# **Supplementary information**

# Acute social isolation evokes midbrain craving responses similar to hunger

In the format provided by the authors and unedited

Supplementary Material

#### Acute social isolation evokes midbrain craving responses similar to hunger.

Livia Tomova<sup>1\*</sup>, Kimberly L. Wang<sup>1</sup>, Todd Thompson<sup>1</sup>, Gillian A. Matthews<sup>3</sup>, Atsushi Takahashi<sup>2</sup>, Kay M. Tye, <sup>3</sup>, Rebecca Saxe<sup>1,2,4</sup>

#### Affiliations:

<sup>1</sup>Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, Massachusetts.

<sup>2</sup>McGovern Institute for Brain Research, Massachusetts Institute of Technology, Cambridge, Massachusetts.

<sup>3</sup>Salk Institute for Biological Studies, La Jolla, California.

<sup>4</sup>Center for Brains, Minds and Machines, Massachusetts Institute of Technology, Cambridge, Massachusetts.

\*Correspondence to: Livia Tomova, tomova@mit.edu

# **Table of Contents**

Supplementary Figures
Craving ratings all sessions
SN/VTA: Full data for all sessions and all cues4
NAcc – functional ROI: Full data for all sessions and all cues
Group level whole brain: session * cue interaction
Correlations between craving ratings
Group level whole brain: main of effects of cue7
Midbrain localizer: group analysis7
Comparison anatomical and functional SN/VTA ROIs
Supplementary Tables
Results: SN/VTA9
Putamen13
NAcc
NAcc – exploratory functional ROI17
Caudate19
Orbitofrontal cortex (OFC)
Amygdala23
Insula25
Anterior Cingulate Cortex (ACC)
Group level whole brain: session * cue interaction
Group level whole brain: main of effects cue

# **Supplementary Figures**



**Craving ratings all sessions** 

Supplementary Figure 1. Craving ratings (n = 40) during the cue induced craving task in response to food cues and social cues for each session. The boxplots in indicate the median (dark center line), the interquartile range (IQR; box) and the 1.5 IQR minima and maxima (whiskers). Datapoints outside the whiskers are shown as individual data points.



SN/VTA: Full data for all sessions and all cues

Supplementary Figure 2. Full data (n = 40): Univariate activity in the SN/VTA (upper row)<sup>1</sup> and the midbrain functional ROI (lower row), for all cues and all sessions. The bar plots depict the mean beta values for food, social and control cues. The grey dots indicate individual data points and the error bars indicate standard errors of the mean. The dashed blue horizontal line indicates zero.

<sup>&</sup>lt;sup>1</sup> Please note that the sign of the activation depends on the implicit baseline when modeling the data which makes the absolute value difficult to interpret (for a discussion on this issue, see Stark & Squire 2001<sup>1</sup>). When compared to the control condition (flower images), we see the expected higher activation in response to the craving cues (food and social).

<sup>1</sup> Stark, C. E. L. & Squire, L. R. When zero is not zero: The problem of ambiguous baseline conditions in fMRI. *Proceedings of the National Academy of Sciences* **98**, 12760-12766, doi:10.1073/pnas.221462998 (2001).



#### NAcc - functional ROI: Full data for all sessions and all cues

Supplementary Figure 3. Univariate activity in the NAcc functional ROI for all cues and all sessions (n = 40). The bar plots depict the mean beta values for food, social and control cues. The dots indicate individual data points and the error bars indicate standard errors of the mean.

# Image: sector provide which it was a way with the way withe way with the way with the way with the way w

Group level whole brain: session \* cue interaction

Supplementary Figure 4. Univariate group-level activity cluster-level corrected over the whole brain (n = 40). Left: contrast food>control: fasting > isolation; Right: contrast social>control: isolation > fasting. Tables 21 (food > control) and 22 (social > control) show the results for this analysis.

#### **Correlations between craving ratings**



Supplementary Figure 5. Correlations between craving ratings during the cue induced craving task for each session (n = 40). fb = food craving, baseline session; ff = food craving, fasting session; fi = food craving, isolation session; sb = social craving, baseline session; sf = social craving, fasting session; si = social craving, isolation session.

Group level whole brain: main of effects of cue



Supplementary Figure 6. Univariate whole brain group-level activity family-wise error corrected at the voxel level (n = 40) : Left: contrast food>control (mean across all sessions: baseline, fasting, isolation). Right: social>control (mean across all sessions). Table 23 shows the results for this analysis.

#### Midbrain localizer: group analysis



Supplementary Figure 7. Univariate group-level activity in the midbrain localizer task within the midbrain for the contrast reward > nonreward (n = 40). All voxels with p<0.001 within the midbrain are displayed (no correction for multiple comparisons).



