Hypothalamic fMRI Responses to Different Sugars under Normal Intake Conditions: A Pilot Study

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INTRODUCTION

Neuronal activity in the hypothalamus is known to change in response to variability in glucose levels. In particular, a significant reduction in brain activity in the hypothalamus was reported following fructose versus glucose ingestion (Page et al., 2013), but not when the sugars were administered intravenously (Purnell et al., 2011).

This reduced hypothalamic activity could be associated with a reduced feeling of satiation. The relevance of these findings is uncertain, as the amount and type of sugar used in the investigations did not represent daily consumption levels or patterns.

STUDY AIMS

Aim #1: To examine hypothalamic activity in five different sugar conditions resembling normal intake.

Aim #2: To evaluate the patterns of functional connectivity of the hypothalamus with the rest of the cortical mantle

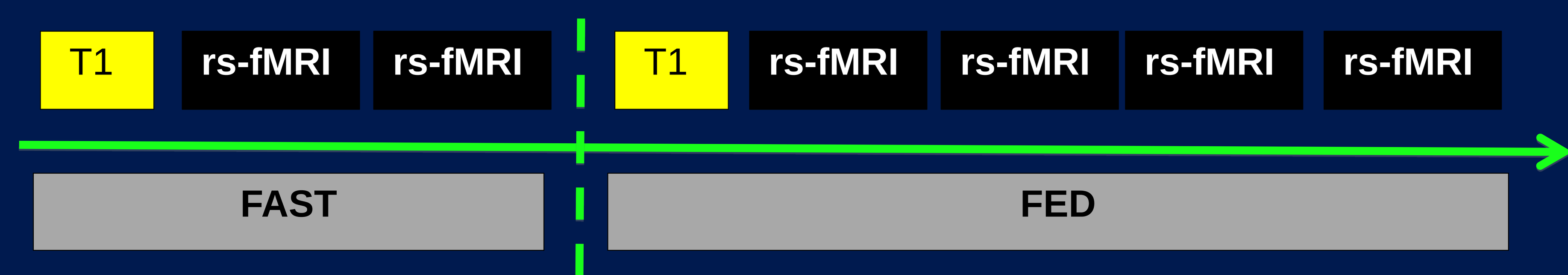
MATERIALS AND METHODS

Sample and Experimental Design

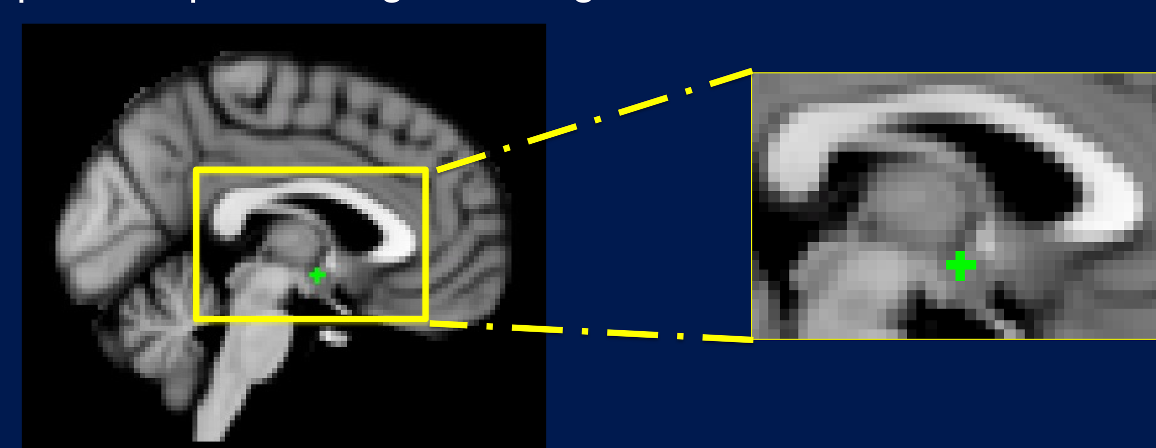
Seven healthy young volunteers underwent six runs of resting-fMRI under 5 different conditions: 9% of energy of fructose, 9% of energy of glucose, 18% of energy of high-fructose corn syrup, 18% of energy of sucrose, and regular 1% milk (control). Conditions took place on five separate days, in a randomized, double-blinded manner and at the same time of day.

