Changes in fMRI Hypothalamic Activity Via Intrinsic Oscillations After Intake of Regular Soda, Diet Soda or Water During a Meal

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INTRODUCTION

The health implications of consuming added sugars, particularly in sugar-sweetened beverages (SSBs), cause considerable controversy and debate within the scientific community.

Recent studies with functional neuroimaging have identified differences in hypothalamic activity and connectivity after ingestion of fructose versus glucose. 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).

The identified reduced hypothalamic activity could be associated with a reduced feeling of satiation. However, the above studies used either sugar in isolation and in amounts that fall within the higher end of the spectrum of population consumption. The relevance of these findings for the case of SSBs remains unknown.

STUDY AIM

The aim of this study was to examine acute changes in hypothalamic activity after intake of different beverages at normal levels of consumption.

MATERIALS AND METHODS

Subjects and Experimental Design

A total of 63 healthy, non-diabetic, normotensive subjects with BMI 21-29.9 kg/m^2, between the ages of 20-50 years took part in an fMRI scanning session. The protocol consisted of six 5-min standard resting-state-fMRI acquisition runs (Figure 1A). During the first two runs subjects were in the fasting state. Subsequently they went out of the scanner and ate a standardized, mixed nutrient, eucaloric meal for 30 minutes. After the meal, subjects were scanned four additional runs. As part of the meal, subjects received one of the following three drinks, based on random allocation (n=21 per group):

- Group 1: 710 ml (24 oz.) of **regular soda** (approximately 14% of calories; mean population level soft drink consumption for this population)
- Group 2: 710 ml (24 oz.) of **diet soda**
- Group 3: 710 ml (24 oz.) of **water**

fMRI analysis

All resting-state images were preprocessed using both AFNI (Cox, 1996) and FSL (www.fmrib.ox.ac.uk) neuroimaging analysis packages. All the preprocessing steps were done using the specific commands that have been released at www.nitrc.org/projects/fcon_1000/.
Figure 1B depicts an overview of fMRI data analysis. Preprocessing included reorientation, motion correction, realignment, skull removing for each subject. Subsequently, a temporal despiking with a hyperbolic tangent squashing function was carried out in order to limit extreme values. Linear trends were removed from data. Finally, spatial smoothing using a 6-mm FWHM Gaussian kernel and grand mean normalization scaling were performed. Temporal filtering was not applied, because the data were examined in the frequency domain within select bands (Yu-Feng et al. 2007). In order to estimate the regional intensity of spontaneous fluctuation in BOLD signal we used two fast-Fourier transformation (FFT) based indices (ALFF and fALFF) (Yu-Feng et al. 2007). The amplitude of low-frequency fluctuation (ALFF) method was estimated on the preprocessed data. Using an FFT the time course for each voxel was transformed to the frequency domain without band-pass filtering. The square root of the power spectrum was calculated and then square averaged across 0.01-0.08 Hz at each voxel. Thus, we obtained an ALFF value (Figure 1B, item II) for each subject at each voxel. Finally, we calculated the fractional amplitude of low-frequency fluctuation (fALFF) which is an improvement of the original ALFF (Zou et al. 2008). fALFF is the normalized ALFF, and is calculated by dividing the ALFF value by the total sum of amplitudes across the entire frequency range measured in the time series (Figure 1B, item III). In other words, fALFF represents the ratio of the 0.01-0.08 Hz frequency range across the entire frequency range.
ALFF and fALFF maps were firstly computed for each subject in native space. Then, the individual maps were normalized to the MNI152 standard brain space with 2-mm isotropic voxel size. To facilitate statistical analysis the individualized maps were transformed into Z-scores (i.e., by subtracting the mean voxelwise ALFF or fALFF obtained for the individual's entire brain, and then dividing by the corresponding SD). Finally, a seed of 3 mm located at the hypothalamus (based on Page et al. 2013) was used to extract the Z-values from these fALFF maps for group-level parametric analyses (Figure 1B, item IV). Subsequent analyses were performed in IBM SPSS Statistics package.

