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Effect of Adolescent Bariatric Surgery on the Brain and Cognition: A Pilot Study

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Abstract

Objective—Neurocognitive deficits in pediatric obesity relate to poor developmental outcomes. We sought preliminary evidence for changes in brain and cognitive functioning relevant to obesogenic behavior following vertical sleeve gastrectomy (VSG) in adolescents relative to wait-listed (WL) and healthy (HC) controls.

Methods—Thirty-six adolescents underwent fMRI twice 4 months apart, during executive, reward, and episodic memory encoding, in addition to behavioral testing for reward-related decision making.

Results—VSG adolescents lost weight, while WL gained weight and HC did not change between timepoints. Gains in executive and reward-related performance were larger in VSG than control groups. Group x Time interaction ($p < 0.05$ corrected) in left prefrontal cortex during N-back showed greater pre-surgical activation and post-surgical reduction comparable to HC levels, but increased in WL between timepoints. Similarly, left striatal parametric response to reward value reduced after surgery to HC levels; WL did not change. Memory-related medial temporal activation did not change in any group.

Conclusion—Results provide pilot evidence for functional brain changes induced by VSG in adolescents with severe obesity. Weight loss and gain was paralleled by reduced and increased prefrontal activation, respectively, suggesting neural plasticity related to metabolic change.

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Keywords

Neuroimaging; executive functioning; reward; memory

Introduction

Severe obesity, defined as body-mass index (BMI) 120% above the 95th percentile cut-off for obesity, is prevalent in 8% of adolescents[1] and confers elevated risk for serious medical comorbidities during adolescence[2] and later in adulthood[3]. Additional risks for adverse developmental outcomes are posed by poor neurocognitive functioning[4], particularly self-regulatory processes important not only for psychosocial health[5] and academic performance[6] but also for controlling obesogenic behaviors (e.g., food and activity choices) that promote and maintain obesity[7,8]. Bariatric surgery is one treatment option[9], with evidence of success for weight loss and improved metabolic health[10,11]. Whether it improves neurocognitive functioning in adolescents, however, is not known. Adolescence is a critical period for maturation of risk/reward-related regulatory function[12] and severe obesity during this period puts youth at far greater risk for poor developmental outcomes. If bariatric surgery improves neurocognitive functioning, it has the potential to reverse the course of maladaptive development in youth with severe obesity.

Studies with adults support neurocognitive changes within a year following weight loss intervention including bariatric surgery[13]. Cognitive processing pertinent to obesity includes executive function, the ability to constrain behavior towards goals mediated by prefrontal-parietal cortices, reward-related function mediated by striatum, and episodic memory mediated by medial temporal lobes (MTL). Together, these processes enable self-control and learning which guides decision-making about food and activity[7]. Meta-analyses of adult studies support improved cognitive function following weight-loss intervention[14] and bariatric surgery[13] for executive and memory functioning. Furthermore, adults reported less food motivation[15,16] and showed activation reductions in reward regions and increases in executive regions in response to food more than non-food images following bariatric surgery[16]. Other evidence suggests that structural[17] and functional[18,19] network properties of the brain resembled healthy adults after surgery. These neurocognitive improvements may hold the key to sustained healthy behaviors for controlling weight gain.

We conducted a pilot study to evaluate the effect of bariatric surgery on executive, reward, and episodic memory functioning and underlying neural substrates in prefrontal-parietal, striatal, and MTL regions, respectively, using functional magnetic resonance imaging (fMRI) in adolescents with severe obesity compared with two age-matched control groups, adolescents with severe obesity wait-listed for surgery (WL) and those with healthy weight (HC). HC group allows estimation of improvement due to effects of repeated testing and familiarity with MRI.

Methods

Participants

Thirty-six participants aged 14–21 years were either healthy weight (HC; n = 12; body-mass index, kg/m2—BMI: M = 21.6, SD = 2.6), were scheduled for vertical sleeve gastrectomy (VSG) as part of clinical standard of care at enrollment (n = 10; BMI: M = 47.2, SD = 7.0), or awaiting VSG due to insurance delays or personal choice (WL; n = 14; BMI: M = 45.3, SD = 8.2) at Children's National Health System (CNHS); HC were recruited from the Washington DC area. Informed consent and assent was acquired according to guidelines of the Institutional Review Boards of Georgetown University and CNHS. Groups did not differ on age, IQ, gender, ethnicity, racial composition, and socio-economic status (measured with family income and maternal education). As expected, BMI was lower in HC than the two groups with obesity, which did not differ from each other (Table 1).

