted from that in the ROIs at every timepoint. For statistical analysis, the data obtained after stimulus ingestion were pooled per minute (28 time points) and Student's t-tests were used to compare the mean signal change at every time point after treatment with that before treatment (the 7 min reference period). To compare treatment effects, the areas under the curve (AUCs) were calculated for every subject and analyzed with a randomized block design. Also, on every study day, 10 blood samples were taken: one before scanning and 9 during scanning at -5 and -3 min (before stimulus ingestion), and at 1, 3, 5, 7, 10, 20 and 29 min after the onset of drinking.

Results

In both ROIs, glucose ingestion resulted in a prolonged significant decrease in the hypothalamic fMRI signal, which started 2-5 min after the onset of drinking and lasted for the remainder of the scan (approx. 30 min). Water, aspartame and maltodextrin had no such effect (Fig. 1 A, B). In the upper hypothalamus, the AUC of glucose differed significantly from that of all other treatments ($P < 0.05$, AUCs did not differ between the 2 ROIs). Glucose and maltodextrin ingestion resulted in similar increases in blood glucose and insulin concentrations, starting 5-10 min after the onset of ingestion (Fig. 1 C).

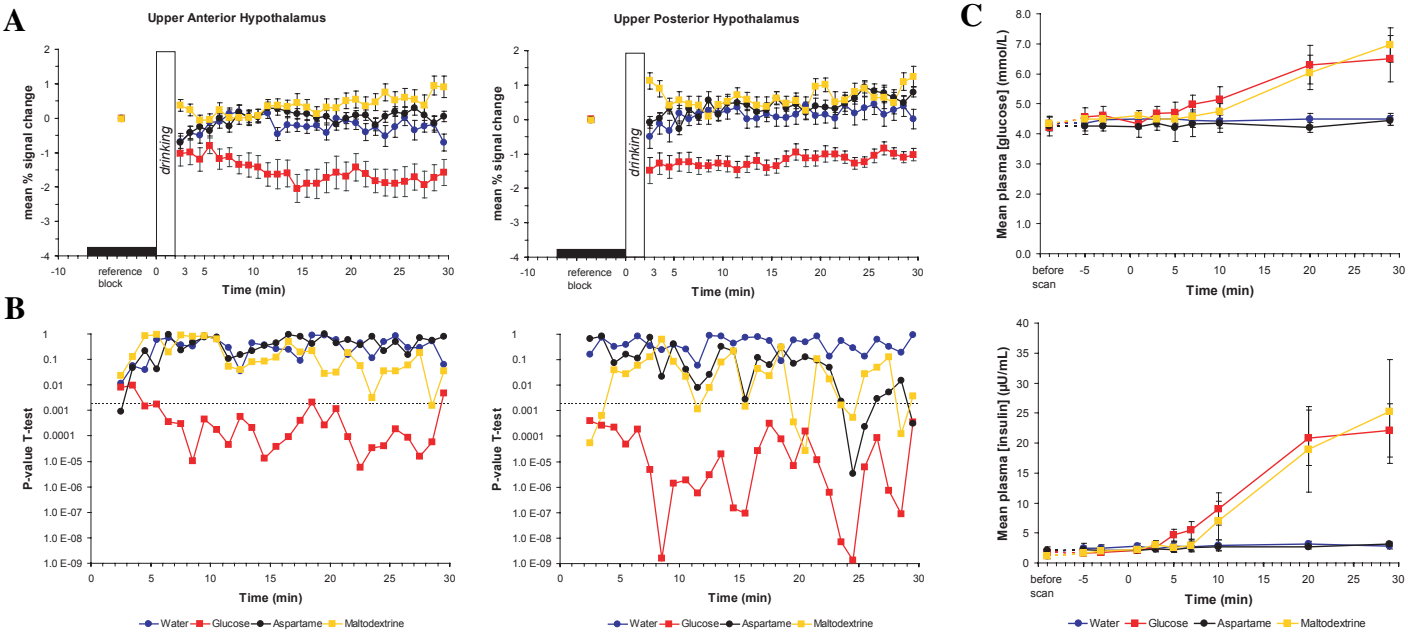

Figure 1. **A**: *Mean % signal change ± SEM in the two ROI's in the upper hypothalamus.* **B**: *P-values of the t-test comparing the treatment effect at every timepoint with the mean signal change in the reference block i.e. before treatment (these signal changes were near zero). The dotted line indicates the Bonferroni-corrected threshold of P = 0.0018.* **C**: *Mean ± SEM glucose and insulin concentrations in the fasted state and after stimulus ingestion.*

Discussion and Conclusion

We aimed to separate the effects of sweet taste and energy content on the response of the hypothalamus to glucose ingestion. Interestingly, we found an effect of glucose but not of maltodextrin on the hypothalamic fMRI signal. Both glucose and maltodextrin, however, resulted in similar increases in blood glucose and insulin concentrations. Subjects were unfamiliar with the maltodextrin solution, which had no distinct taste. Therefore, conditioned responses to maltodextrin's post-ingestive effects might be absent. The hypothalamic response to glucose was similar but smaller than reported previously [3]. A possible reason for this is that the stress caused by the blood sampling affected the response of the hypothalamus [5,6]; otherwise the experimental setup of both studies was the same.

Taken together, our findings suggest that both sweet taste and energy content are required for a hypothalamic response. Whether other sweet carbohydrates also elicit such a response remains to be investigated. A learned combination of taste (sweetness) and energy content could be crucial in triggering adaptive responses to sweetened beverages.

References

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