Supplementary Information

Materials and Methods

Peripheral hormone measurement

Blood samples were collected into EDTA-coated tubes and protease inhibitors were immediately added (10 mM DDP-IV and 1.3% Aprotinin, both dissolved with 0.9% NaCl). The protease inhibitors were prepared according to the kit manufacturer's recommendation (Bio-Plex). After mixing inhibitors and blood, samples were centrifuged at 1400 × g per 10 min at 4°C, and the supernatants were stored at -80°C before analysis.

Plasma concentrations of total ghrelin, GLP-1, glucagon, leptin and insulin were measured using a Bio-Plex 200TM suspension array system (BIO-RAD, Inc, Hercules, California, USA). The principle of the Bio-Plex Pro bead-based assays is similar to capture sandwich immunoassays. The capture antibody-coupled beads were first incubated with the sample followed by incubation with biotinylated detection antibodies. After washing away the unbound biotinylated antibodies, the beads were incubated with a reporter streptavidin-phycoerythrin conjugate. The beads were then passed through the Bio-Plex array reader, which measures the fluorescence of the bound streptavidin-phycoerythrin on each bead. Measurements were provided as the median fluorescence intensity for a given bead population. Bead populations were identified by fluorescence to determine the analyte being measured. All assay incubations were performed at room temperature as described in the instruction manual (Bio-Rad part number 10024929). All washes were performed using a Bio-

Plex Pro Wash Station with cycles of 200 µL of wash buffer per well. Data acquisition was done using the Bio-Plex Manager 6.1 software. The inter-assay variation (% coefficient of variation (CV)) was 4%, and the intra-assay variation (%CV) was 5%.

Supplementary Tables

Supplementary Table 1. Genotype analysis of SNPs of FTO and MC4-R.

Genotype		***FTO***				***MC4-R***	
		rs8050136: AA/AC/CC	*rs17817449:* GG/GT/TT	*rs1421085:* CC/CT/TT	*rs1121980:* TT/TC/CC	*rs17782313:* CC/CT/TT	*rs12970134:* AA/AG/GG
FTO-rs9939609	AT:16	0/11/5	0/12/4	0/11/5	0/15/1	0/6/10	0/6/10
	TT:26	0/0/26	0/0/26	0/0/26	0/0/26	0/5/21	1/6/19

Supplementary Table 2. Group comparison of BMI within FTO and MC4-R variants.

