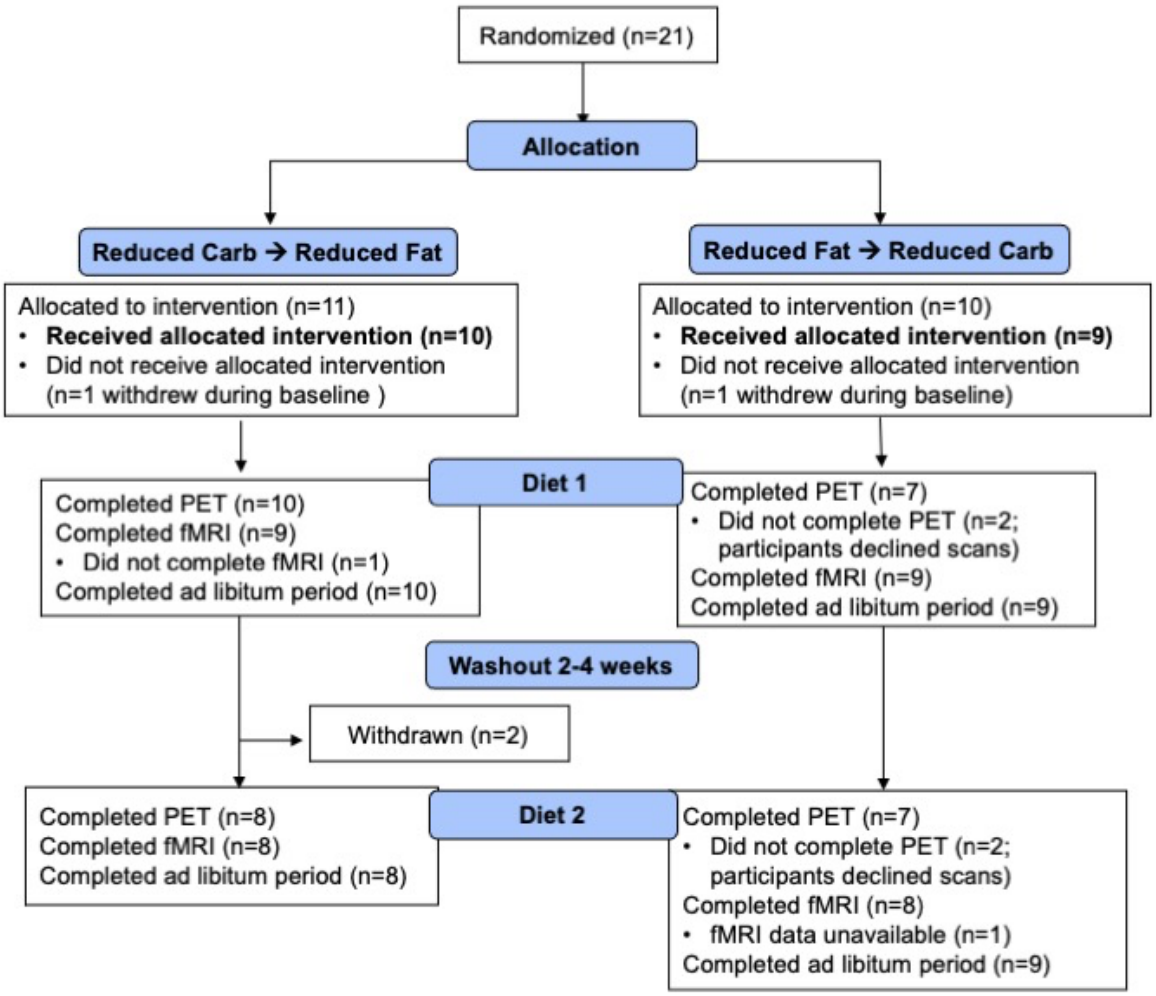
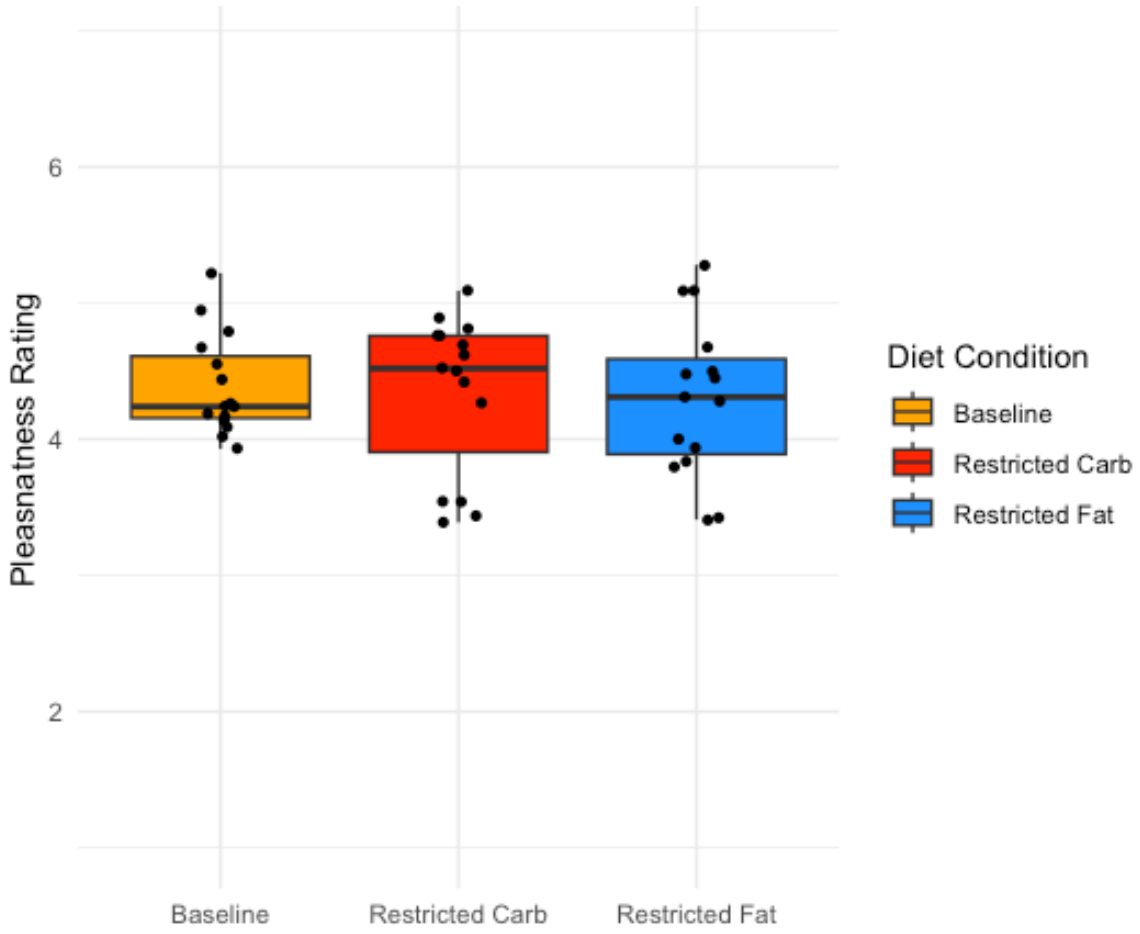
Supplemental Information

Restriction of dietary fat affects brain reward regions in adults with obesity: A randomized crossover trial

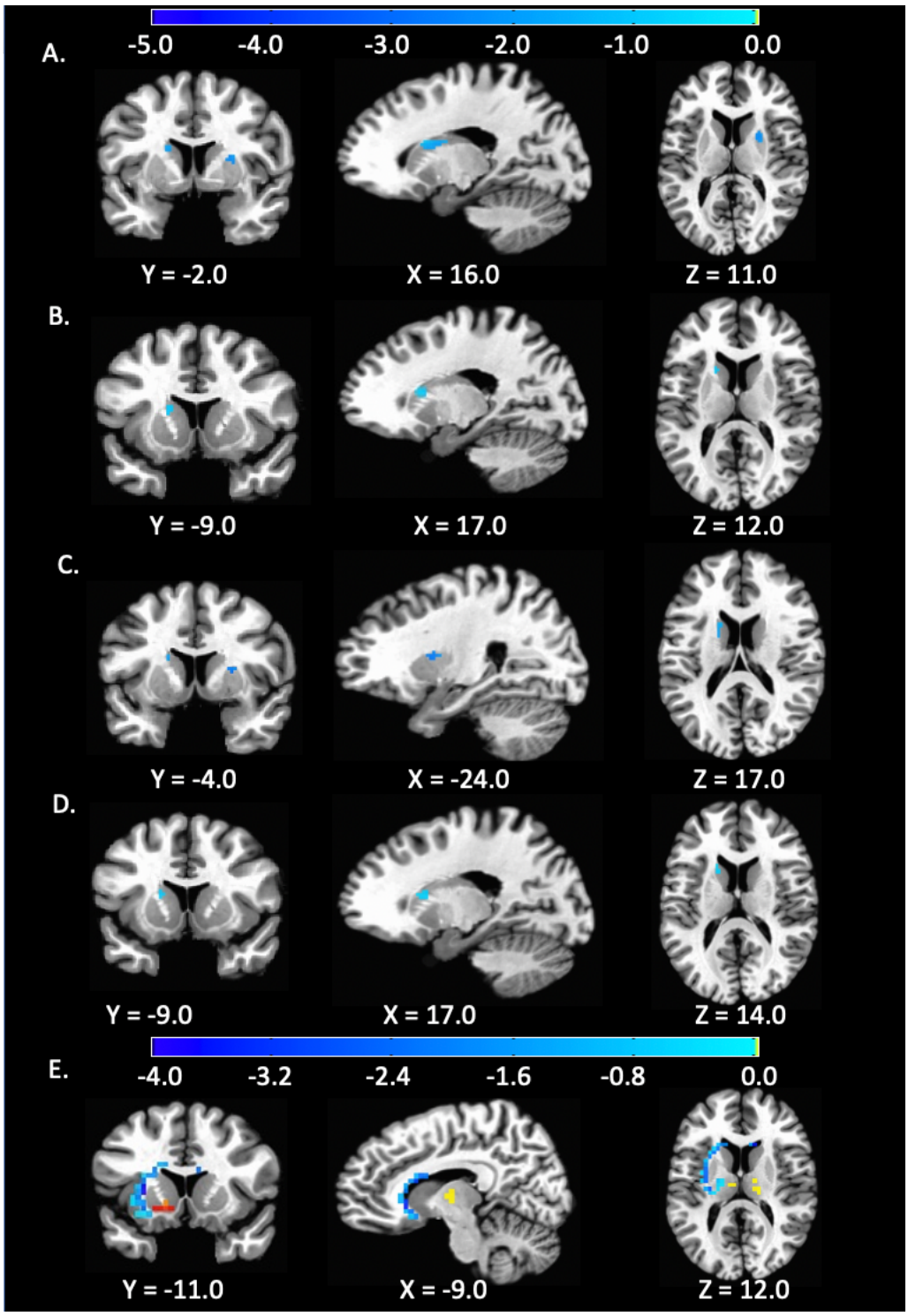
Valerie L. Darcey, Juen Guo, Amber Courville, Isabelle Gallagher, Jason A. Avery, W. Kyle Simmons, John E. Ingeholm, Peter Herscovitch, Alex Martin, Kevin D. Hall



Supplementary Figure 1. CONSORT diagram of participant randomization in crossover trial. Full neuroimaging data (PET and fMRI) across all 3 diet conditions are available for n=13 participants and the results are provided in Supplementary Materials. Complete PET data across 3 diet conditions are available in n=15 participants and complete fMRI data across 3 diet conditions are available from n=15 participants.