All participants completed two testing sessions 2.5–7 months apart, with average interval matched across groups (HC=4.6 (3–7), Surgery = 4.5 (3–7), WL = 3.8 (2–5). Surgery participants' first session (Time 1) was 1–4 weeks before VSG and the second session (Time 2) was 3–4 months after VSG. Only youth with BMI below 50 were able to fit in the MRI bore. Including those with acceptable head motion in at least one task, final samples with two fMRI sessions were - VSG: n = 6; WL: n = 9; HC: n = 12. Successful behavioral data was acquired from participants unable to fit in the MRI yielding larger behavioral than fMRI samples. Thus, sample sizes are listed for each result.

Participants with obesity met standard criteria for VSG listed in Supplementary Materials (SM). Criteria met by all participants included full-scale IQ ≥ 74, no past or current diagnosis of Type 2 diabetes, psychiatric or neurological disorder and/or prescription of psychotropic medication.

Measures and Procedure

fMRI protocol comprised tasks probing executive, reward, and memory function administered in E-Prime[20] via a magnet-compatible projector through a mirror mounted on the head coil. Participants practiced each task outside the scanner. Tasks were presented in a fixed order as listed below across subjects. Two versions of each task were created from the same stimulus set and randomly assigned and counterbalanced across sessions. A reward-related decision making task was administered on a laptop outside the MRI scanner. Tasks are described briefly below in light of space limits with more design details found in SM.

Episodic Memory—During fMRI, participants classified 46 color scenes as indoor/outdoor. Outside the scanner, participants encoded additional 46 new scenes, which were included as distractors to increase interference on the recognition memory test, during which participants indicated whether 184 serially presented scenes (46 in-scanner, 46 outside-scanner, 96 foils) were "New" (i.e., not previously seen) or "Old" (i.e., previously seen during either encoding). For fMRI analysis, activation during encoding was compared between in-scanner scenes that were remembered (correct "old") relative to those that were forgotten (encoded scenes rated as "new").

Executive Function—The verbal N-back task with three load blocks (1-back, 2-back, 3-back) was used to probe activation during dynamic working memory, a component process of executive function. Participants viewed consonant letters and were instructed to press a right-hand button when the current letter matched the letter presented *n* trials ago, with higher *n* reflecting higher load.

Reward Function—The commonly used Monetary Incentive Delay (MID) task[21] was used to probe activation during anticipation of monetary reward. Each trial presented a cue signaling gain/loss and points at stake followed by the target, which participants were instructed to respond to a fast as possible (target timing parameters were calibrated to ensure 66% success rate). Points gained/lost and the current total number of points were presented after each trial. Participants were informed at the outset that points earned could be exchanged for a monetary reward; unbeknownst to participants all received a $5 gift card. Since the fMRI task evokes evaluation of reward in the brain but does not provide a measure of performance related to reward, a decision-making task, the Balloon Analog Risk Taking (BART)[22] task was administered outside the scanner. A Bayesian model was applied to performance to derive parameters related to response consistency and reward sensitivity[23] (see SM).

fMRI Acquisition and Analyses

Imaging was performed on a 3T Trio Siemens scanner (Erlangen, Germany). A high resolution T1-weighted structural scan (MPRAGE) was acquired lasting 7.23 mins with the parameters: TR/TE=2300/2.94ms, TI=900ms, 90-degree flip angle, 1 slab, 160 sagittal slices with a 1.0mm thickness, FOV=256×256mm^2, resulting in an effective resolution of 1.03mm isotropic voxels. Functional MRI used a T2*-sensitive gradient echo pulse sequence with parameters: TR/TE=2000/30ms, 90-degree flip angle, 43 interleaved slices (width = 2.5mm, gap width = 0.5mm, effective width = 3mm) ascending in the transverse plane, FOV=192×192mm^2. Slice acquisition was angled in the plane of the hippocampus to optimize MTL signal and parallel to orbitofrontal cortex for N-back and MID to minimize susceptibility artifacts. Head movement was minimized with padding between the head and coil.