#### Comparison anatomical and functional SN/VTA ROIs

Supplementary Figure 8. Number of overlapping voxels between the functional and anatomical midbrain ROI (n = 40). The overlap ranged between 0-30 voxels out of a possible 100 voxels.



Supplementary Figure 9. Correlation between activity in functional and anatomical ROIs across subjects (n = 40).

### **Supplementary Tables**

#### **Results: SN/VTA**

#### Fasting vs Isolation contrast, anatomical SN/VTA

Predictors	Estimates	t	р
Session: Isolation > Fasting	0.009	1.2	0.230
Cue: Food	0.08	7.0	3.13e-11
Cue: Social	0.06	5.2	4.28e-7
Interaction: session - cue (food)	-0.03	-4.0	0.0005
Interaction: session – cue (social)	0.006	0.6	0.535

Supplementary Table 1. *Output mixed effects model: Fasting vs. Isolation contrast, SN/VTA anatomical ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

#### Fasting vs Isolation contrast, midbrain functional ROI

Predictors	Estimates	t	р
Session: Isolation > Fasting	0.006	0.36	0.720
Cue: Food	0.11	6.7	1.60e-10
Cue: Social	0.13	7.2	1.04e-11
Interaction: session – cue (food)	-0.03	-3.3	0.001
Interaction: session – cue (social)	0.03	2.5	0.015

Supplementary Table 2. *Output mixed effects model: Fasting vs. Isolation contrast, midbrain functional ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р
Session: Fasting	0.01	0.3	0.795
Session: Isolation	0.01	0.7	0.496
Cue: Food	0.09	4.0	8.06e-5
Cue: Social	0.06	3.0	0.003
Interaction: session (fasting) – cue	0.005	0.2	0.836
(food)			
Interaction: session (isolation) – cue	-0.05	-2.1	0.038
(food)	-0.05		
Interaction: session (fasting) – cue	-0.01	-0.6	0 576
(social)	-0.01		0.570
Interaction: session (isolation) - cue	0.002	0.1	0 941
(social)	-0.002	-0.1	0.241

#### Fasting and Isolation compared to baseline session, anatomical SN/VTA

Supplementary Table 3. *Output mixed effects model: Fasting and Isolation compared to Baseline, SN/VTA anatomical ROI*. Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р
Session: Fasting	0.005	0.2	0.857
Session: Isolation	0.02	0.6	0.531
Cue: Food	0.14	5.2	2.67e-7
Cue: Social	0.16	5.8	1.14e-8
Interaction: session (fasting) – cue	0.004	0.14	0.900
(food)			
Interaction: session (isolation) – cue	-0.06	-2.4	0.018
(food)	-0.00		
Interaction: session (fasting) – cue	-0.05	-1.8	0.070
(social)	-0.03		
Interaction: session (isolation) – cue	0.004	0.14	0.000
(social)	0.004	0.14	0.200

#### Fasting and Isolation compared to baseline session, midbrain functional ROI

Supplementary Table 4. *Output mixed effects model: Fasting and Isolation compared to Baseline, midbrain functional ROI*. Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

#### Putamen

#### Fasting vs Isolation contrast

Predictors	Estimates	t	р
Session: Isolation > Fasting	0.003	0.3	0.751
Cue: Food	0.024	1.8	0.077
Cue: Social	-0.006	-0.4	0.673
Interaction: session * cue (food)	-0.033	-3.2	0.002
Interaction: session * cue (social)	0.016	1.4	0.173

Supplementary Table 5. *Output mixed effects model: Fasting vs. Isolation contrast, Putamen ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р
Session: Fasting	0.004	0.1	0.886
Session: Isolation	0.012	0.4	0.676
Cue: Food	0.047	2.2	0.031
Cue: Social	0.011	0.6	0.535
Interaction: session (fasting) – cue	0.010	0.3	0.742
(food)			
Interaction: session (isolation) – cue	0.060	-2.5	0.012
(food)	-0.000		
Interaction: session (fasting) – cue	0.022	1.2	0.222
(social)	-0.033	-1.2	
Interaction: session (isolation) – cue	0.002	0.1	0.025
(social)	-0.002	-0.1	0.955

Supplementary Table 6. *Output mixed effects model: Fasting and Isolation compared to Baseline, Putamen ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

#### NAcc

#### Fasting vs Isolation contrast

Predictors	Estimates	t	р
Session: Isolation > Fasting	0.033	1.9	0.060
Cue: Food	0.128	6.4	1.09e-9
Cue: Social	0.114	5.2	3.70e-7
Interaction: session * cue (food)	-0.080	-4.7	4.51e-6
Interaction: session * cue (social)	0.038	2.1	0.040