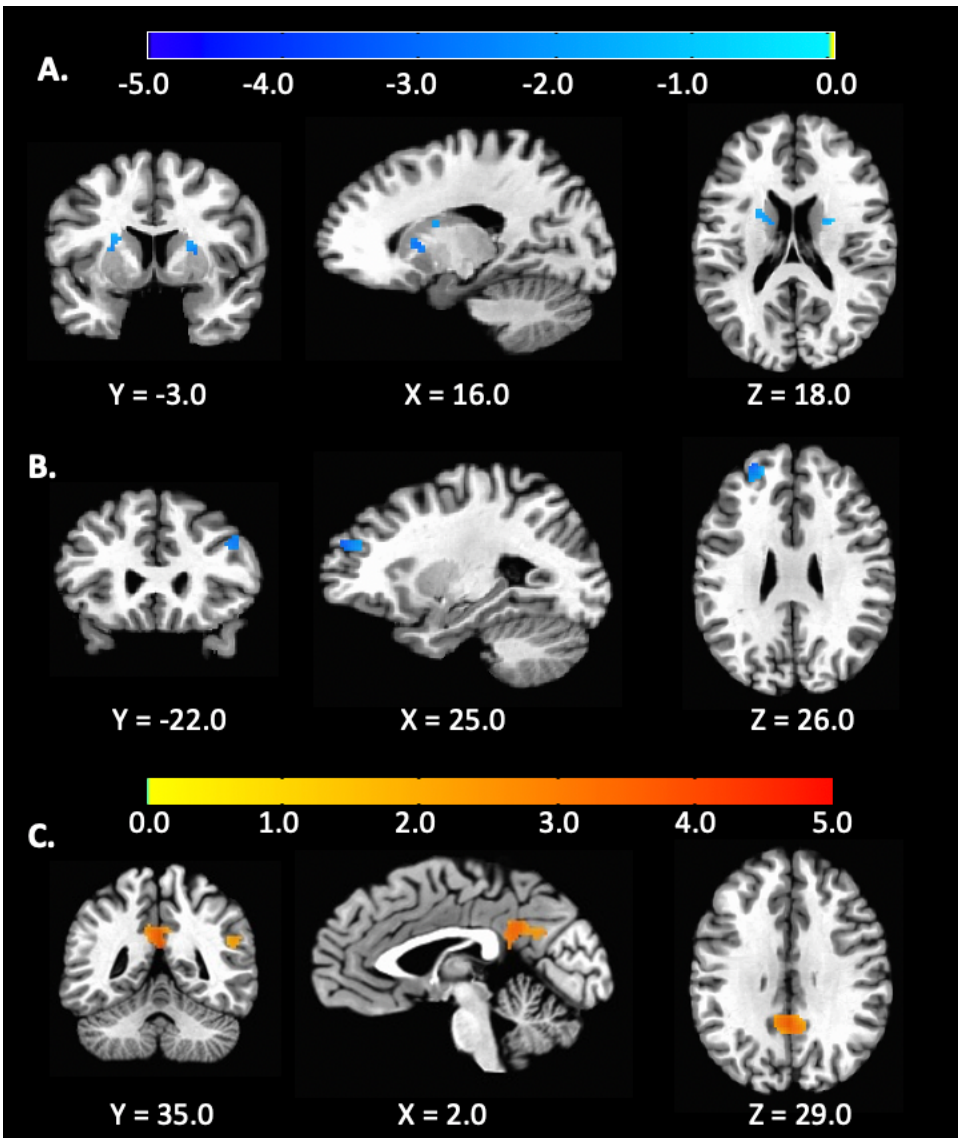
Supplementary Figure 2. Diet condition did not significantly impact in-scanner pleasantness ratings of visual food cues. Mean food pleasantness ratings on a scale of 1-7 during fMRI scanning for n=15 participants. Means: 4.39 ± 3.7 at Baseline, 4.35 ± 0.58 at RC, 4.30 ± 0.58 at RF; Repeated measures ANOVA Wilks' Lambda 0.29, *F* 0.498, *p*=0.619.



Supplementary Figure 3. Reduced-fat diet decreased both striatal activity in response to visual food cues and dopamine D2BP. fMRI ANOVA analyses including 15 participants with complete fMRI data, contrasting (A) RF versus Baseline diets and (B) RF versus RC diets. fMRI ANOVA analyses including 13 participants with both complete fMRI and PET data, contrasting (C) RF versus Baseline diets, and (D) RF versus RC diets. (E) Analysis of D2BP in 13 participants with complete fMRI and PET data, contrasting RF versus baseline diets via ANOVA. See Supplementary Table 1 for corresponding cluster details.

Supplementary Table 1. Locations of clusters displaying changes in BOLD responses within *a priori* reward region mask or D2BP to reduced fat or reduced carbohydrate diet within individuals completing all diets and all fMRI (n=15), all diets and all PET scans (n=15), and all diets, fMRI and PET (n=13).