Functional images were analyzed using SPM12 (Wellcome Department of Cognitive Neurology, London, UK). The first 4 TRs were discarded from analysis for signal stabilization. Images were corrected for motion as recommended by Wilke[24], slice-time corrected, co-registered to each participant's MPRAGE, and smoothed with an 8mm FWHM Gaussian kernel. fMRI responses were modeled using a canonical hemodynamic response function which was convolved with trial/block onset vectors specific to each task. For each subject, a General Linear Model for each functional task modeled the following contrasts of interest: Episodic memory: encoded scenes that were subsequently remembered > forgotten; Executive function: 2-Back > 1-Back (the 3-back blocks were not included because of below chance mean accuracy); Reward: gain cues parametrically modeled according to point value (0 pts., 0.5 pts., 1 pt., and 5 pts.). Additionally, each model included 7 motion regressors of no interest (6 realignment parameters derived estimate of effect of head motion on signal[24] and 1 which de-weighted volumes with greater than 1.5 mm scan-to-scan (STS) motion).

Participants with more than 10% of volumes with half a voxel (1.5mm) or higher STS motion were excluded from analyses. Resulting contrast maps were normalized into MNI standard stereotaxic space by applying the deformation field derived from participants' MPRAGE.

Group x Time interactions for each task, controlling for mean STS, were examined using separate mixed effects analyses of variance (ANOVAs) models for VSG vs HC and VSG vs. WL using GLM Flex Fast2 (http://mrtools.mgh.harvard.edu/). Controlling for age did not impact results (Table S1). These models were constrained by anatomical masks encompassing regions derived from meta-analyses targeting MTL (episodic memory)[25], fronto-parietal (N-back)[26–28], and thalamo-striatal (MID)[29] regions for hypothesis-testing (see SM for details). Multiple comparisons were controlled at $p < .05$ using Monte Carlo simulation using 3dclustsim (2-sided, nearest neighbor 2)[30] and Tukey-corrected pairwise post-hoc tests of significant interactions. As the size of the anatomical masks differed for each task, the cluster threshold satisfying the corrected threshold differed across tasks and is listed in results below. Since 12 HC participants were scanned twice successfully, 6 were randomly selected to match the smaller sample size of the VSG group for Group x Time analysis. The same participants (n=6/group) with acceptable head motion were included across all three fMRI tasks by using listwise deletion. Only Group x Time interaction results at the corrected threshold are presented in the main text, but for an exploratory picture of time comparisons within each group, we have presented Time 1 vs Time 2 paired t-tests at an uncorrected threshold in SM (Tables S3–S5).

Behavioral Analyses

Time differences were assessed with paired t-tests for all performance measures while the non-parametric BART decision-making parameters were assessed with paired Wilcoxon Rank Sum tests; effect sizes, t, and p values are listed in tables and not repeated below.

Results

Head Motion

Group x Time ANOVA did not show significant effect of Time, Group, or interaction for STS motion during any task (see full report in SM Table S1).

Weight change

Change in weight was significant for youth with obesity, who lost 9.06 BMI units after VSG ($t(9) = 12.96$, $d = 4.10$, $p<0.001$), and in WL participants who gained 1.27 BMI units ($t(13) = -3.33$, $d = 0.89$, $p = 0.005$). HC participants gained 0.56 BMI units between Time 1 and Time 2, which was not statistically significant ($t(11) = -2.08$, $d = 0.60$, $p = 0.062$).

Episodic Memory—Twenty-seven participants had complete behavioral data for the subsequent memory paradigm at both time points (VSG = 6; HC = 12; WL = 9). Corrected accuracy (%remembered - %false alarms) did not differ between timepoints significantly in VSG and WL groups but was significantly lower at Time 2 than Time 1 in the HC group (Table 2). In the MTL, comparison did not show any clusters with significant Group x Time

interactions (p = 0.02; k = 88) for VSG vs HC or VSG vs WL groups. Within-group comparison at uncorrected threshold showed that MTL activation in HC and WL reduced at Time 2 relative to Time 1, but did not change in the VSG group (see SM Figure S1 and Table S3).

Executive Function—Twenty-nine participants had behavioral data at both time points for the N-Back task (VSG = 8; HC = 10; WL = 11). While non-significant, effect sizes for improvement in balanced accuracy (percent correct mean target and non-target responses) were larger for high (2-back) than low (1-Back) or very high (3-Back) loads across all groups, with the VSG group showing the largest effect size, suggesting VSG-related effects above and beyond practice or familiarity effects (Table 3). Reaction time showed no significant time-related differences and generally small magnitudes of change in any group (Table 3).

Due to poor accuracy during 3-back load (20% of sample with obesity showed <50% correct hits), only 1- and 2-Back loads were analyzed for fMRI. Comparison of the VSG group with HC showed a significant Group x Time interaction in the left anterior insula/inferior frontal gyrus (p=0.02, k=242; Table 4; Figure 1A), where load-related activation (2-back > 1-back) reduced from Time 1 to Time 2 in the VSG group and was greater than HC at Time 1 but not at Time 2. Thus, after weight loss due to VSG, participants showed a similar pattern of activation to healthy peers than before surgery.

