SUPPLEMENTARY DATA

Supplementary Table 1. Metabolic and hormonal parameters during fMRI session.

Group	Lean			Obese			T2DM		
Treatment	Placebo	Exe	Ex9-39	Placebo	Exe	Ex9-39	Placebo	Exe	Ex9-39
Glucose* (mmol/l)	4.9 ± 0.06	4.8 ± 0.07	4.9 ± 0.06	4.9 ± 0.05	4.9 ± 0.03	4.9 ± 0.04	5.2 ± 0.17	5.1 ± 0.16	5.0 ± 0.06
GIR* (mg/kg/min)	8.0 ± 0.7	8.1 ± 0.8	8.3 ± 0.8	4.7 ± 0.5‡	5.4 ± 0.5	5.0 ± 0.4	1.4 ± 0.2‡	1.3 ± 0.2	1.6 ± 0.2
Insulin* (pmol/l)	314 ± 12	335 ± 15	313 ± 13	390 ± 15‡	396 ± 12	383 ± 13	377 ± 12‡	374 ± 14	374 ± 14
Glucagon* (pmol/l)	11.3 ± 0.7	10.2 ± 0.8	11.4 ± 1.0	8.9 ± 0.5‡	8.6 ± 0.6	8.5 ± 0.4	10.8 ± 0.6	10.5 ± 0.7	11.9 ± 0.7
NEFA† (mmol/l)	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.05 ± 0.01	0.05 ± 0.01	0.06 ± 0.02	0.15 ± 0.03§	0.16 ± 0.03	0.13 ± 0.03
Growth hormone† (mU/l)	1.7 ± 0.1	1.9 ± 0.2	1.6 ± 0.2	1.8 ± 0.1	1.7 ± 0.1	1.8 ± 0.1	1.7 ± 0.1	1.9 ± 0.1	1.7 ± 0.2
Cortisol† (nmol/l)	293 ± 39	373 ± 60	259 ± 30	266 ± 29	315 ± 25	284 ± 34	256 ± 27	321 ± 26	239 ± 20

Data are presented as means ± SEM.
*Mean of time point t=90 until t=180 min (during fMRI and lunch buffet) [E]
†Mean of time point t=120 min (during fMRI)
‡Statistically significant different from lean (post-hoc Bonferroni corrected $p<0.05$)
§Statistically significant different from lean and obese (post-hoc Bonferroni corrected $P<0.05$)
GIR, glucose infusion rate; Exe, exenatide; Ex9-39, exendin 9-39

SUPPLEMENTARY DATA

Supplementary Table 2. Main effect of tasks over all groups.

Contrast	Region	Side	Cluster	Z	p_{FWE}	MNI (x, y, z)
Food > non-food						
	Occipital, parietal, temporal cortex	L	1160	>8	<0.001	-45, -70, -8
				>8	<0.001	-35, -52, -17
				7.55	<0.001	-27, -85, 10
	Occipital, parietal, temporal cortex	R	828	>8	<0.001	48, -73, -5
				>8	<0.001	42, -70, -11
				>8	<0.001	39, -82, 4
	Precentral gyrus	L	90	6.67	<0.001	-57, -25, 31
	Superior parietal cortex	R	50	6.27	<0.001	30, -55, 55
	Inferior frontal operculum	L	83	5.75	<0.001	-48, 8, 22
	Supplementary motor area	L	35	5.56	<0.001	-6, 11, 52
	Precuneus (BA 7)	L	59	5.40	0.001	-3, -52, 19
	Superior parietal cortex (BA 40)	L	22	5.06	0.004	-33, -55, 55
	Amygdala	L	2	4.70	0.018	-21, -4, -17
	Postcentral (BA 3)	R	4	4.67	0.021	63, -19, 31
	Amygdala	R	3	4.60	0.028	21, -1, -14
HC > non-food						
	Occipital, parietal, temporal cortex	L	882	>8	<0.001	-45, -70, -8
				>8	<0.001	-35, -52, -17
				5.57	<0.001	-9, -76, 7
	Occipital, parietal, temporal cortex	R	801	>8	<0.001	48, -73, -5
				>8	<0.001	42, -70, -11
				>8	<0.001	51, -51, 8
	Postcentral gyrus	L	106	6.56	<0.001	-57, -25, 31
	Middle occipital lobe	L	119	6.05	<0.001	-24, -67, 31
	Inferior frontal operculum	L	71	5.69	<0.001	-48, 8, 22
	Superior parietal lobe	R	39	5.51	<0.001	30, -55, 55
	Posterior cingulate cortex	L	52	5.48	<0.001	-3, -52, 22
	Amygdala	L	6	5.44	0.001	-24, -1, -17
	Postcentral (BA3) gyrus	R	18	5.27	0.001	60, -19, 31
	Superior parietal lobe	L	18	5.17	0.002	-33, -52, 55
	Supplementary motor area	L	12	4.89	0.008	-6, 11, 52
	Amygdala	R	5	4.83	0.010	21, -1, -17
	Precuneus (BA 19)	R	3	4.66	0.021	27, -79, 34
	Hippocampus (BA 27)	L	2	4.62	0.026	-21, -34, -5
	Orbitofrontal cortex	L	1	4.55	0.034	-30, 35, -14
	Orbitofrontal cortex	**L**	1	4.45	0.050	-36, 26, -17

