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Cortical thickness of the cognitive control network in obesity and successful weight loss maintenance: A preliminary MRI study

Jason J. Hassenstab^{1,2,*}, Lawrence H. Sweet³, Angelo Del Parigi⁴, Jeanne M. McCaffery¹, Andreana P. Haley⁵, Kathryn E. Demos¹, Ronald A. Cohen¹, and Rena R. Wing¹

¹The Miriam Hospital and Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University, Providence, RI

²Knight Alzheimer's Disease Research Center, Washington University School of Medicine, St. Louis, MO

³Butler Hospital and Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University, Providence, RI

⁴Medical Affairs, Pfizer, Inc., New York, NY

⁵Department of Psychology, The University of Texas at Austin, Austin, TX

Abstract

Cortical thickness of the cognitive control network was contrasted between obese (OB), successful weight loss maintainers (SWLM), and lean individuals. OB had significant thinning, most notably in the anterior cingulate and posterior parietal cortices. SWLM exhibited trends towards thicker cortex than OB, which may be important in future studies.

Keywords

obese; magnetic resonance imaging; Freesurfer

1. Introduction

Successful weight loss maintainers (SWLM) exert more behavioral control to maintain their achieved weight than never-obese lean (NOL) individuals. For example, we found that SWLMs had increased brain activation in response to pictures of high calorie foods in prefrontal and temporal regions associated with selective monitoring and inhibitory control (McCaffery et al., 2009). We have also shown that currently obese individuals (OB) exhibit low levels of attention bias in response to high calorie stimuli, whereas SWLM exhibit higher levels (Phelan et al., 2011). These findings suggest that control of several cognitive processes is related to weight status and may be crucial for weight loss maintenance.

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Corresponding Author: Jason Hassenstab, Ph.D., Knight ADRC, 4488 Forest Park Ave, Suite 130, St. Louis, MO, 63108 Phone: (314) 286-2881 Fax: (314) 286-2763 hassenstabj@wustl.edu.

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Obesity and related metabolic dysfunction has been linked to poor performance on tests of cognitive control (Elias et al., 2003; Hassenstab et al., 2010) and reduced global and regional brain volumes (Ho et al., 2010; Pannacciulli et al., 2006; Raji et al., 2010). Cognitive control refers to mechanisms that can adjust the selection, biasing, and maintenance of reflexive and habitual reactions in order to configure behavior for the performance of specific tasks (Botvinick et al., 2001) and a functionally connected network of regions that comprise the cognitive control network (CCN) has been identified, including the dorsal anterior cingulate cortex (DACC), the dorsal lateral prefrontal cortex (DLPFC), the anterior insular cortex (AIC) and the posterior parietal cortex (PPC; (Cole and Schneider, 2007).

It is currently unknown if obesity is associated with structural alterations that are specific to the CCN and whether these alterations remain following sustained weight loss. Our goal was to determine if current and past obesity status are associated with brain structure in the CCN. Cortical thickness was chosen because it has high sensitivity to individual variation in neuroanatomy and to cognitive functioning in normal aging and disease (Dickerson et al., 2008; Salat et al., 2004). Based on our prior studies in this sample and recent literature supporting brain changes in response to behavioral interventions (e.g., (Erickson et al., 2011), we hypothesized that OBs would show greater cortical thinning in all areas of the CCN relative to NOLs and that SWLMs would more closely resemble NOLs, possibly reflecting their reduction in body weight.

2. Methods

2.1. Participants

Study participants included 17 SWLM (ages 27-65), 17 OB (ages 35-64), and 19 age and gender matched NOL (ages 27-56). SWLM had a history of overweight or obesity (BMI > 30 kg/m²), subsequent weight loss (> 13 kg), maintenance of a normal body weight for at least 3 years (BMI 18.5-25 kg/m²). NOLs were currently normal weight (BMI 18.5-25 kg/m²) with no history of obesity and OB were currently in the obese range (BMI >30 kg/m²). All participants were weight stable for at least 2 years. Participants were excluded for standard MRI contraindications, major neurological or psychiatric conditions, and psychiatric and/or weight loss medications.

2.2. Procedures

T1-weighted MP-RAGE structural scans were acquired on a Siemen's 3T Tim Trio (1mm slice thickness, TE=3.9ms, TR=1.57s, flip angle=15deg, FOV=256mm², matrix=256 × 256). Scans were processed using the default settings in the Freesurfer Imaging Analysis Suite (v. 4.5; <http://surfer.nmr.mgh.harvard.edu>), described in detail elsewhere (Fischl and Dale, 2000). Mean thicknesses were generated by combining adjacent labels from the Destrieux atlas (Destrieux et al., 2010) using weighted averaging, based on the number of vertices in each label. Four cortical regions were selected *a priori* and combined bilaterally into the AIC, the DACC, the DLPFC, and the PPC. To verify that our results were not due to more generalized global effects, global cortical thickness, and volumes of CSF, white matter, and gray matter were compared. In addition, two theoretically unrelated comparison regions were selected and combined bilaterally (occipital pole and postcentral gyrus).

2.3. Statistical analysis

Basic demographics and descriptive variables were examined using analysis of variance, Chi-Square tests, and t-tests. Regions were analyzed using multivariate analysis of covariance (MANCOVA) comparing mean cortical thickness across the regions. Due to potential effects on brain structure, models included age, gender, and use of

antihypertensives. *Post hoc* contrasts were completed when main effects ($P < .05$) were found. To reduce Type 1 error, $P < .01$ was considered significant for all *post hoc* contrasts.