Comparison of the VSG group with WL, revealed Group x Time interaction in several fronto-parietal clusters (Table 4; Figure 1A), which showed that the WL, but not VSG group significantly increased load-related activation from Time 1 to Time 2. These clusters included left superior frontal gyrus (WL: $p_{TukeyCorrected} = 0.09$) and right inferior parietal lobule (WL: $p_{TukeyCorrected} = 0.050$). The VSG group significantly reduced activation from Time 1 to Time 2 in the right inferior parietal lobule (VSG: $p_{TukeyCorrected} = 0.045$). Further, activation was significantly greater for WL relative to VSG participants at Time 2, but not Time 1, in the left superior frontal gyrus ($p_{TukeyCorrected} = 0.008$) and right inferior parietal lobule ($p_{TukeyCorrected} = 0.026$). Lastly, although there was a significant interaction in a cluster that extended to the inferior triangularis, post-hoc tests revealed no significant pair-wise difference. Together, this pattern of results suggests that weight loss was associated with reductions in activation whereas weight gain was associated with increase in activation in fronto-parietal regions associated with executive function.

Reward Function—A total of 25 participants (VSG = 6, HC = 12, WL = 7) had behavioral data at both sessions during the MID task. Surgery participants showed significantly faster response speed and marginal improvement in total points on the MID between timepoints; no differences were observed in the control groups (Table 5).

Group x Time interaction was observed in the left ventral caudate and thalamus (p < .02, k=99; Table 4; Figure 1B) such that response to reward value decreased from Time 1 to Time 2 (left caudate: $p_{TukeyCorrected} = 0.017$; thalamus: $p_{TukeyCorrected} <0.001$; right putamen: $p_{TukeyCorrected} = 0.080$) in the VSG group. It was significantly higher than HC participants at Time 1 (caudate: $p_{TukeyCorrected} = 0.01$; thalamus: $p_{TukeyCorrected} = 0.005$) but

not at Time 2 (caudate: $p_{TukeyCorrected} = 0.892$; putamen: $p_{TukeyCorrected} = 0.431$). VSG has less activation in thalamus at Time 2 than HC ($p_{TukeyCorrected} = 0.021$). These results indicate that weight loss due to VSG normalized sensitivity to value of anticipated reward in the ventral striatum, a region related to reward evaluation[29] and magnitude[21]. No regions showed significant Group x Time interaction for VSG vs. WL participants.

Thirty-four participants completed the BART assessing reward-related decision-making at both time points (VSG = 9; HC = 12; WL = 13). While not significant, it is notable that both VSG and HC participants' performance suggested gains (decreased Total Points and number Balloons Popped at Time 2 than Time 1) whereas WL participants showed the opposite pattern (Table 5). To examine decision-making processes, a decision-making model[23] was used to estimate two parameters of interest: Response Consistency (β): the extent to which a participants' responses matches prior responses with lower values indicating more variable behavior; and Reward Sensitivity (γ^{+}): sensitivity to potential gains. Although all groups showed increases in Response Consistency at Time 2 suggesting less erratic reward-related responding, the VSG group showed the largest effect, which was statistically significant. In contrast, while VSG and HC groups showed only small effects of Time on Reward Sensitivity, the WL group showed a very large effect with greater Reward Sensitivity at Time 2 than Time 1 (Table 5). Together with the behavioral outcomes, these results suggest that after weight loss due to VSG, participants adopted a more consistent, less reward-driven strategy at Time 2 while after weight gain the WL group's performance suggested greater reward sensitivity at Time 2.

Discussion

Results of our pilot study suggest normalization of prefrontal-parietal and striatal engagement associated with executive function and reward anticipation, respectively, 3–4 months following VSG relative to repeated testing at the same time interval in two age-matched control groups, wait-listed surgery candidates who were severely obese and healthy controls. Surgery participants lost significant weight and showed reduction in cortico-striatal activation, whereas wait-listed participants gained weight during the 4-month interval and increased prefrontal-parietal activation during that period. MTL regions associated with episodic memory did not reveal significant time-related change. Improvement of a larger magnitude was observed for the surgery group for high-load executive performance, statistically significant for speed and some parameters of reward-related decision-making relative to that in the control groups. These results must be considered preliminary until their stability is established with replication in larger samples. They are useful for estimating effects sizes and generating hypotheses to guide the future work.