BA, Brodmann Area; Z, Z-score; p_{FWE}, p-value Family-Wise Error corrected for multiple comparisons across whole brain; R, right; L, left; MNI, Montreal Neurological Institute coordinates in mm

SUPPLEMENTARY DATA

Supplementary Table 3. Between-group differences in CNS responses to food pictures.

Interaction	**Contrast**	**Region**	**Side**	**Cluster**	**T**	**p_{-FWE}**	**MNI coordinates (x, y, z)**
Obese > lean							
	Food > non-food	Insula	L	222	3.55	0.009	-33, 17, -17
		Insula (BA 38)	R	134	3.50	0.011	45, 8, -11
		Insula	R	17	3.15	0.028	36, -22, 10
		Amygdala	R	7	2.82	0.019	18, -4, -17
	HC > non-food	Insula	L	136	3.18	0.025	-33, 17, -17
					2.99	0.042	-45, -7, -5
		Insula (BA 38)	R	63	3.33	0.018	45, 5, -11
T2DM > lean							
	Food > non-food	Insula	L	26	2.75	0.020	-45, 5, -11
	HC > non-food	NA					
Obese > T2DM							
	Food > non-food	Insula	R	9	3.27	0.021	30, 14, -17
	HC > non-food	Insula	R	17	3.46	0.012	30, 11, -17
T2DM > obese							
	Food > non-food	NA					
	HC > non-food	NA					

BA, Brodmann Area; T, t-statistic; p_{-FWE}, p-value Family-Wise Error corrected for multiple comparisons on the basis of cluster extent; R, right; L, left; MNI, Montreal Neurological Institute coordinates in mm; NA, not applicable