MATERIALS AND METHODS

The first 2 runs were carried out under fasting. Subsequently, subjects ate a standardized meal (sugar administered in a liquid formula). After the meal (30 min), subjects underwent 4 runs of resting-fMRI (5 min each). For image analysis, we performed standard preprocessing methods using FSL and AFNI software. Briefly, we applied motion correction, normalization to MNI, smoothing and temporal filtering (<0.08 Hz). We also removed several sources of spurious variance: (a) 6 parameters to correct for rigid-body head motion, (b) the global brain signal, (c) the average signal of ventricles, and (4) the average signal white matter.

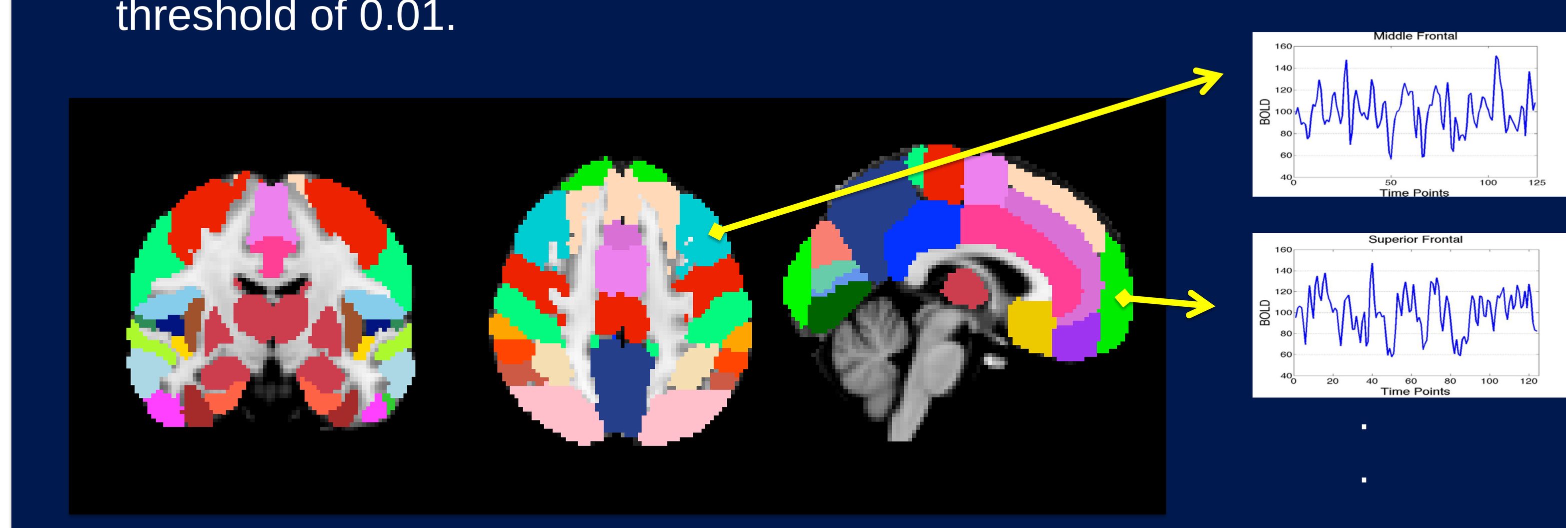


A seed of 4 mm was placed in the hypothalamus, based on a previous study (Page et al., 2013) to compute the percent signal change.



Talairach Coordinates:
X=0 Y=-3 Z=-6

A Pearson R correlation was computed between the time series of 96 brain regions (cortical and subcortical) generated from the Oxford atlas (FSL) and the hypothalamus region of interest(ROI). We only used used positive correlations exceeding a positive and false discovery rate (FDR)-corrected threshold of 0.01.

