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Changes in Cerebral Cortical Thickness Related to Weight Loss Following Bariatric Surgery

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Abstract

Cerebral cortical thickness is associated with memory recall and intelligence test scores and serves as a measure for changes in cortical grey matter. Previous studies suggest reduced cortical thickness in patients with obesity. This study aimed to investigate changes in cortical thickness following bariatric surgery. Magnetic resonance imaging (MRI) data of five patients were analyzed preoperatively and six months postoperatively to assess changes in global measures of cortical thickness. No patients were lost to follow-up. Preliminary trends of brain change following surgery suggest increases in cerebral cortical thickness in patients with greater excess weight loss. The results of this study suggest increases in cortical thickness may be an additional benefit of bariatric surgery for those with greatest weight loss and indicate the need for further investigation using larger samples and correlation with neurocognitive measures, such as memory recall.

Introduction:

Obesity is associated with functional and structural brain deficits such as diminished memory recall and reduced grey matter volume, as well as neurocognitive disorders like dementia [1–5]. Prior studies have demonstrated these associations in patients with obesity of various ages, even after controlling for comorbid conditions like diabetes [3–4, 6–7]. Although the exact mechanism underlying the relationship between obesity and structural and neurocognitive changes remains unknown, previous research underscores the possible role of inflammation, adipokines like leptin and ghrelin, and oxidative damage [4–5, 8].

Understanding structural brain changes with weight loss is vital to considering the long-term implications of these previously detected associations between obesity and brain function and structure. Neuroimaging studies are essential for investigating structural brain changes. Such studies often assess cerebral cortical thickness (CT), which serves as a sensitive measure for changes in cortical grey matter [9]. Prior research has documented reductions in CT in patients with obesity relative to individuals at healthier weights [6], in addition to an inverse association between CT and body mass index (BMI) [7]. Previous studies have also demonstrated positive associations between CT and memory recall and intelligence quotient

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test scores [10–11]. Therefore, a growing body of evidence suggests not only that patients with obesity may be at increased risk for diminished cognitive function due to weight-related cerebral cortical thinning, but also that CT may be crucial for maintaining healthy cognitive function.

The relationship between obesity and reduced CT should be considered in conjunction with previous literature regarding anorexia nervosa (AN). Patients with AN typically engage in self-starvation, which leads to emaciation, and the literature suggests not only that AN is associated with cerebral cortical thinning, but also that cerebral cortical thickness is restored following weight regain [12–13]. Thus, the AN literature contributes evidence that supports the importance of maintaining a healthy weight to achieve optimal cortical thickness and, consequently, healthy cognition. Further, these findings also suggest the influence of nutritional change on CT. Given that both very low weight in AN and very high weight in obesity are associated with reduced CT compared to healthy weight, it may be that change into a healthier weight range is directly related to structural brain change. It is also vital to ensure that caloric restriction that accompanies bariatric surgery does not result in cortical thinning, as it does in patients with AN.

Given past research showing lower CT in patients with obesity, the utility of CT as a quantifiable and surrogate measure for cognitive health, and the role of bariatric surgery as the only intervention presently available for durable weight loss, it is important to investigate changes in cortical thickness in patients undergoing bariatric surgery. Whether cerebral cortical thickness improves or is restored following bariatric surgery remains unknown, and to our knowledge, no prior studies have measured cortical thickness in the same patients before and after bariatric surgery. We hypothesized that greater weight loss would be positively associated with improvements in CT after surgery.