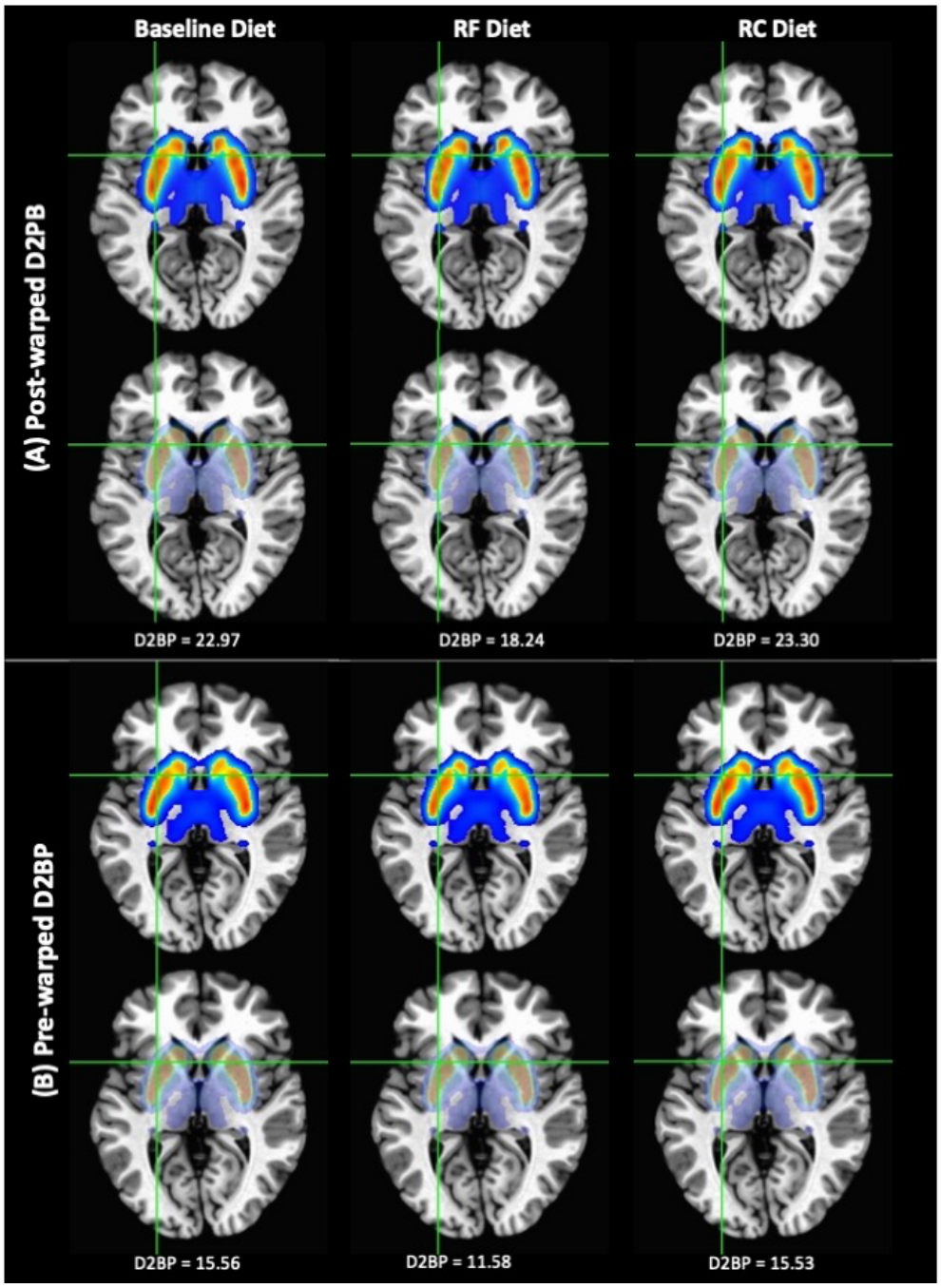
	Location of peak			***Voxels***	***Size (mm^3)***	***Z-score (fMRI) t-stat (PET)***	***alpha***
	x	***y***	***z***				
fMRI							
Reduced Fat vs. Reduced Carbohydrate v. Baseline							
(ANOVA, n=15 with complete fMRI; k_e*=5,* $p_{uncorrected}$ *= 0.001)*							
RF diet vs. Baseline							
Left caudate	15.0	1.0	18.0	38	304	-3.43	<0.01
Right putamen	-23.0	-5.0	10.0	21	168	-3.31	<0.02
Right mid. orbital gyrus	-25.0	-45.0	-10.0	6	48	-3.38	<0.09
Right ventromedial putamen	-23.0	-5.0	0.0	6	48	-3.51	<0.09
RF diet vs. RC diet							
Left caudate	17.0	-9.0	12.0	16	128	-3.33	<0.03
RC diet vs. Baseline							
No clusters	--	--	--	--	--	--	--
Reduced Fat vs. Reduced Carbohydrate v. Baseline							
(ANOVA, n=13 with complete PET & fMRI; k_e*=5,* $p_{uncorrected}$ *= 0.001*)							
RF diet vs. Baseline							
Right putamen	-23.0	-3.0	10.0	17	136	-3.30	<0.02
Left caudate	17.0	-7.0	16.0	18	144	-3.34	<0.02
RF diet vs. RC diet							
Left caudate	17.0	-9.0	14.0	11	88	-3.45	<0.04
RC diet vs. Baseline							
No clusters	--	--	--	--	--	--	--
PET D2BP							
Reduced Fat vs. Reduced Carbohydrate v. Baseline							
(ANOVA, n=15 with complete PET**;** k_e*=20,* $p_{uncorrected}$ *= 0.1*)							
RF diet vs. RC diet							
No clusters	--	--	--	--	--	--	--
RC diet vs. Baseline							
No clusters	--	--	--	--	--	--	--
Reduced Fat vs. Reduced Carbohydrate v. Baseline							
(ANOVA, n=13 with complete PET & fMRI **;** k_e*=20,* $p_{uncorrected}$ *= 0.1*)**)**							
RF diet vs. Baseline							
Left putamen	26.2	-9.5	6.5	172	7375	-2.33	<0.01