Our pilot results must be viewed in the context of the following factors. First, the small sample sizes illustrate the challenges of conducting successful fMRI in a well-controlled, within-subjects design with two control groups in a 1-year period. Youth with BMIs above 50 could not fit in the Trio scanner bore. Furthermore, compliance to restricting head motion was more difficult in youth with obesity. Furthermore, follow up and compliance to multiple testing visits that were months apart was also more challenging for youth with obesity. Together, these limitations reduced the final sample providing two fMRI sessions with high

quality data for participants with obesity to half (6) of that for healthy controls (12). Thus, physical discomfort and challenges to compliance of testing requirements are higher in youth with obesity, and must be factored into estimation of sample sizes for future studies. While this limited recruitment, evidence of neurocognitive changes for those in the lower BMI range of eligibility for bariatric surgery (35/40–50) bolsters its potential for intervention and reversing maladaptive developmental outcomes. Potential for neural plasticity may be higher in those with relatively better metabolic health compared to those with more severe obesity and/or medical comorbidities. Second, small sample sizes limit statistical power and therefore, our results must be interpreted with caution. Despite slightly larger behavioral samples, neural activation was more sensitive to weight-loss/gain-related changes than behavioral performance, which reached statistical significance in the surgery group only for response speed and the BART decision parameter. However, fMRI results in small sizes may be unstable, and therefore, replication in larger samples is necessary. Thus, our results must be considered as preliminary and suggestive of surgery-related changes in brain function beyond those observed upon repeated testing.

Weight gain/loss related neural changes were observed for executive and reward functioning but not for episodic memory. The N-back task, a common fMRI probe for a key component process of executive function in both adult and pediatric fMRI studies, yielded time-related activation changes in frontal-parietal regions that suggest an association between weight and neural inefficiency. Greater activation prior to weight-loss and its reduction after it in the surgery group to the same level as the healthy-weight controls, suggests a more efficient neural response to task demand, as performance accuracy and speed improved, albeit not significantly. This pattern of activation change was paralleled in the wait-listed surgery candidates with widespread increased activation after weight gain during the 4-month interval. Their performance did not change and therefore, the more widespread recruitment suggests a more inefficient neural response to task demands following weight gain. Striatal response to reward value also showed reduced engagement following surgery, suggesting that weight-loss related neural efficiency generalized across brain regions, in the small set of surgery candidates included in this study. Whether this pattern of results is generalizable remains to be tested with better-powered studies in the future.

Further work is needed to probe the basis of these activation reductions, whether they are driven by changes in vasculature or insulin receptor activity associated with metabolic changes induced by weight-loss following bariatric surgery. Association with insulin activity is suggested by hypothalamic activation reduction following glucose ingestion in humans[31], which is attenuated in obese rats[32]. Our small sample sizes preclude examination of correlation of activation changes with insulin parameter changes, but could be examined in future work as a first step to hypothesis generation about the metabolic basis of activation change in obesity. Activation in MTL during memory encoding and recognition memory was not sensitive to surgery. Perhaps neural plasticity in this region takes longer, beyond the 3–4 month post-surgery interval. Alternately, our fMRI encoding probe may not have been optimal in detecting changes and future studies should examine memory retrieval after longer delays.

Executive and reward-related functioning is central to behaviors such as food and activity choices, which promote and maintain obesity[7]. Our fMRI probes did not use food related stimuli and thus, the extent to which the observed neurocognitive changes may impact food-related decisions remains to be tested. Upon replication, these results point to the potential of surgical intervention for altering domain-general regulatory and motivational processes. Whether those changes support improvement in adaptive function and psychosocial health remains to be investigated in future work.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Study Importance Questions

What is already known about this subject?

- Executive and motivational performance is often lower in adolescents with severe obesity.
- Bariatric surgery results in weight loss and metabolic improvement in adults and adolescents.
- Preliminary neuroimaging in adults shows neurocognitive changes after bariatric surgery relative to before surgery.

What does your study add?

- Provides first pilot neuroimaging evidence supporting neurocognitive functional change due to bariatric surgery in adolescents using two control groups, wait-listed surgical candidates with obesity and healthy-weight controls.
- Surgery-related reduction of prefrontal and striatal engagement to the same levels as healthy controls, provides a basis for formulating neurocognitive hypotheses for future work.
- Provides pilot data for estimating effect sizes of neural and cognitive change following surgical weight-loss and weight gain during 4 month interval in adolescents with severe obesity.