Supplementary Table 7. *Output mixed effects model: Fasting vs. Isolation contrast, NAcc ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р
Session: Fasting	-0.051	-1.2	0.241
Session: Isolation	0.020	0.5	0.643
Cue: Food	0.161	5.7	2.87e-8
Cue: Social	0.104	3.3	0.001
Interaction: session (fasting) – cue	0.049	1.1	0.260
(food)	0.048		
Interaction: session (isolation) – cue	0.112	-3.0	0.004
(food)	-0.115		
Interaction: session (fasting) – cue	0.028	-0.8	0 455
(social)	-0.028		0.433
Interaction: session (isolation) – cue	0.050	1.2	0.102
(social)	0.030	1.3	0.192

Supplementary Table 8. *Output mixed effects model: Fasting and Isolation compared to Baseline, NAcc ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

#### NAcc – exploratory functional ROI

#### Fasting vs Isolation contrast

Predictors	Estimates	t	р
Session: Isolation > Fasting	0.030	1.6	0.122
Cue: Food	0.142	6.1	4.70e-9
Cue: Social	0.100	4.2	3.40e-5
Interaction: session * cue (food)	-0.090	-4.3	2.23e-5
Interaction: session * cue (social)	0.038	1.9	0.061

Supplementary Table 9. *Output mixed effects model: Fasting vs. Isolation contrast, NAcc functional ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р
Session: Fasting	-0.042	-0.9	0.384
Session: Isolation	0.020	0.4	0.657
Cue: Food	0.176	6.1	2.71e-9
Cue: Social	0.100	3.3	0.001
Interaction: session (fasting) – cue	0.052	1.1	0.292
(food)			
Interaction: session (isolation) – cue	0 121	-3.0	0.004
(food)	-0.121		
Interaction: session (fasting) – cue	0.040	-1.0	0.315
(social)	-0.040		
Interaction: session (isolation) – cue	0.040	1.0	0.222
(social)	0.040	1.0	0.322

Supplementary Table 10. *Output mixed effects model: Fasting and Isolation compared to Baseline, NAcc functional ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

#### Caudate

#### Fasting vs Isolation contrast

Predictors	Estimates	t	р
Session: Isolation > Fasting	-0.003	-0.2	0.849
Cue: Food	0.058	4.0	8.49e-5
Cue: Social	0.023	1.3	0.181
Interaction: session * cue (food)	-0.025	-1.9	0.061
Interaction: session * cue (social)	0.035	3.0	0.003

Supplementary Table 11. *Output mixed effects model: Fasting vs. Isolation contrast, Caudate ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р	
Session: Fasting	0.011	0.3	0.740	
Session: Isolation	0.006	0.2	0.860	
Cue: Food	0.077	4.0	8.12e-5	
Cue: Social	0.010	0.5	0.614	
Interaction: session (fasting) – cue	0.007	0.2	0.922	
(food)	0.007	0.2	0.832	
Interaction: session (isolation) – cue	0.044	2.0	0.053	
(food)	-0.044	-2.0	0.055	
Interaction: session (fasting) – cue	0.022	0.8	0.440	
(social)	-0.022	-0.8	0.440	
Interaction: session (isolation) – cue	0.048	2.2	0.022	
(social)	0.048	2.2	0.055	

Supplementary Table 12. *Output mixed effects model: Fasting and Isolation compared to Baseline, Caudate ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

#### **Orbitofrontal cortex (OFC)**

#### Fasting vs Isolation contrast

Predictors	Estimates	t	р
Session: Isolation > Fasting	-0.006	-0.2	0.857
Cue: Food	0.249	5.5	1.26e-7
Cue: Social	0.968	12.5	1.09e-27
Interaction: session * cue (food)	-0.033	-1.0	0.337
Interaction: session * cue (social)	0.112	2.5	0.0121

Supplementary Table 13. *Output mixed effects model: Fasting vs. Isolation contrast, OFC ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р
Session: Fasting	0.079	1.0	0.311
Session: Isolation	0.078	1.0	0.330
Cue: Food	0.288	4.6	6.35e-6
Cue: Social	0.897	9.5	2.56e-19
Interaction: session (fasting) – cue (food)	-0.006	-0.1	0.926
Interaction: session (isolation) – cue (food)	-0.072	-0.8	0.416
Interaction: session (fasting) – cue (social)	-0.041	-0.5	0.601
Interaction: session (isolation) – cue (social)	0.184	2.1	0.039