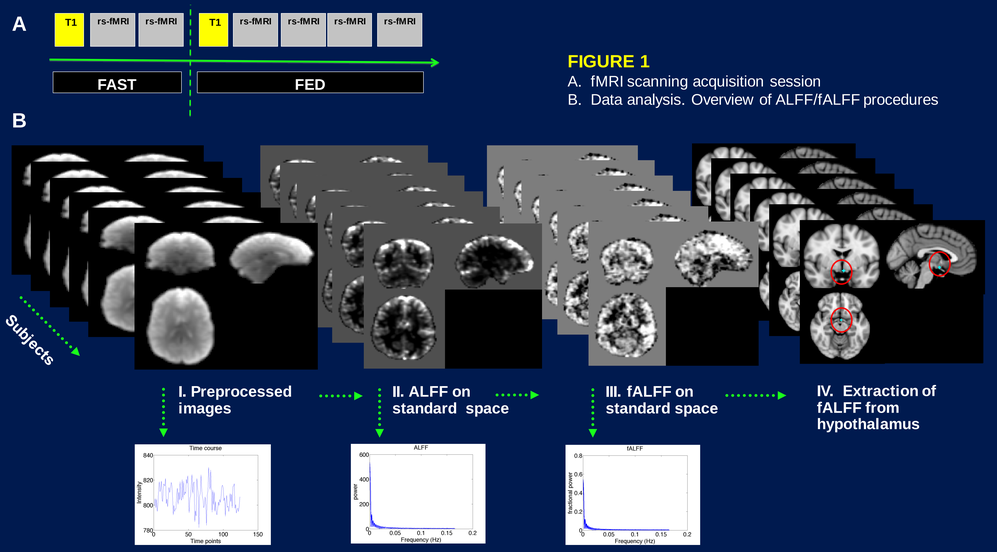

FIGURE 1
A. fMRI scanning acquisition session
B. Data analysis. Overview of ALFF/fALFF procedures

RESULTS

Figure 2A shows all available data (n=63, 3 groups, 6 time points per subject), summarized by mean ± SEM (error bars). Modelling all available data and time points as a repeated measures 3x6 ANOVA we did not find any effect of group (F=0.47, p=0.63), time (F=1.26, p=0.26) or interaction group x time (F=0.99, p=0.38). There was no effect either when time was reduced to two conditions only (fast/fed) [condition effect (F=1.99, p=0.16); group effect (F=0.77, p=0.46); interaction (F=0.57, p=0.56)]. Finally, we adjusted fed (post-meal) values to a baseline average specific for each individual. A summary graph corresponding to that adjusted data is presented in Figure 2B. Even with this adjustment to baseline we could not detect any significant difference: group effect (F=0.63, p=0.53), time effect (F=0.62, p=0.60), interaction (F=1.36, p=0.23).

These results suggest that the previously identified differences in acute hypothalamic activity following ingestion of sugars (Purnell et al. 2011; Page et al. 2013) may not apply to the case of SSBs under conditions that are more representative of normal daily intake levels and patterns.

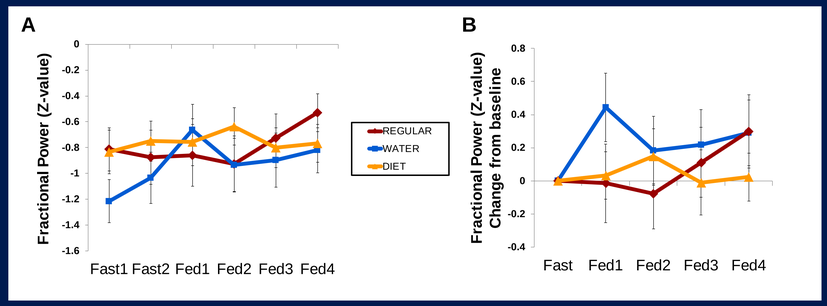

FIGURE 2
A. Changes in hypothalamic activity estimated by fALFF
B. Changes in hypothalamic activity, estimated by fALFF and adjusted for baseline

CONCLUSION

In this pilot study mimicking the conditions of a regular meal and mean population levels of soft drink consumption, we did not find any significant differences between changes in hypothalamic activity between water, regular soda and diet soda.

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