

# Supporting Information

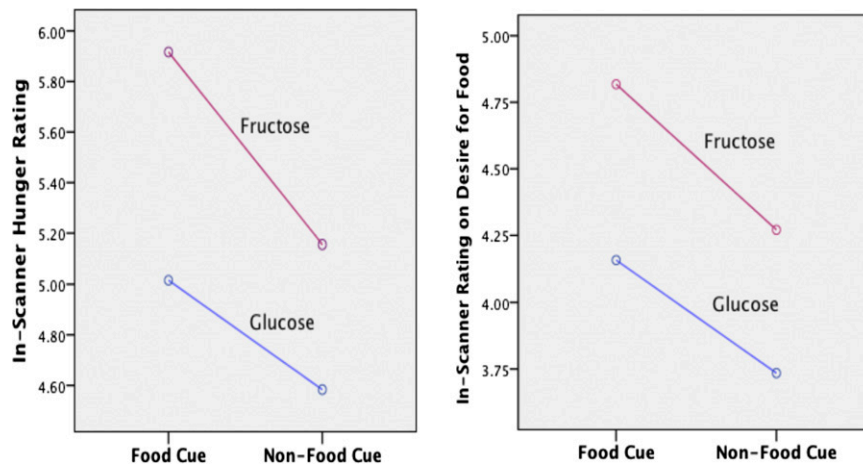
Luo et al. 10.1073/pnas.1503358112

## SI Materials and Methods

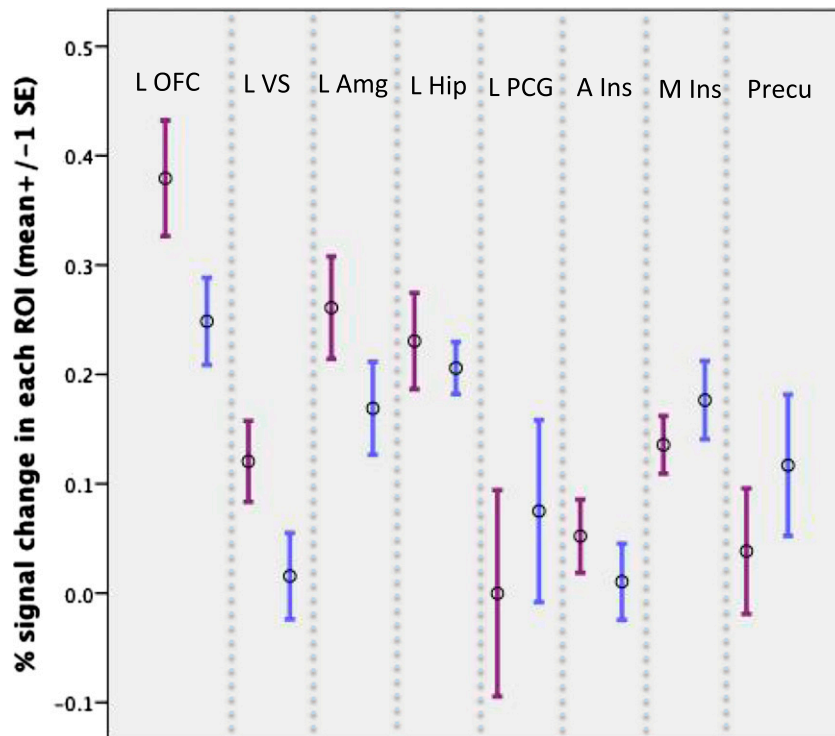
**In-Scanner Food-Cue Reactivity Ratings.** To explore drink effects on each individual appetite question, a  $2 \times 2$  ANOVA with drink (fructose or glucose) and condition (food or nonfood cues) as within-subject factors was performed for ratings on hunger and desire for food, respectively. There was a significant main effect of condition [ $F(1, 23) = 14.141, P = 0.001$ ] and marginally significant main effect of drink [ $F(1, 23) = 3.898, P = 0.06$ ] on hunger rating, and the interaction of drink and condition was

also marginally significant [ $F(1, 23) = 3.844, P = 0.06$ ]. There was a significant main effect of drink [ $F(1, 23) = 6.003, P = 0.022$ ] and condition [ $F(1, 23) = 10.438, P = 0.004$ ] on desire for food, and the interaction of drink and condition was not significant ( $P = 0.33$ ). The overall pattern is shown in Fig. S1.