Genotype		PreLSG	PostLSG-1	PostLSG-6	PostLSG-12	PostLSG-24	PostLSG-36	PostLSG-48	PostLSG-60
FTO-rs9939609	**AT: 16**	39.25±1.07	34.98±1.07	30.06±1.24	29.11±1.25	29.30±1.24	30.27±1.19	31.23±1.19	32.53±1.17
	TT: 26	38.76±0.83	34.09±0.80	28.43±0.61	26.35±0.46	26.81±0.46	27.28±0.59	28.11±0.68	28.26±0.69
	AT vs TT (t/P)	0.36/0.717	0.67/0.504	1.31/0.197	**2.43/0.020**	**2.18/0.035**	**2.49/0.017**	**2.44/0.019**	**3.33/0.002**
FTO-rs8050136	**AC: 11**	39.87±1.47	35.41±1.53	30.80±1.73	30.02±1.68	30.13±1.72	31.03±1.64	31.91±1.64	33.09±1.60
	CC: 31	38.62±0.71	34.08±0.67	28.43±0.53	26.47±0.42	26.92±0.41	27.49±0.52	28.38±0.60	28.75±0.64
	AC vs CC (t/P)	0.84/0.402	0.91/0.365	1.75/0.087	**2.91/0.006**	**2.60/0.013**	**2.70/0.010**	**2.51/0.016**	**3.01/0.005**
FTO-rs17817449	**GT: 12**	39.51±1.39	35.21±1.41	30.49±1.61	29.53±1.61	29.84±1.60	30.69±1.54	31.63±1.52	32.71±1.51
	TT: 30	38.72±0.73	34.11±0.69	28.47±0.54	26.55±0.43	26.93±0.43	27.51±0.54	28.37±0.62	28.76±0.66
	GT vs TT (t/P)	0.53/0.594	0.77/0.445	1.51/0.138	**2.45/0.019**	**2.40/0.021**	**2.45/0.018**	**2.36/0.023**	**2.78/0.008**
FTO-rs1421085	**CT: 11**	39.87±1.47	35.41±1.53	30.80±1.73	30.02±1.68	30.13±1.72	31.03±1.64	31.91±1.64	33.09±1.60
	TT: 31	38.62±0.71	34.08±0.67	28.43±0.53	26.47±0.42	26.92±0.41	27.49±0.52	28.38±0.60	28.75±0.64
	CT vs TT (t/P)	0.84/0.402	0.91/0.365	1.75/0.087	**2.91/0.006**	**2.60/0.013**	**2.70/0.010**	**2.51/0.016**	**3.01/0.005**
FTO-rs1121980	**TC: 15**	39.28±1.14	34.99±1.14	30.24±1.30	29.43±1.28	29.56±1.30	30.54±1.24	31.44±1.25	32.77±1.23
	CC: 27	38.76±0.80	34.11±0.76	28.38±0.59	26.28±0.44	26.76±0.45	27.24±0.57	28.11±0.66	28.29±0.66
	TC vs CC (t/P)	0.37/0.707	0.65/0.515	1.48/0.146	**2.80/0.008**	**2.46/0.018**	**2.75/0.009**	**2.59/0.013**	**3.49/0.001**
MC4-R-rs17782313	**CT: 11**	40.20±1.38	35.74±1.30	30.29±1.70	28.96±1.59	29.49±1.40	30.02±1.48	30.97±1.52	31.44±1.69
	TT: 31	38.50±0.72	33.96±0.72	28.61±0.56	26.85±0.53	27.15±0.58	27.85±0.63	28.71±0.69	29.34±0.71
	CT vs TT (t/P)	1.15/0.257	1.24/0.222	1.22/0.229	1.63/0.111	1.83/0.074	1.56/0.125	1.54/0.131	1.34/0.187
MC4-R-rs12970134	**AA/AG: 13**	39.58±1.13	35.33±1.11	30.05±1.42	28.57±1.33	28.94±1.17	29.63±1.24	30.17±1.29	30.73±1.44
	GG: 29	38.66±0.80	34.02±0.77	28.60±0.61	26.88±0.58	27.23±0.64	27.88±0.69	28.91±0.75	29.51±0.77
	AA/AG vs TT (t/P)	0.64/0.520	0.94/0.350	1.10/0.276	1.35/0.182	1.37/0.176	1.32/0.194	0.88/0.381	0.80/0.425

Supplementary Table 3. Time effects and post-hoc tests for behavioral measurements.