Methods:

Adult bariatric patients ($n = 5$) at a single academic medical center in California were recruited for participation in this study. All patients were female, of whom four underwent laparoscopic Roux-en-Y gastric bypass (RYGB) and one underwent laparoscopic sleeve gastrectomy (SG). For each patient, anthropometric measures were assessed, and MRI scans were completed preoperatively and six months after surgery. Data were summarized using means. Given the small sample size, means were reported alongside minimum and maximum values to describe the spread of the data. Scans were conducted on a 3.0 Tesla GE scanner. T1-weighted 1mm voxel high resolution scans were completed. Images were subsequently analyzed using FreeSurfer 5.3.0, a previously validated and open source software for estimating the thickness of cortical matter [14]. Global measures of cerebral cortical thickness were obtained for each hemisphere separately to examine possible lateral differences. Standard linear regression was conducted in SPSS Version 23 to examine the relationship between percentage of excess weight loss and changes in cortical thickness six months postoperatively. Approval for this study was provided by Stanford University's Institutional Review Board, and participants completed written, informed consent.

Results:

At baseline, the average participant age, BMI, and excess body weight (EBW) were 48.8 years (35 – 69), 45.0 kg/m² (41.0 – 51.3) and 113 kg (99 – 131), respectively (Table 1). No patients were lost to follow-up. Six months after bariatric surgery, the average participant BMI was 34.9 kg/m² (30.4 – 39.4), the average percent excess weight loss (%EWL) was 51.7% (30.7 – 68.6), and the average percent total body weight loss was 22.5% (12.8 – 27.8). The average change in BMI was 10.2 kg/m² (5.5 – 11.9). Table 2 summarizes individual measures of cerebral CT, %EWL, and absolutely weight. Changes in CT seemed related to percentage excess weight loss following surgery, with independent regressions yielding non-significant trends between %EWL and changes in the CT of the right ($F(1,3) = 4.10$; $p = .136$; $R^2 = .578$) and left ($F(1,3) = 4.82$; $p = .116$; $R^2 = .617$) hemispheres (Figure 1). Given the small sample size in this pilot study, we focused on effect sizes, revealing that %EWL explained approximately 60% of the variance in the change of cerebral CT among these five patients. No major differences in the right and left hemispheres were observed. Interestingly, when percent total weight loss (rather than excess weight loss) was utilized as the outcome variable, the effect size dropped to $R^2 = .275$ ($p > .05$). (Figure 2 illustrates the results of FreeSurfer cortical thickness estimates.)

Conclusion:

This study is first to investigate changes in cerebral CT in patients with obesity following bariatric surgery. The results obtained from this preliminary sample demonstrated a positive trend relation between %EWL after bariatric surgery and improvements in CT, which supports previous literature demonstrating an inverse relationship between obesity and CT [6]. Greater excess weight loss may therefore result in the successful increase of CT in patients undergoing bariatric surgery, and CT may, in turn, serve as an objective marker for improved cognitive function. This study complements previous research examining functional brain changes in patients with obesity after bariatric surgery and adds to the literature early evidence of improved CT after surgical intervention. A recent study by Alosco et al. [15] demonstrated improvements in memory in patients who underwent bariatric surgery even up to 24 months postoperatively, and a systematic review conducted by Thiara et al. [8] found evidence to suggest improvements in attention and executive function following bariatric surgery. Given previous research regarding CT and cognitive performance, increases in CT after significant weight loss from bariatric surgery may partially mediate these neurocognitive improvements.

It is important to note that the observed effect was strongest when considering excess weight loss, rather than total weight loss. This finding suggests that it is not total weight loss alone—but rather moving closer towards a healthier weight—that is important for structural brain change. Taken together with results from the AN literature, these findings suggest that deviations towards abnormally high or low BMIs may compromise neuronal structure and function, underscoring the importance of maintaining healthy weight for achieving optimal cognition. Importantly, preliminary evidence from these five patients suggests that restrictive dietary intake following bariatric surgery does not result in reductions in CT, as is observed

in patients with AN. Despite the novelty of these results, further research is necessary to replicate this trend in a larger sample.

A limitation of the study is the lack of healthy weight comparisons. Because prior investigations of CT in the general population have used a variety of methods to measure CT, there is no clear norm for a healthy CT measure. Some data suggest that an overall average CT of 2.5mm is a reasonable estimate [16], but the significant and meaningful deviations from that value are not clearly defined or understood. Thus, this study cannot provide a valid understanding of whether these patients showed reduced CT values preoperatively that were then restored after weight loss. Instead, each participant serves as her own comparison, with the goal to study within patient change rather than shifts toward a healthy comparison value.