**Region-of-Interest Analysis.** We report ROI analysis results in the main text and display in Fig. S2 the signal change in each ROI separately for fructose and glucose day.



**Fig. S1.** Fructose vs. glucose effects on hunger and desire for food. The x axis indicates condition, food cue, and nonfood cue. (Left) The y axis indicates mean hunger scores separately for fructose (purple line) and glucose (blue line). (Right) The y axis indicates mean rating scores on desire for food separately for fructose and glucose.



**Fig. S2.** Percent signal change in each ROI separately for fructose (purple) and glucose (blue). A Ins, anterior insula; L Amg, left amygdala; L Hip, left hippocampus; L OFC, left orbital frontal cortex; L PCG, left postcentral gyrus; L VS, left ventral striatum; M Ins, middle insula; Precu, precuneus.

**Table S1. Metabolic and hormonal response**

| Circulating levels of hormone or metabolite | Glucose drink, mean (±SE) |                    |                    |                       | Fructose drink, mean (±SE) |                    |                    |                       | P*     |
|---|---------------------------|--------------------|--------------------|-----------------------|----------------------------|--------------------|--------------------|-----------------------|--------|
|   | Baseline                  | 30 min             | 60 min             | AUC                   | Baseline                   | 30 min             | 60 min             | AUC                   |        |
| Insulin (μU/mL)                             | 15.04 (2.45)              | 63.52 (13.26)      | 62.62 (8.90)       | 3070.53 (535.38)      | 13.09 (1.74)               | 20.08 (3.07)       | 22.68 (2.87)       | 1139.08 (159.48)      | <0.001 |
| GLP-1 (pg/mL)                               | 25.20 (3.10)              | 44.79 (8.31)       | 40.39 (5.22)       | 2327.59 (333.86)      | 21.25 (2.38)               | 43.33 (9.35)       | 33.80 (4.50)       | 2125.82 (346.52)      | 0.53   |
| PYY (pg/mL)                                 | 74.68 (10.27)             | 87.27 (10.99)      | 80.05 (9.40)       | 4939.26 (621.44)      | 72.64 (11.02)              | 91.56 (12.54)      | 127.01 (12.71)     | 5741.38 (706.99)      | 0.07   |
| Ghrelin (pg/mL)                             | 102.58 (13.20)            | 78.13 (10.24)      | 69.02 (10.73)      | 4917.86 (651.95)      | 118.37 (12.84)             | 88.46 (8.99)       | 66.54 (6.58)       | 5427.56 (523.93)      | 0.22   |
| Glucose (mg/dL)                             | 86.06 (1.06)              | 112.74 (4.89)      | 102.20 (6.58)      | 6206.13 (197.39)      | 84.64 (1.04)               | 89.78 (1.28)       | 85.50 (2.06)       | 5245.66 (71.32)       | <0.001 |
| Fructose (mg/dL)                            | 9.71 (1.04)               | 9.76 (0.97)        | 10.02 (0.96)       | 588.64 (59.98)        | 8.95 (1.08)                | 11.44 (1.17)       | 14.35 (0.94)       | 692.64 (61.17)        | <0.05  |
| Leptin (pg/mL)                              | 13331.41 (3032.08)        | 13414.70 (3202.57) | 12706.64 (2728.64) | 793011.86 (185819.13) | 13011.79 (3044.18)         | 12384.16 (2807.45) | 11967.74 (2897.88) | 746217.68 (176748.65) | 0.38   |
| Lactate (mg/dL)                             | 9.87 (0.87)               | 9.62 (0.71)        | 11.38 (0.60)       | 607.39 (38.91)        | 7.95 (0.66)                | 11.63 (1.16)       | 16.50 (1.06)       | 715.78 (48.51)        | <0.01  |

SI conversion factors: to convert glucose values to mmol/L, multiply by 0.0555; to convert fructose values to mol/L, multiply by 55.506; to convert insulin values to pmol/L, multiply by 6.945. AUC, area under the curve; GLP-1, glucagon-like polypeptide 1; PYY, peptide YY.  
 \*For comparisons of mean AUC of fructose vs. glucose level.