	Time effects		Post-hoc tests	PreLSG vs PostLSG-1		PostLSG-1 vs PostLSG-6		PostLSG-6 vs PostLSG-12		PreLSG vs PostLSG-12	
	F	*P*		t	*P*	t	*P*	t	*P*	t	*P*
Weight (kg)	370.81	< 0.001	AT	12.62	<0.001	11.38	<0.001	2.34	0.033	15.65	<0.001
			TT	17.117	<0.001	12.463	<0.001	6.367	<0.001	17.80	<0.001
WC (cm)	202.08	< 0.001	AT	3.53	0.003	7.86	<0.001	3.02	0.009	14.12	<0.001
			TT	6.298	<0.001	10.684	<0.001	8.234	<0.001	13.57	<0.001
BMI	399.38	< 0.001	AT	13.88	<0.001	9.93	<0.001	3.32	0.005	9.82	<0.001
			TT	19.9	<0.001	12.28	<0.001	6.62	<0.001	13.04	<0.001
HAMA	18.05	< 0.001	AT	1.992	0.065	2.22	0.042	-1.46	0.165	1.42	0.177
			TT	3.28	0.003	2.78	0.010	0.66	0.515	2.81	0.009
HAMD	8.3	< 0.001	AT	-0.57	0.575	2.17	0.046	-0.25	0.809	1.78	0.095
			TT	0.63	0.534	2.73	0.011	2.11	0.045	3.94	0.001
HiCal Craving	12.63	< 0.001	AT	3.09	0.007	0.82	0.425	-1.15	0.269	-0.46	0.65
			TT	2.96	0.007	1.24	0.225	-2.57	0.016	-0.07	0.94
LoCal Craving	1.54	0.208	AT	0.78	0.449	0.47	0.642	-1.55	0.142	-1.07	0.3
			TT	1.46	0.158	0.31	0.755	-0.4	0.693	0.02	0.983
YFAS	25.19	< 0.001	AT	3.36	0.004	1.47	0.162	-0.14	0.889	1.62	0.127
			TT	3.53	0.002	2.89	0.008	-1.51	0.142	1.68	0.105
Glucose	26.23	< 0.001	AT	3.57	0.003	2.50	0.024	2.76	0.015	3.47	0.003
			TT	4.22	<0.001	3.46	0.002	4.33	<0.001	5.48	<0.001
Glucagon	1.41	0.244	AT	1.64	0.122	-0.29	0.775	1.21	0.246	1.38	0.186
			TT	1.07	0.293	-1.09	0.285	0.25	0.806	0.57	0.571
Insulin	14.81	< 0.001	AT	1.31	0.208	1.31	0.208	-1.16	0.263	3.22	0.006
			TT	3.95	<0.001	-0.71	0.480	2.21	0.037	4.49	<0.001
Leptin	61.95	< 0.001	AT	3.89	0.001	2.27	0.038	0.25	0.806	4.67	<0.001
			TT	9.58	<0.001	3.48	0.002	1.41	0.172	8.80	<0.001
GLP-1	2.05	0.110	AT	-0.98	0.339	0.81	0.426	-1.34	0.20	-1.25	0.23
			TT	-2.13	0.043	-1.18	0.248	0.95	0.350	-1.88	0.071
Ghrelin	43.02	< 0.001	AT	4.21	<0.001	1.93	0.073	-4.92	<0.001	4.36	<0.001
			TT	6.56	<0.001	0.37	0.714	0.66	0.512	5.77	<0.001

Supplementary Table 4. Group effects and post-hoc tests for behavioral measurements.

	Group effects		**PreLSG: AT vs. TT**		**PostLSG-1: AT vs. TT**		**PostLSG-6: AT vs. TT**		**PostLSG-12: AT vs. TT**	
	F	P	t	*P*	t	*P*	t	*P*	t	*P*
Weight (kg)	0.76	0.389	0.59	0.559	0.89	0.380	1.30	0.200	2.14	0.039
WC (cm)	0.49	0.486	0.53	0.603	0.54	0.594	0.49	0.627	1.13	0.267
BMI	1.46	0.235	0.37	0.717	0.67	0.504	1.31	0.197	2.38	0.022
HAMA	0.18	0.676	-1.16	0.251	-0.05	0.956	-0.34	0.739	0.66	0.514
HAMD	0.23	0.635	-0.59	0.559	0.26	0.796	0.64	0.527	1.456	0.154
HiCal Craving	0.44	0.512	0.21	0.831	0.26	0.799	0.84	0.406	0.576	0.5694
LoCal Craving	<0.01	0.992	-0.77	0.445	-0.02	0.984	-0.18	0.857	0.92	0.364
YFAS	2.66	0.111	0.42	0.68	1.57	0.123	1.44	0.158	1.15	0.258
Glucose	0.72	0.401	-1.33	0.191	-0.82	0.414	-0.18	0.852	0.24	0.805
Glucagon	0.31	0.581	0.74	0.459	0.66	0.511	0.39	0.696	-0.59	0.559
Insulin	0.32	0.578	-1.06	0.293	0.89	0.377	-1.39	0.172	0.41	0.677
Leptin	0.01	0.929	-0.66	0.508	0.01	0.996	0.41	0.678	1.37	0.178
GLP-1	0.08	0.773	1.31	0.195	0.37	0.713	-0.89	0.374	0.79	0.435
Ghrelin	0.31	0.579	0.15	0.879	-0.54	0.592	-1.66	0.105	-0.06	0.954