3. Results

A MANCOVA contrasting mean cortical thickness across the four ROIs revealed a significant main effect of group (Wilk's Lambda: $F[8,88] = 2.87$, $P = .007$), with a robust effect size ($\eta_p^2 = .21$) (Table 1). Univariate contrasts revealed significant main effects of group in the AIC ($F[2,47] = 3.81$, $P = .029$, $\eta_p^2 = .14$), the DACC ($F[2,47] = 4.28$, $P = .020$, $\eta_p^2 = .15$), and the PPC ($F[2,47] = 5.08$, $P = .010$, $\eta_p^2 = .18$). *Post hoc* contrasts revealed that the OB group, when compared to NOL, had significantly thinner DACC ($P = .008$), PPC ($P = .004$), and AIC ($P = .009$). The SWLM were mostly intermediate between the NOL and OB groups. Compared to NOL, the SWLM showed trends towards thinner cortex in the PPC ($P = .040$), but did not differ significantly from the NOL or OB group in any regions.

4. Discussion

Building on our prior studies of obesity and weight loss maintenance, we chose a highly sensitive region-of-interest approach to test the hypothesis that cortical thickness in the cognitive control network (CCN) is associated with present or former obesity status. OB individuals exhibited significant thinning in the DACC, PPC, and the AIC when compared to NOLs. These findings appear to be regionally specific, as there were no group differences in total CSF, gray or white matter volume, overall cortical thickness, and thickness of two unrelated regions. Previous investigations have found smaller global and regional brain volumes in obese populations (Ho et al., 2010; Pannacciulli et al., 2006; Raji et al., 2010), however, perhaps due statistical power and other methodological considerations, we did not find global brain volumes differences. However, we provide the first known description of reduced cortical thickness associated with obesity specifically in CCN regions.

It is notable that the SWLMs tended to have thinner cortex than NOLs in nearly all regions, yet tended to have thicker cortex than the OBs. SWLM are frequent exercisers and rigorously monitor their food intake (McGuire et al., 1999), and recent work has shown that diet and exercise modification can lead to increases in brain volumes (e.g., Erickson et al., 2011). This suggests that lifestyle modifications necessary to maintain weight reduction may have beneficial effects on the central nervous system and may encourage gray matter recovery. However, the cross-sectional design of the study does not support any causal inferences, and our results may be related to pre-existing characteristics that enabled SWLM to be better dieters. This study highlights the need for prospective studies examining the association between long-term weight reduction and changes in brain structure and function. Other important limitations include our small sample size, no directly correlated behavioral data, and underrepresentation of males and ethnic minorities.

In conclusion we have detected structural differences in the CCN between OB and NOL, but not SWLM. These findings expand upon our prior studies with these same subjects showing differences between OB and SWLM in behavioral control and attention bias in response to food related stimuli (McCaffery et al., 2009; Phelan et al., 2011). Taken together, these preliminary results suggest an association between behavior, structural differences in the CCN, and past or present obesity status that should be explored in future studies.

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Table 1

Sample characteristics and morphology measures (M, SD).

Variable	Never obese lean (NOL)	SWLM	Obese (OB)	Overall <i>P</i> value
N	19	17	17	--
Female, %	89.5	88.2	88.2	.991
Age, years	43.6(8.4)	48.4(11.3)	47.8(7.6)	.171
Race, % White	100	94.4	82.4	.743
Education, levels ^a	5.9(1.1)	5.8(1.5)	5.3(1.4)	.404
Body Mass Index (kg/m ²)	21.7(1.9)	23.7(1.5)	34.0(3.6)	<0.001**
Lifetime highest BMI (kg/m ²)	22.8(2.1)	33.0(3.0)	35.4(3.5)	<0.001**
Current Smoker, %	5.3	5.9	0	.615
Antihypertensive medication, %	5.3	11.8	35.3	.054
Antidiabetic medication, %	10.5	0	0	.103
CESD Total	6.2(5.5)	5.2(5.7)	9.0(9.1)	.310
Total cortical gray matter volume, cm ³	479(42)	456(31)	467(46)	.374 ^b
Total white matter volume, cm ³	424(53)	412(48)	414(54)	.790 ^b
Total Cerebrospinal Fluid volume, cm ³	1164(277)	1044(210)	1275(276)	.243 ^b
Total mean cortical thickness, mm	2.52(.09)	2.48(.06)	2.52(.07)	.135
Comparison regions cortical thickness ^c , mm				
Occipital pole	2.12(.09)	2.11(.14)	2.08(.13)	.226
Postcentral gyrus	2.31(.09)	2.29(.17)	2.27(.13)	.282
Cognitive control network cortical thickness ^c , mm				
Dorsal Anterior Cingulate	2.73(.16)	2.63(.13)	2.59(.12) ^d	.020*
Dorsal Lateral Prefrontal	2.54(.16)	2.48(.12)	2.45(.11)	.154
Anterior Insular	2.85(.09)	2.82(.11)	2.74(.12) ^d	.029*
Posterior Parietal	2.55(.09)	2.48(.09) ^e	2.44(.10) ^d	.010*

^aEducation Levels, 1 = Grade School, 2 = Jr. High School, 3 = High School, 4 = Vocational Training, 5 = Some College, 6 = College, 7 = Graduate/Professional Degree,

^bCalculated using analysis of covariance with total intracranial volume as covariate,

^cCalculated using multivariate analysis of variance with age, gender, and antihypertensive medication as covariates,

^dObese vs. Never obese lean $P < .01$,

^eSWLM vs. Never obese lean trend at $P < .05$