**Table S2. Whole-brain analysis results showing regions with increased activation for food vs. nonfood contrast after each drink and fructose vs. glucose direct comparison**

| Condition                    | Regions                      | MNI coordinate               | Maximum Z score |      |
|------------------------------|------------------------------|------------------------------|-----------------|------|
| After fructose drink         | Right nucleus accumbens      | 6,12,-8                      | 2.99            |      |
|                              | Left nucleus accumbens       | -6,14,-6                     | 2.61            |      |
|                              | Medial prefrontal cortex     | -2,36,16                     | 4.01            |      |
|                              | Right orbital frontal cortex | 22,30,-16                    | 4.38            |      |
|                              | Left orbital frontal cortex  | -24,30,-16                   | 4.55            |      |
|                              | Right amygdala               | 22,-4,-16                    | 3.91            |      |
|                              | Left amygdala                | -22,-6,-16                   | 4.27            |      |
|                              | Right insular cortex         | 38,-4,8                      | 4.05            |      |
|                              | Left insular cortex          | -36,-8,12                    | 4.44            |      |
|                              | Right hippocampus            | 24,-32,-2                    | 4.27            |      |
|                              | Left hippocampus             | -22,-34,-2                   | 3.68            |      |
|                              | Right occipital cortex       | 14,-96,26                    | 4.96            |      |
|                              | Left occipital cortex        | -6,-96,26                    | 4.37            |      |
|                              | Left inferior frontal gyrus  | -40,38,6                     | 3.62            |      |
|                              | Precuneus                    | -4,-58,12                    | 3.27            |      |
|                              | Anterior cingulate cortex    | 0,36,2                       | 4.06            |      |
|                              | After glucose drink          | Medial prefrontal cortex     | -2,40,-12       | 4.02 |
|                              |                              | Left orbital frontal cortex  | -24,32,-16      | 4.71 |
|                              |                              | Left amygdala                | -22,-4,-16      | 4.04 |
| Right occipital cortex       |                              | 10,-96,24                    | 4.92            |      |
| Left occipital cortex        |                              | -12,-96,24                   | 4.76            |      |
| Right inferior frontal gyrus |                              | 58,8,32                      | 3.11            |      |
| Left inferior frontal gyrus  |                              | -46,36,6                     | 3.65            |      |
| Right postcentral gyrus      |                              | 62,-6,32                     | 2.95            |      |
| Left postcentral gyrus       |                              | -60,-24,32                   | 3.47            |      |
| Right hippocampus            |                              | 20,-32,2                     | 3.24            |      |
| Left hippocampus             |                              | -20,-34,2                    | 3.61            |      |
| Precuneus                    |                              | -4,-54,14                    | 3.30            |      |
| Precentral gyrus             |                              | 0,-22,64                     | 3.46            |      |
| After water drink            |                              | Right nucleus accumbens      | 10,10,-12       | 3.03 |
|                              |                              | Left nucleus accumbens       | -6,6,12         | 2.85 |
|                              |                              | Medial prefrontal cortex     | -2,38,-16       | 4.00 |
|                              |                              | Right orbital frontal cortex | 20,32,-16       | 4.16 |
|                              |                              | Left orbital frontal cortex  | -26,34,-16      | 4.36 |
|                              |                              | Right amygdala               | 28,-4,-16       | 2.98 |
|                              | Left amygdala                | -20,-6,-16                   | 3.46            |      |
|                              | Right insular cortex         | 38,6,-12                     | 3.75            |      |
|                              | Left insular cortex          | -36,4,-12                    | 3.35            |      |
|                              | Left caudate                 | -10,14,0                     | 2.62            |      |
|                              | Right occipital cortex       | 12,-96,18                    | 4.63            |      |
|                              | Left occipital cortex        | -12,-102,18                  | 4.23            |      |
|                              | Right frontal pole           | 52,44,6                      | 3.96            |      |
|                              | Left inferior frontal gyrus  | -40,34,12                    | 3.42            |      |
|                              | Left superior frontal gyrus  | -18,46,42                    | 3.19            |      |
|                              | Precuneus                    | -6,-56,18                    | 2.99            |      |
|                              | Fructose vs. glucose         | Right occipital pole         | 6,-92,26        | 5.30 |
|                              |                              | Left occipital pole          | -6,-84,42       | 4.21 |