Right caudate	-12.2	-20.0	13.5	50	2144	-1.93	<0.01
Right thalamus	-1.8	18.5	3.0	34	1457	2.87	<0.05
Left putamen	19.2	-6.0	-4.0	26	1115	3.78	<0.14
RF diet vs. RC diet							
No clusters	--	--	--	--	--	--	--
RC diet vs. Baseline							
No clusters	--	--	--	--	--	--	--



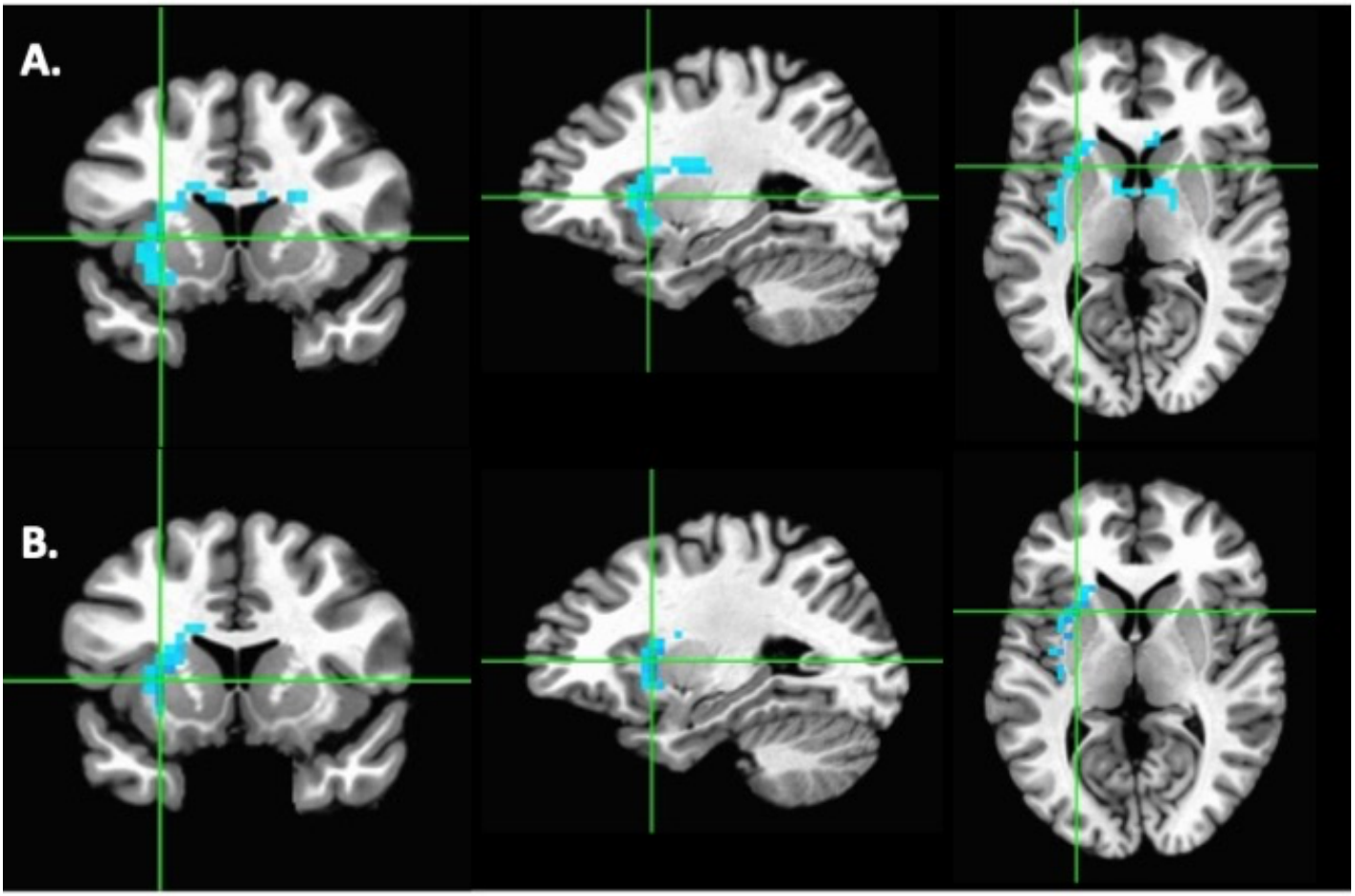
Supplementary Figure 4. Whole-brain fMRI analyses. Paired t-test fMRI analyses contrasting (A) RF versus Baseline (n=17), (B) RF versus RC (n=15), and (C) RC versus Baseline (n=17).

Supplementary Table 2. Locations of clusters displaying changes in whole-brain BOLD responses to reduced fat or reduced carbohydrate diets.

	Location of peak			*Voxels*	*Size (mm^3)*	*Z-score*	*alpha*
	x	***y***	***z***				
Reduced Fat v. Reduced Carbohydrate v. Baseline							
RF diet vs. Baseline (*paired t-test, n=17; k_e=40, $p_{uncorrected}$ = 0.001)*							
Left putamen	19.0	-9.0	6.0	77	616	-3.48	<0.06
Right putamen	-23.0	3.0	10.0	50	400	-3.41	>0.10
RC diet vs. Baseline (*paired t-test, n=17; k_e=40, $p_{uncorrected}$ = 0.001)*							
Right posterior cingulate/precuneus	-1.0	45.0	20.0	234	1872	3.33	<0.01
Right middle temporal gyrus	-49.0	-1.0	-22.0	80	640	3.80	<0.07
Left middle temporal gyrus	61.0	31.0	0.0	64	512	3.58	<0.10
Right supramarginal gyrus	-49.0	45.0	26.0	58	464	3.45	>0.10
Right angular gyrus	-39.0	57.0	26.0	54	432	3.79	>0.10
Right medial temporal pole	-37.0	-3.0	-24.0	46	368	3.56	>0.10
RF diet vs. RC diet (*paired t-test, n=15; k_e=40, $p_{uncorrected}$ = 0.001)*							
Left superior frontal gyrus	25.0	-51.0	26.0	72	576	-3.49	<0.07