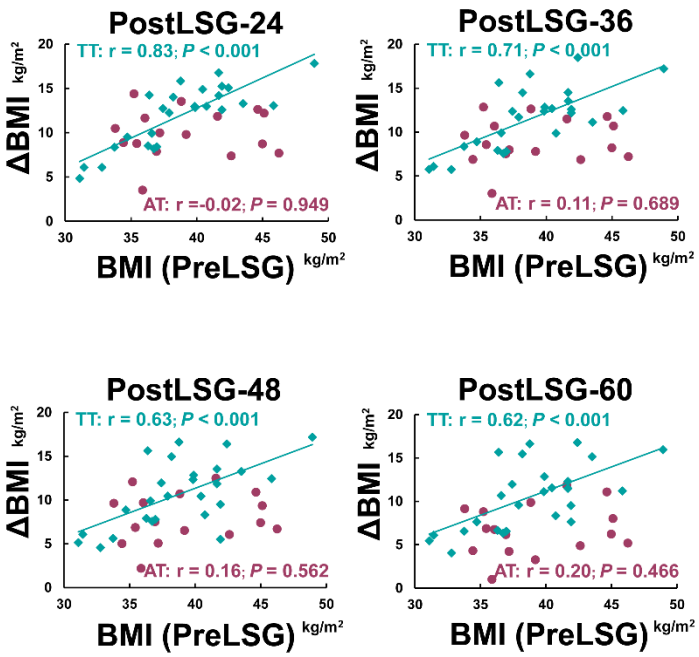
Supplementary Table 5. Group effects of ANOVA for resting state functional connectivity and PPI connectivity in responses to food cues.

Functional Connectivity	HEM	Cluster Size	MNI			Peak T-value
			X	Y	Z	
Resting State: Group effects						
PCC-DLPFC	L	136	-21	48	33	-5.97
PCC-ANG	L	191	-45	-66	48	-10.61
Food Cue Task: Group effects						
DLPFC- Hippocampus	L	91	-27	-30	-9	4.42
DMPFC- Caudate	L	85	-18	9	12	3.95

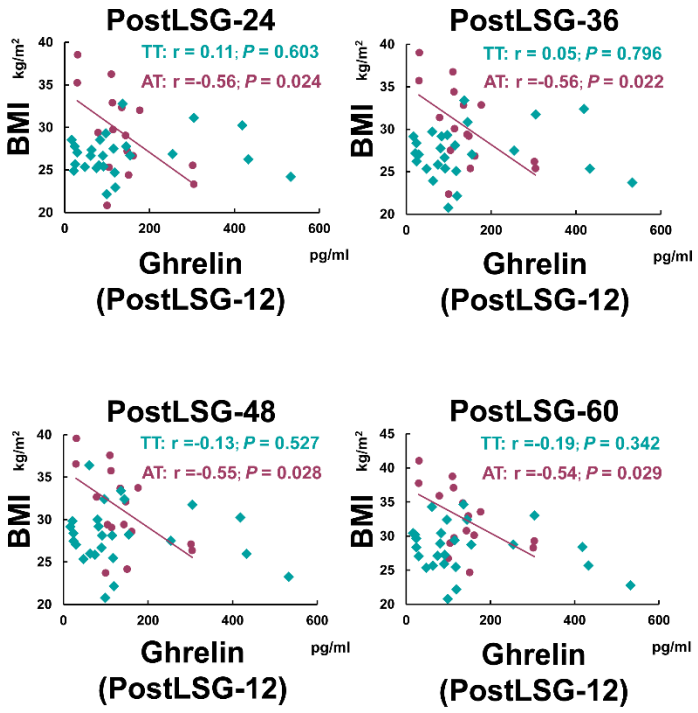
Abbreviation: PCC, posterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; ANG, angular gyrus; DMPFC, dorsomedial prefrontal cortex.