**Table S3. Regions showed stronger responses to food cues than nonfood cues**

| Left/right | Brain region            | Volume, mm <sup>3</sup> | Peak voxel MNI coordinate | Radius of ROI, mm |
|------------|-------------------------|-------------------------|---------------------------|-------------------|
| L          | Lateral OFC             | 1,304                   | -25,31,-17                | 4                 |
| L          | Anterior insula         | 328                     | -35,14,10                 | 4                 |
| R          | Anterior insula         | 752                     | 40,6,-10                  | 4                 |
| L          | Anterior insula         | 432                     | -38,5,-8                  | 4                 |
| L          | Ventral striatum        | 184                     | -9,6,-6                   | 2                 |
| L          | Middle insula           | 496                     | -37,-5,7                  | 4                 |
| R          | Middle insula           | 2,736                   | 39,-6,8                   | 4                 |
| L          | Amygdala                | 832                     | -19,-8,-16                | 4                 |
| L          | Parahippocampal gyrus   | 936                     | -21,-34,0                 | 4                 |
|            | Precuneus               | 240                     | 2,-50,35                  | 4                 |
| L          | Postcentral gyrus; BA 2 | 272                     | -39,-50,59                | 4                 |
| R          | Precuneus               | 480                     | 29,-57,54                 | 4                 |
| R          | Fusiform gyrus          | 896                     | 38,-71,-14                | NA*               |
| L          | Occipital lobe; BA 19   | 408                     | -24,-85,-15               | NA*               |
| L          | Lingual gyrus           | 1,288                   | -14,-92,-5                | NA*               |
| R          | Lingual gyrus           | 688                     | 12,-93,-6                 | NA*               |

Based on Tang et al. (table 4) (1). NA, not available.

\*The current study's slice position did not have signal coverage for these regions.

1. Tang DW, Fellows LK, Small DM, Dagher A (2012) Food and drug cues activate similar brain regions: A meta-analysis of functional MRI studies. *Physiol Behav* 106(3):317-324.

**Table S4. Correlations between demographics and fructose vs. glucose differences using Spearman's correlation analysis**

| Demographics    |                           | Behavioral rating* | WTP <sup>†</sup> | Neural food-cue reactivity <sup>‡</sup> |
|-----------------|---------------------------|--------------------|------------------|---|
| Age             | Correlation coefficient   | 0.08               | 0.03             | -0.034                                  |
|                 | Significance (two-tailed) | 0.71               | 0.888            | 0.875                                   |
|                 | <i>N</i>                  | 24                 | 24               | 24                                      |
| Education       | Correlation coefficient   | 0.202              | -0.151           | -0.104                                  |
|                 | Significance (two-tailed) | 0.344              | 0.481            | 0.629                                   |
|                 | <i>N</i>                  | 24                 | 24               | 24                                      |
| Body mass index | Correlation coefficient   | 0.038              | -0.119           | -0.278                                  |
|                 | Significance (two-tailed) | 0.861              | 0.579            | 0.188                                   |
|                 | <i>N</i>                  | 24                 | 24               | 24                                      |
| Waist           | Correlation coefficient   | 0.037              | -0.113           | -0.338                                  |
|                 | Significance (two-tailed) | 0.865              | 0.598            | 0.106                                   |
|                 | <i>N</i>                  | 24                 | 24               | 24                                      |
| Hip             | Correlation coefficient   | 0.087              | -0.095           | -0.296                                  |
|                 | Significance (two-tailed) | 0.687              | 0.658            | 0.16                                    |
|                 | <i>N</i>                  | 24                 | 24               | 24                                      |
| Waist/hip       | Correlation coefficient   | 0.048              | -0.09            | -0.143                                  |
|                 | Significance (two-tailed) | 0.823              | 0.674            | 0.506                                   |
|                 | <i>N</i>                  | 24                 | 24               | 24                                      |

\*Fructose vs. glucose difference in hunger and desire for food ratings to food cues.

<sup>†</sup>Fructose vs. glucose difference in willingness to pay (WTP).

<sup>‡</sup>Fructose vs. glucose difference in the composite ROI response to food cues.