Supplementary Table 14. *Output mixed effects model: Fasting and Isolation compared to Baseline, OFC ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

#### Amygdala

#### Fasting vs Isolation contrast

Predictors	Estimates	t	р
Session: Isolation > Fasting	0.026	1.4	0.160
Cue: Food	0.145	6.4	1.04e-9
Cue: Social	0.259	9.2	1.78e-17
Interaction: session * cue (food)	-0.035	-1.9	0.055
Interaction: session * cue (social)	0.019	1.0	0.334

Supplementary Table 15. *Output mixed effects model: Fasting vs. Isolation contrast, Amygdala ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р	
Session: Fasting	-0.022	-0.6	0.548	
Session: Isolation	0.029	0.7	0.463	
Cue: Food	0.142	5.3	1.89e-7	
Cue: Social	0.275	6.6	1.78e-10	
Interaction: session (fasting) – cue	0.027	0.7	0.200	
(food)	0.037	0.7	0.300	
Interaction: session (isolation) – cue	0.032	0.8	0.404	
(food)	-0.032	-0.8	0.404	
Interaction: session (fasting) – cue	-0.035	0.0	0 301	
(social)	-0.035	-0.9	0.391	
Interaction: session (isolation) – cue	0.003	0.1	0.041	
(social)	0.005	0.1	0.741	

Supplementary Table 16. *Output mixed effects model: Fasting and Isolation compared to Baseline, Amygdala ROI*. Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

#### Insula

#### Fasting vs Isolation contrast

Predictors	Estimates	t	р
Session: Isolation > Fasting	0.015	0.8	0.433
Cue: Food	0.165	7.1	1.47e-11
Cue: Social	-0.223	-9.6	9.81e-19
Interaction: session * cue (food)	-0.034	-2.0	0.052
Interaction: session * cue (social)	-0.021	-1.0	0.324

Supplementary Table 17. *Output mixed effects model: Fasting vs. Isolation contrast, Insula ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р	
Session: Fasting	0.020	0.6	0.583	
Session: Isolation	0.051	1.1	0.266	
Cue: Food	0.196	6.6	1.26e-10	
Cue: Social	-0.186	-5.5	6.36e-8	
Interaction: session (fasting) - cue	0.004	0.1	0.024	
(food)	0.004	0.1	0.924	
Interaction: session (isolation) – cue	0.065	1 8	0.070	
(food)	-0.005	-1.0	0.070	
Interaction: session (fasting) – cue	0.016	0.4	0 701	
(social)	-0.010	-0.4	0.701	
Interaction: session (isolation) – cue	0.057	1 /	0 151	
(social)	-0.037	-1.4	0.131	

Supplementary Table 18. *Output mixed effects model: Fasting and Isolation compared to Baseline, Insula ROI*. Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

#### Anterior Cingulate Cortex (ACC)

#### Fasting vs Isolation contrast

Predictors	Estimates	t	р
Session: Isolation > Fasting	0.007	0.3	0.766
Cue: Food	0.117	3.6	0.0004
Cue: Social	0.034	1.0	0.337
Interaction: session * cue (food)	-0.073	-2.9	0.005
Interaction: session * cue (social)	-0.007	-0.3	0.787

Supplementary Table 19. *Output mixed effects model: Fasting vs. Isolation contrast, ACC ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

Predictors	Estimates	t	р	
Session: Fasting	0.034	0.6	0.542	
Session: Isolation	0.057	1.1	0.253	
Cue: Food	0.139	3.4	0.0008	
Cue: Social	0.022	0.5	0.634	
Interaction: session (fasting) – cue	0.052	1 1	0 272	
(food)	0.052	1.1	0.273	
Interaction: session (isolation) – cue	0.005	1 0	0.078	
(food)	-0.093	-1.0	0.078	
Interaction: session (fasting) – cue	0.010	0.2	0 726	
(social)	0.019	0.3	0.730	
Interaction: session (isolation) – cue	0.005	0.1	0.000	
(social)	0.005	0.1	0.908	

Supplementary Table 20. *Output mixed effects model: Fasting and Isolation compared to Baseline, ACC ROI.* Results are shown for a mixed effects regressions (using Matlab 2019b's *fitlme* function) to estimate the fixed effects of cue, deprivation session, and their interaction on response magnitude in the ROI, controlling for each session's average framewise displacement (i.e. head motion), with participant included as a random effect with both random intercepts and random slopes. The reported p-values (two-tailed) are not corrected for multiple comparisons.