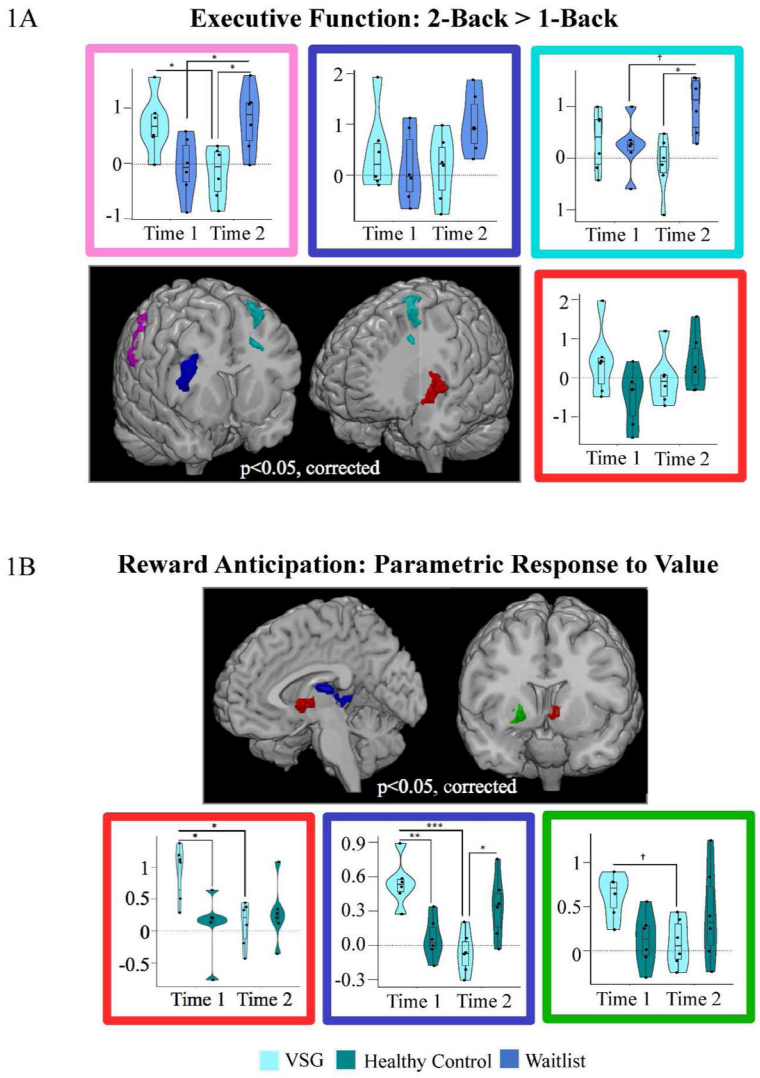

Figure 1.

Regions showing significant Group x Time interaction ($p < .05$ corrected) during the N-back task indexing executive function (1A) and during reward anticipation on the Monetary Incentive Delay task (1B) in ANOVA models comparing VSG vs. Healthy Controls and VSG vs. Wait-list controls. Colors surrounding graphs correspond to colors depicting activation clusters. Graphs depict mean beta values of activated clusters in the VSG group (light blue), Healthy Control (green), and Wait-list controls (dark blue). †p<0.10, *p<0.05, **p<0.01, ***p<0.005

Table 1

Demographic Characteristics

	Healthy Control Mean (SD)	VSG Mean (SD)	Wait List Mean (SD)	One-Way ANOVA F	eta_p^2	P
BMI Baseline[a]	21.57 (2.59)	47.18 (6.98)	45.32 (8.19)	57.53	0.78	<0.001
Age, yrs	16.51 (1.27)	17.00 (1.37)	16.42 (1.33)	0.613	0.04	0.548
IQ	97.75 (9.53)	92.20 (19.04)	93.71 (11.45)	0.518	0.03	0.601
Maternal Ed, yrs	14.83 (2.62)	13.30 (4.81)	13.92 (4.86)	0.373	0.02	0.692
	Healthy Control	VSG	Wait List	p[b]		
Gender, *N*				0.534		
Male	6	4	4			
Female	6	6	10			
Handedness, *N*				0.402		
Right	11	10	11			
Left	2	0	3			
Ethnicity, *N*				0.418		
Hispanic/Latino	1	2	4			
Not Hispanic/Latino	11	6	10			
Not Reported	0	2	0			
Race, *N*				0.294		
Black/AA	6	5	5			
White	4	3	3			
Other/Mixed	2	0	5			
Not Reported	0	2	1			
SES, *N*				0.384		
>$80,000	4	2	6			
$50,000–$80,000	3	1	4			
<$50,000	5	7	4			

[a]Healthy Control vs. VSG and Healthy Control vs. Wait List p<0.05

Obesity (Silver Spring). Author manuscript; available in PMC 2018 November 01.