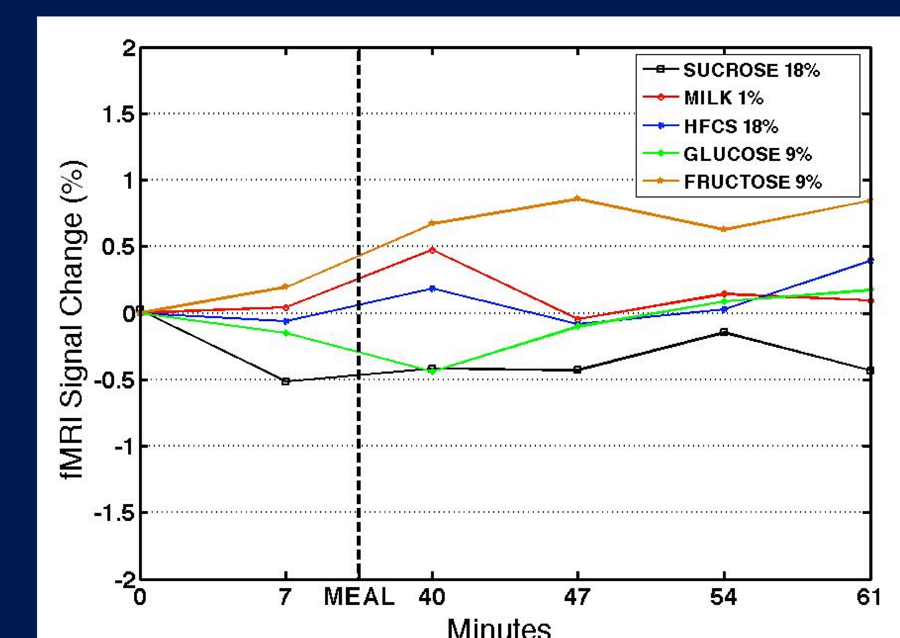


96 time series

$$r_{ij} = \frac{\sum_{t=1}^{T} (x_i(t) - \overline{x_i})(x_j(t) - \overline{x_j})}{\sqrt{\sum_{t=1}^{T} (x_i(t) - \overline{x_i})^2}\sqrt{\sum_{t=1}^{T} (x_j(t) - \overline{x_j})^2}}.$$

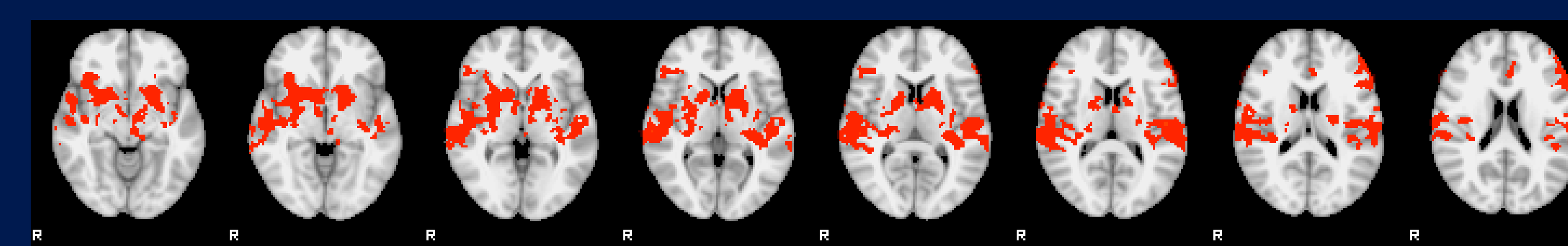
Pearson correlation formula applied between the time courses of the hypothalamic ROI (x_i) and the rest of cortical areas (x_j).

RESULTS



In this pilot study mimicking the conditions of a regular meal, we did not find any significant differences between the five sugar conditions and baseline activity on hypothalamic activation. There was only an overall increase of variability after the consumption of the meal.
The graph shows % signal change (PSC) throughout the runs of resting-state for each condition. To compute the PSC the baseline activity is the hypothalamic signal in the first run of fasting for each condition.

Below is the general pattern of connectivity between the hypothalamic ROI and the rest of brain areas. Significant connectivity was found with caudate, putamen, and insula.



However, there was no effect of condition: the correlation between the hypothalamic ROI and the rest of brain areas did not differ on the basis of sugar composition.

CONCLUSION

Although these results should be considered preliminary, they suggest that the previously identified differences in hypothalamic response to sugars may not occur under conditions that are more representative of normal daily intake levels and patterns.

REFERENCES

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