Subsequent studies with adequately powered sample sizes and longer follow up are necessary to corroborate the relationship between weight loss, cerebral CT, and neurocognitive outcomes following bariatric surgery. If replicated, these results provide evidence of additional improvements beyond weight loss associated with bariatric surgery and may reduce concerns regarding dietary restriction on brain health.

References

1. Gunstad J, Paul RH, Cohen RA, Tate DF, Spitznagel MB, Grieve S, Gordon E. Relationship between body mass index and brain volume in healthy adults. *Int J Neurosci* 2008 11;118(11):1582–93. doi: 10.1080/00207450701392282. [PubMed: 18853335]
2. Hawkins MAW, Alosco ML, Spitznagel MB, et al. The association between reduced inflammation and cognitive gains after bariatric surgery. *Psychosomatic medicine* 2015;77(6):688–696. doi: 10.1097/PSY.000000000000125. [PubMed: 25478707]
3. Stillman CM, Weinstein AM, Marsland AL, Gianaros PJ, Erickson KI. Body-Brain Connections: The Effects of Obesity and Behavioral Interventions on Neurocognitive Aging. *Front Aging Neurosci* 2017 5 1;9:115. doi: 10.3389/fnagi.2017.00115 eCollection 2017. [PubMed: 28507516]
4. Spitznagel MB, Hawkins M, Alosco M, Galioto R, Garcia S, Miller L, Gunstad J. Neurocognitive Effects of Obesity and Bariatric Surgery. *Eur Eat Disord Rev* 2015 11;23(6):488–95. doi: 10.1002/erv.2393. [PubMed: 26289991]
5. Shalev D, Arbuckle MR. Metabolism and Memory: Obesity, Diabetes, and Dementia. *Biol Psychiatry* 2017 12 1;82(11):e81–e83. doi: 10.1016/j.biopsych.2017.09.025. [PubMed: 29110819]
6. Marqués-Iturria I, Pueyo R, Garolera M, Segura B, Junqué C, García-García I, José Sender-Palacios M, Vernet-Vernet M, Narberhaus A, Ariza M, Jurado MÁ. Frontal cortical thinning and subcortical volume reductions in early adulthood obesity. *Psychiatry Res* 2013 11 30;214(2):109–15. doi: 10.1016/j.pscychresns.2013.06.004. [PubMed: 24041490]
7. Veit R, Kullmann S, Heni M, Machann J, Häring HU, Fritsche A, Preissl H. Reduced cortical thickness associated with visceral fat and BMI. *Neuroimage Clin* 2014 9 26;6:307–11. doi: 10.1016/j.nicl.2014.09.013. [PubMed: 25379443]
8. Thiara G, Cigliobianco M, Muravsky A, Paoli RA, Mansur R, Hawa R, McIntyre RS, Sockalingam S. Evidence for Neurocognitive Improvement After Bariatric Surgery: A Systematic Review. *Psychosomatics* 2017 May-Jun;58(3):217–227. doi: 10.1016/j.psym.2017.02.004. [PubMed: 28410777]
9. Pereira JB, Ibarretxe-Bilbao N, Marti MJ, Compta Y, Junqué C, Bargallo N, Tolosa E. Assessment of cortical degeneration in patients with Parkinson's disease by voxel-based morphometry, cortical folding, and cortical thickness. *Hum Brain Mapp* 2012 11;33(11):2521–34. doi: 10.1002/hbm.21378. [PubMed: 21898679]