[b] p-value derived from Fisher Exact or chi^2 Test;

VSG: Vertical Sleeve Gastrectomy

Table 2

Effect of Time on Recognition Memory for Encoded Scenes During fMRI for VSG, Wait List, and Healthy Control Groups

	Time1	Time2	Time 1 vs Time 2		
	Mean (SD)	Mean (SD)	Mean Diff (95% CI)	d[a]	P[b]
		Episodic Memory			
Corrected Accuracy[c], %					
VSG	56.9 (22.9)	55.8 (23.4)	1.1 (−27.8, 30.0)	0.04	0.927
Wait List	51.9 (21.2)	45.9 (23.8)	6.0 (−3.0, 15.1)	0.51	0.162
Healthy Control	54.7 (14.9)	44.9 (13.6)	9.8 (2.1, 17.4)	0.81	0.017*

[a]Cohen's d;

[b]p-value from paired t-test;

[c]hits– false alarms

VSG: Vertical Sleeve Gastrectomy;

*p<0.05

Table 3

Effect of Time on Accuracy and Speed During the N-Back task for VSG, Wait List, and Healthy Control Groups

	Time1	Time2	Time 1 vs Time 2		
	Mean (SD)	Mean (SD)	Mean Diff (95% CI)	d[a]	P[b]
		N-Back			
1-Back Accuracy, %					
VSG	96.6 (8.9)	97.6 (3.6)	−1.0 (−9.8, 7.7)	0.10	0.786
Wait List	93.2 (12.3)	95.6 (8.0)	−2.4 (−8.6, 3.8)	0.26	0.414
Healthy Control	97.8 (4.4)	97.9 (5.2)	−0.8 (−4.3, 2.6)	0.17	0.601
2-Back Accuracy, %					
VSG	87.9 (15.3)	92.2 (11.7)	−4.3 (−13.4, 4.7)	0.40	0.299
Wait List	92.0 (8.5)	95.2 (10.7)	−3.2 (−11.4, 4.9)	0.27	0.400
Healthy Control	96.0 (7.0)	96.3 (6.0)	−0.3 (−6.4, 5.8)	0.04	0.909
3-Back Accuracy, %					
VSG	75.3 (17.4)	79.7 (15.8)	−4.3 (−17.8, 9.2)	0.26	0.474
Wait List	81.5 (10.2)	83.8 (16.0)	−2.3 (−13.1, 8.5)	0.17	0.643
Healthy Control	90.1 (13.6)	89.9 (7.9)	0.2 (−6.3, 6.8)	0.02	0.939
1-Back Reaction Time, ms					
VSG	692 (218)	664 (361)	28 (−288, 345)	0.08	0.838
Wait List	654 (191)	650 (260)	4 (−126, 134)	0.02	0.946
Healthy Control	552 (111)	505 (64)	47 (−31, 125)	0.43	0.204
2-Back Reaction Time, ms					
VSG	750 (286)	692 (331)	58 (−175, 291)	0.21	0.574
Wait List	631 (228)	643 (374)	−12 (−224, 201)	0.04	0.908
Healthy Control	547 (180)	495 (149)	52 (−119, 223)	0.21	0.507
3-Back Reaction Time, ms					
VSG	734.1 (386.2)	700.7 (280.0)	33.4 (−202.4, 269.5)	0.10	0.748
Wait List	736.9 (324.2)	731.5 (300.1)	5.4 (−146.1, 156.9)	0.02	0.938
Healthy Control	670.5 (237.7)	640.3 (297.5)	30.1 (−198.3, 258.5)	0.11	0.772

[a]Cohen's d

^{b}p-value from paired t-test

VSG: Vertical Sleeve Gastrectomy

Table 4

Peak Activations from clusters showing Group x Time interaction: N-back task indexing Executive Function and Reward Anticipation during the Monetary Incentive Delay Task VSG vs. Healthy Control and VSG vs. Wait-list controls