SUPPLEMENTARY DATA

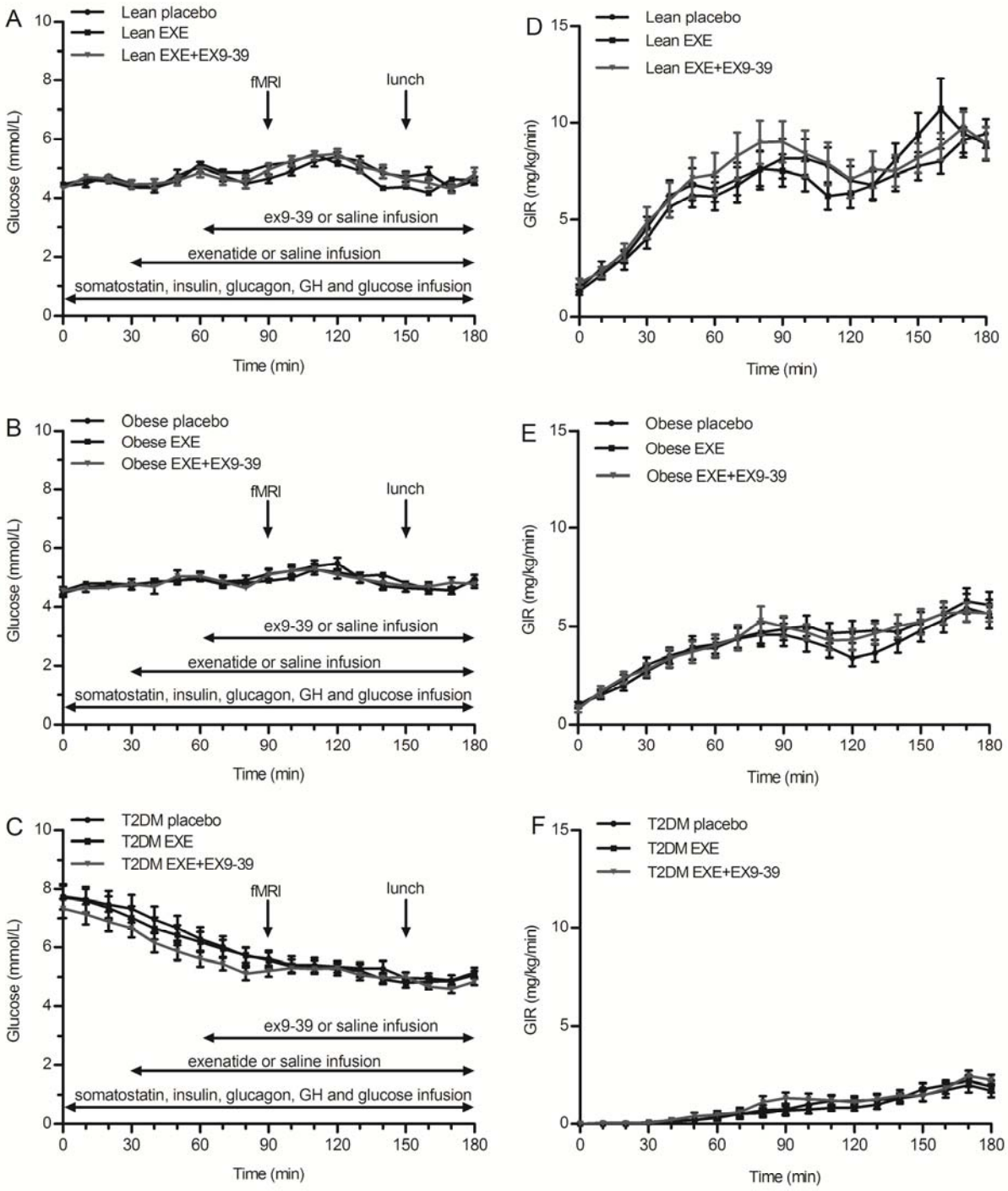
Supplementary Table 4. Brain regions with a positive correlation between exenatide-induced reductions in caloric intake and exenatide-induced reductions in CNS responses to food pictures (food > non-food)

	Correlation	**Region**	**Side**	**Cluster**	**T**	**p_{-FWE}**	**MNI (x, y, z)**
Lean							
Placebo > EXE (food > non-food)	Positive correlation with change in caloric intake	NA					
Obese							
Placebo > EXE (food > non-food)	Positive correlation with change in caloric intake	OFC	L	60	5.31	0.006	-48,29,-8
		Insula	R	184	4.15	0.026	42,-13,-8
		OFC	R	184	3.83	0.040	51,17,-11
		Caudate	R	10	3.71	0.046	21,20,10
		Insula	L	76	3.92	0.035	-45,-13,-8
T2DM							
Placebo > EXE (food > non-food)	Positive correlation with change in caloric intake	Caudate nucleus	R	8	3.74	0.046	21,14,16
		Insula	L	54	3.86	0.039	-42,2,13
		Insula	R	12	4.80	0.011	33,-10,19

BA, Brodmann Area; T, t-statistic; p_{-FWE}, p-value Family-Wise Error corrected for multiple comparisons on the basis of cluster extent; R, right; L, left; MNI, Montreal Neurological Institute coordinates in mm; NA, not applicable