Right inferior frontal gyrus	-45.0	-15.0	32.0	42	336	-3.34	>0.10



Supplementary Figure 5. Mean D2BP maps by diet condition in each column. (A) Data processed according to the pipeline reported in the main text where D2BP was computed after linear warping individual subject data to Talairach coordinates. Top row indicates the mean D2BP>1.5 overlaid on the template brain and the bottom row depicts the results with increased transparency of the D2BP map to visualize anatomical overlap. Peak D2BP was located within striatal nuclei, but regions with nonzero D2BP were found outside these regions, including in white matter. Crosshairs indicate coordinates within the cluster defining maximum significant differences between RF and Baseline diets indicating that this occurred at regions close to gray/white border (26.2, -9.5, 6.5). D2BP at this location for each diet condition is indicated below each column. (B) Data processed according to a pipeline where D2BP was first computed in native space and then nonlinear warped to Talairach coordinates and produces similar results for the location of the cluster defining maximum significant differences between RF and Baseline diets (26.2, -9.5, 3).



Supplementary Figure 6. D2BP contrast between RF and Baseline diets (n=15) using D2BP calculated using (A) a processing pipeline where D2BP was computed after linear warping individual subject data to Talairach coordinates (peak: 26.2, -9.5, 6.5) and (B) a pipeline where D2BP was computed in native space and then nonlinear warped to Talairach coordinates (peak: 26.2, -9.5, 3), producing a similar cluster.