# Group level whole brain: session \* cue interaction

Area	MNI coordinates cluster peak			t value
	х	у	Z	
Right cerebellum	14	-48	-46	5.90
Left anterior cingulate cortex	-4	6	32	5.21
Right occipital cortex	26	-84	20	5.11
Left cerebellum	-24	-68	-52	5.06
Left superior parietal cortex	-26	-82	48	4.74
Left midbrain (periaqueductal gray)	-8	-30	-12	4.73
Left amygdala	-18	-2	-10	4.72
Right premotor cortex	4	-2	72	4.60
Left dorsolateral prefrontal cortex	-30	38	30	4.57
Left superior parietal cortex	-14	-54	62	4.52
Right nucleus accumbens	14	12	-10	4.46
Right superior parietal cortex	20	-54	60	4.06

Supplementary Table 21. *Group level whole brain session* \* *cue interaction - Food: Fasting* > *Isolation.* Flexible factorial model using the first-level contrasts food > control and social > control from each session. Statistical inference was performed using a threshold of p < 0.05 corrected for multiple comparisons over the whole brain, using cluster-level correction. Supplementary Figure 4 (left) depicts the results from this table.

MNI	t value		
cluster peak			
х	у	Z	
-10	64	24	5.93
34	-96	6	5.15
-8	22	0	4.58
-2	40	-24	4.47
-14	-100	-8	4.19
-38	-94	-6	4.12
-26	-104	0	3.85
	MNI cluste x -10 34 -8 -2 -14 -38 -26	MNI coordin cluster peak x y -10 64 34 -96 -8 22 -2 40 -14 -100 -38 -94 -26 -104	MNI coordinatescluster peakxyz10642434-966-8220-240-24-14-100-8-38-94-6-26-1040

Supplementary Table 22. *Group level whole brain session* \* *cue interaction - Social: Isolation* > *Fasting.* Flexible factorial model using the first-level contrasts food > control and social > control from each session. Statistical inference was performed using a threshold of p < 0.05 corrected for multiple comparisons over the whole brain, using cluster-level correction. Supplementary Figure 4 (right) depicts the results from this table.

# Group level whole brain: main of effects cue

Food > Control

Area	Peak	Peak MNI coordinates		
	Х	у	Z	
Left fusiform gyrus	-30	-54	-12	19.04
Left orbitofrontal cortex	-24	36	-14	15.01
Left dorsolateral prefrontal cortex	-46	36	14	12.96
Left anterior cingulate cortex	-4	4	30	11.68
Right orbitofrontal cortex	22	32	-16	10.37
Right cerebellum	18	-40	-44	10.29
Left postcentral gyrus	-64	-18	30	9.98
Left cerebellum	-22	-38	-42	9.81
Left anterior cingulate cortex	-2	34	10	9.13
Right parietal cortex	28	-76	48	7.87
Left perirhinal cortex	-24	-2	-32	7.74
Left frontal cortex	-20	34	48	7.15
Right fusiform gyrus	52	-50	-18	6.19
Right supramarginal gyrus	66	-16	24	6.04
Left frontal cortex	-8	50	52	5.47
Left premotor cortex	-24	22	68	5.46
Left perirhinal cortex	-18	-20	-24	5.30
Right dorsolateral prefrontal cortex	42	42	8	5.27
Left premotor cortex	-20	24	70	5.23
Left premotor cortex	-32	16	66	5.19
Right parietal cortex	26	-62	62	5.18
Left caudate nucleus	-10	14	2	5.17

#### Social > Control

Area	Peak	Peak MNI coordinates		
	Х	У	Z	
Left fusiform gyrus	40	-48	-18	34.95
Right inferior frontal gyrus	48	22	22	12.77
Right frontal cortex	24	34	50	7.98
Right premotor cortex	48	2	58	7.46
Right premotor cortex	40	0	50	7.04
Left posterior cingulate cortex	-4	-16	38	6.27
Cerebellum	0	-96	-24	5.78
Left superior parietal cortex	-2	-64	-50	5.77
Left cerebellum	-30	-64	-50	5.75
Left frontal cortex	-4	36	64	5.55
Left inferior temporal gyrus	-42	4	-44	5.50
Left premotor cortex	-10	6	78	5.25
Left premotor cortex	-14	28	68	5.24
Right dorsolateral prefrontal cortex	12	56	48	5.18

Supplementary Table 23. *Main effects of cue (food > control and social > control)*. Flexible factorial model using the first-level contrasts food > control and social > control. Statistical inference was performed using a threshold of p < 0.05 corrected for multiple comparisons over the whole brain, using family-wise error correction at the voxel level. Supplementary Figure 6 depicts the results for this analysis.