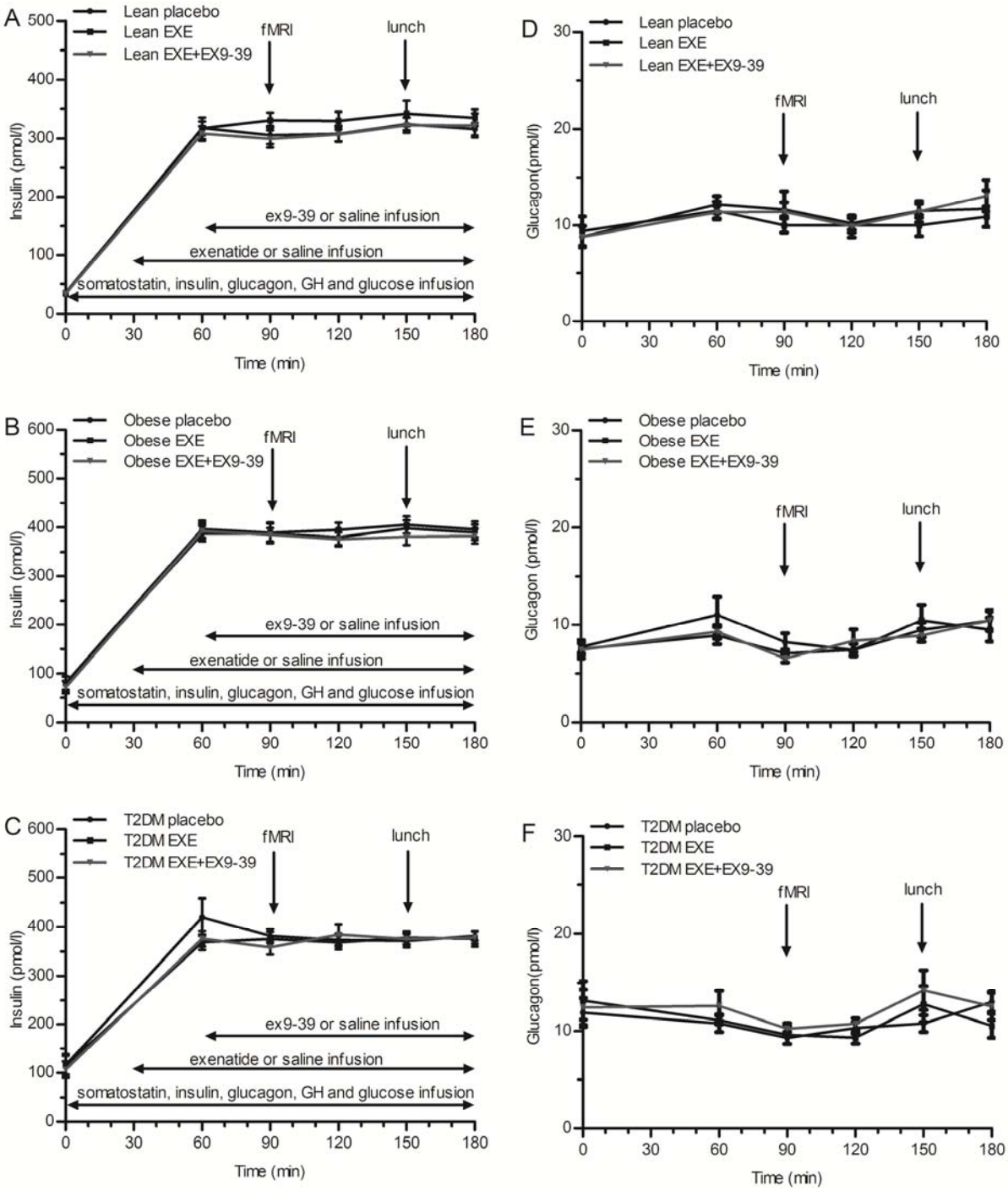
SUPPLEMENTARY DATA

Supplementary Figure 1. Glucose levels and glucose infusion rates during the pancreatic clamp. Mean glucose levels (mmol/l) in lean (A), obese (B) and T2DM (C) subjects. Mean glucose infusion rate(GIR; mg/kg/min) in lean (D), obese (E) and T2DM (F) subjects. EXE, exenatide; EX9-39, exendin 9-39 Data are means ± SEM.



SUPPLEMENTARY DATA

Supplementary Figure 2. Insulin and glucagon levels during the pancreatic clamp.
Mean insulin levels (pmol/l) in lean (A), obese (B) and T2DM (C) subjects.
Mean glucagon levels (pmol/l) in lean (D), obese (E) and T2DM (F) subjects.
EXE, exenatide; EX9-39, exendin 9-39 Data are means ± SEM



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