Region (BA)	H	Volume[a]	F[b]	x	y	z
Executive Function: 2-Back > 1-Back						
VSG vs. Healthy Control						
Anterior Insula (13)	L	275	25.21	−37	−2	6
VSG vs. Wait List						
Superior Frontal Gyrus (6)	L	277	22.73	−20	14	38
Inferior Triangularis (9, 44)	R	322	22.79	46	16	18
Inferior Parietal Lobe (40)	R	424	28.93	62	−26	34
Reward Anticipation: Parametric Response to Reward Value						
VSG vs Healthy Control						
Putamen	R	125	17.40	20	10	−4
Caudate	L	119	77.34	−6	4	−4
Thalamus	R/L	165	29.78	4	−20	12

[a] volume measured in mm^3;

[b] F-value derived from the Group x Time interaction term

BA: Broadmann's Area; H: hemisphere

Table 5

Effect of Time on Performance during the Monetary Incentive Delay and Balloon Analog Risk Taking Tasks for VSG, Wait List and Healthy Control Groups

	Time1	Time2	Time 1 vs Time 2		
	Mean (SD)	**Mean (SD)**	**Mean Diff (95% CI)**	**d**[a]	**p**[b]
Monetary Incentive Delay Task					
Total Points					
VSG	13.0 (4.2)	18.3 (3.1)	−5.3 (−11.5, 1.0)	0.88	0.084[†]
Wait List	14.3 (8.0)	14.6 (7.6)	−0.3 (−2.8, 2.2)	0.10	0.777
Healthy Control	15.1 (5.1)	12.7 (5.7)	2.4 (−6.6, 11.4)	0.28	0.521
Reaction Time, ms					
VSG	199.9 (20.1)	180.0 (13.1)	19.9 (5.2, 34.6)	1.42	0.018[*]
Wait List	190.7 (22.7)	180.6 (29.1)	10.1 (−15.9, 36.2)	0.32	0.389
Healthy Control	175.3 (28.2)	168.6 (18.6)	6.6 (−6.0, 19.3)	0.55	0.237
Balloon Analog Risk Taking Task					
Total Points					
VSG	6,483 (2,093)	5,216 (2,829)	1,266 (−1,237, 3,771)	0.51	0.298
Wait List	6,655 (1,737)	7.015 (1,199)	−360 (−1,573, 853)	0.24	0.544
Healthy Control	6,199 (2,322)	5,801 (1,953)	398 (−1,421, 2,218)	0.19	0.654
Adjusted Number of Pumps					
VSG	30.64 (11.47)	24.83 (16.74)	5.81 (−8.68, 20.31)	0.41	0.404
Wait List	36.37 (18.18)	40.94 (13.87)	−4.28 (−17.41, 8.86)	0.26	0.507
Healthy Control	31.34 (14.49)	28.00 (15.85)	3.38 (−9.48, 16.24)	0.22	0.591
Balloons Popped					
VSG	8.22 (2.68)	6.89 (3.79)	1.33 (−1.98, 4.64)	0.41	0.403
Wait List	9.15 (5.96)	11.77 (3.81)	−2.62 (−6.70, 1.47)	0.52	0.197
Healthy Control	8.92 (3.42)	6.92 (0.48)	2.00 (−1.53, 5.53)	0.48	0.251
	Median (IQR)	**Median (IQR)**	**Difference (95% CI)**[c]	**R**[d]	**p**[e]

Response Consistency: β

	Time1	Time2	Time 1 vs Time 2		
	Mean (SD)	Mean (SD)	Mean Diff (95% CI)	d^a	p^b
VSG	0.09 (0.12)	0.12 (0.16)	−0.06 (−0.36, 0.00)	0.55	0.055 †
Wait List	0.09 (0.07)	0.10 (0.06)	−0.01 (−0.04, 0.034)	0.09	0.735
Healthy Control	0.14 (0.08)	0.14 (0.17)	0.01 (−0.06, .13)	0.06	0.850
Reward Sensitivity: γ^+					
VSG	0.43 (0.68)	0.49 (0.63)	0.003 (−0.21, 0.34)	0.00	1.00
Wait List	0.69 (0.66)	0.92 (0.61)	−0.21 (−0.45, 0.04)	0.42	0.127
Healthy Control	0.57 (0.31)	0.40 (0.94)	0.06 (−0.28, 0.26)	0.16	0.622

[a] Cohen's d;

[b] p-value from paired t-test;

d: Difference in location from Wilcoxon Rank Sum Z;

[c] Difference in location from Wilcoxon Rank Sum Z;

[d] r derived from Wilcoxon Rank Sum Z;

[e] Wilcoxon Rank Sum Test

VSG: Vertical Sleeve Gastrectomy;

† p<0.01,

* p<0.05