10. Narr KL, Woods RP, Thompson PM, Szeszko P, Robinson D, Dimtcheva T, Gurbani M, Toga AW, Bilder RM. Relationships between IQ and regional cortical gray matter thickness in healthy adults. *Cereb Cortex* 2007 9;17(9):2163–71. [PubMed: 17118969]
11. Walhovd KB, Fjell AM, Dale AM, Fischl B, Quinn BT, Makris N, Salat D, Reinvang I. Regional cortical thickness matters in recall after months more than minutes. *Neuroimage* 2006 7 1;31(3): 1343–51. [PubMed: 16540346]
12. Bernardoni F, King JA, Geisler D, Stein E, Jaite C, Nätsch D, Tam FI, Boehm I, Seidel M, Roessner V, Ehrlich S. Weight restoration therapy rapidly reverses cortical thinning in anorexia nervosa: A longitudinal study. *Neuroimage* 2016 4 15;130:214–222. doi: 10.1016/j.neuroimage.2016.02.003. [PubMed: 26876474]
13. King JA, Geisler D, Ritschel F, Boehm I, Seidel M, Roschinski B, Soltwedel L, Zwipp J, Pfuhl G, Marxen M, Roessner V, Ehrlich S. Global cortical thinning in acute anorexia nervosa normalizes following long-term weight restoration. *Biol Psychiatry* 2015 4 1;77(7):624–32. doi: 10.1016/j.biopsych.2014.09.005. [PubMed: 25433902]
14. Fischl B FreeSurfer. *Neuroimage* 2012 8 15;62(2):774–81. doi: 10.1016/j.neuroimage.2012.01.021. [PubMed: 22248573]
15. Alosco ML, Spitznagel MB, Strain G, Devlin M, Cohen R, Paul R, Crosby RD, Mitchell JE, Gunstad J. Improved memory function two years after bariatric surgery. *Obesity (Silver Spring)* 2014 1;22(1):32–8. doi: 10.1002/oby.20494. [PubMed: 23625587]
16. Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proc Natl Acad Sci U S A* 2000 9 26;97(20):11050–5. [PubMed: 10984517]

Figure 1:
Linear Regression of Percent Excess Weight Loss and Change in Cortical Thickness

Figure 2: Participant Brain Images Preoperatively (left) and 6-Months Postoperatively (right). Yellow corresponds to greater cortical thickness. Images are arranged by greatest improvement in cortical thickness, in descending order.

Table 1:

Patient Characteristics Prior to and Six Months After Bariatric Surgery

	Preoperative $\bar{x}$ (min – max)	6-Months Postoperative $\bar{x}$ (min – max)
BMI (kg/m ²)	-	10.2 (5.5 – 11.9)
Percent Total Body Weight Loss (%)	-	22.5 (12.8 – 27.8)
Weight (kg)	115 (99 – 131)	89 (78 – 101)
BMI (kg/m ²)	45.0 (41.0 – 51.3)	34.9 (30.4 – 39.4)
HbA1c (%)	6.1 (5.9 – 6.4)	5.7 (5.4 – 6.0)
Left Cortical Thickness (mm) *	2.36 (2.24 – 2.51)	2.36 (2.27 – 2.46)
Right Cortical Thickness (mm) **	2.40 (2.27 – 2.55)	2.39 (2.23 – 2.48)

* $R^2=.617$ (F(1,3) = 4.82; p=.116)

** $R^2=.578$ (F(1,3) = 4.10; p=.136)

Table 2:

Summary of Average Cortical Thickness, Percent Excess Weight Loss, and Weight, by Participant

	<u>Left Cerebral Hemisphere</u>		<u>Right Cerebral Hemisphere</u>		Initial Weight (kg)	Final Weight (kg)	%EWL
	Initial Cortical Thickness (mm ³)	Final Cortical Thickness (mm ³)	Initial Cortical Thickness (mm ³)	Final Cortical Thickness (mm ³)			
Participant 1	2.24	2.31	2.27	2.32	246	185	63.5
Participant 2	2.38	2.46	2.42	2.47	237	171	68.6
Participant 3	2.34	2.31	2.43	2.47	289	222	45.2
Participant 4	2.32	2.27	2.34	2.23	219	191	30.7
Participant 5	2.51	2.43	2.55	2.48	278	211	50.5