Supplementary Figure

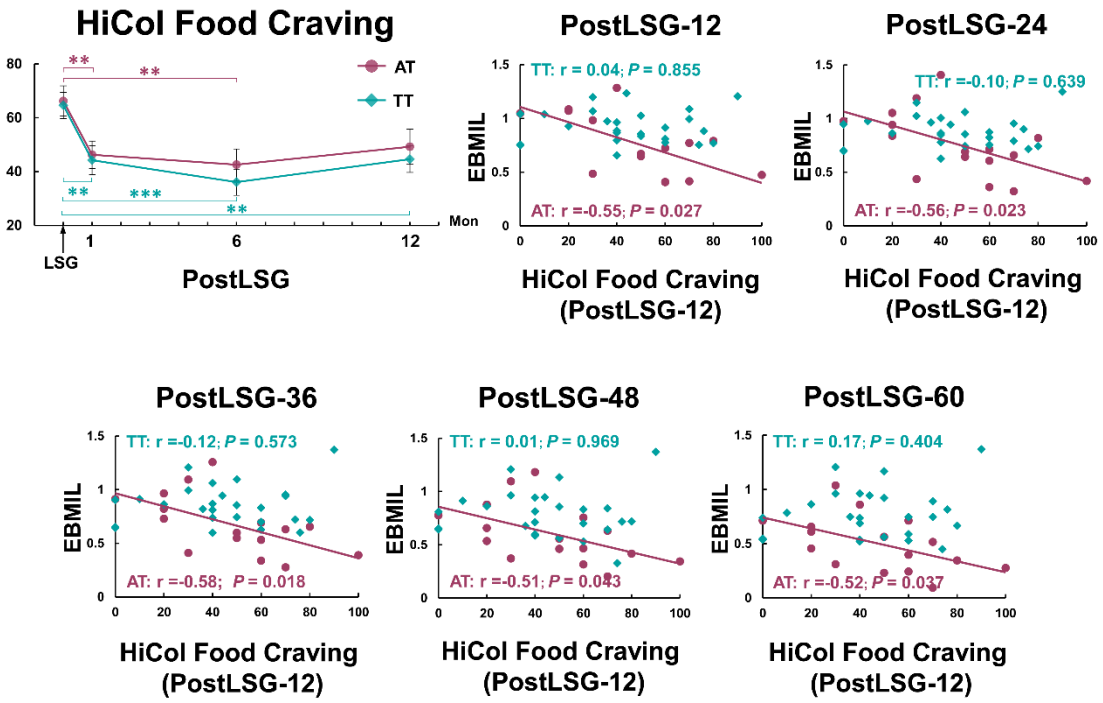
Supplementary Figure 1. The correlation between basal BMI and BMI reductions at, 24-, 36-, 48- and 60- months after LSG in the TT group.



Supplementary Figure 2. The correlation between the rebounding ghrelin at PostLSG-12 and BMI at, 24-, 36-, 48- and 60- months after LSG in the AT group.



Supplementary Figure 3. Time effects of ANOVA for HiCal food craving. In the AT group, HiCal food craving at PostLSG-12 was negatively correlated with the EBMIL at 12-, 24-, 36-, 48- and 60- months after LSG.



Supplementary Figure 4. Group effects of ANOVA for resting state functional connectivity and PPI connectivity in responses to food cues.