RESEARCH ARTICLE

Neuroanatomical correlates of food addiction symptoms and body mass index in the general population

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Abstract

The food addiction model suggests neurobiological similarities between substance-related and addictive disorders and obesity. While structural brain differences have been consistently reported in these conditions, little is known about the neuroanatomical correlates of food addiction. We therefore aimed to determine whether symptoms of food addiction related to body mass index (BMI), personality, and brain structure in a large population-based sample. Participants of the LIFE-Adult study ($n = 625$; 20–59 years old, 45% women) answered the Yale Food Addiction Scale (YFAS) and further personality measures, underwent anthropometric assessments and high-resolution 3T-neuroimaging. A higher YFAS symptom score correlated with higher BMI, eating behavior traits, neuroticism, and stress. Higher BMI predicted significantly lower thickness of (pre)frontal, temporal and occipital cortex and increased volume of left nucleus accumbens. In a whole-brain analysis, YFAS symptom score was not associated with significant differences in cortical thickness or subcortical gray matter volumes. A hypothesis-driven Bayes factor analysis suggested a small, additional contribution of YFAS symptom score to lower right lateral orbitofrontal cortex thickness over the effect of BMI. Our study indicates that symptoms of food addiction do not account for the major part of the structural brain differences associated with BMI in the general population. Yet, symptoms of food addiction might explain additional variance in orbitofrontal cortex, a hub area of the reward network. Longitudinal studies implementing both anatomical and functional MRI could further disentangle the neural mechanisms of addictive eating behaviors.

KEYWORDS

body mass index, cohort studies, eating, food addiction, gray matter, neuroimaging, obesity

1 | INTRODUCTION

The food addiction model provides a theoretical framework that explains the development of obesity based on observed similarities between substance addictions and overeating behavior (Gearhardt,

Corbin, & Brownell, 2009; Randolph, 1956). Essentially, this model proposes that some individuals exhibit eating patterns, elicited by certain types of food, that resemble addictive behaviors with regard to loss of control over eating and continued food consumption despite harmful consequences (Schulte, Joyner, Potenza, Grilo, & Gearhardt, 2015; Volkow, Wang, Tomasi, & Baler, 2013). Yet, specific aspects and implications of the concept have been critically discussed (Fletcher & Kenny, 2018).

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Evidence in support of this hypothesis has been found in patients with eating disorders but also in epidemiological cohorts (Flint et al., 2014; Pedram et al., 2013) where self-reported food addiction correlated with higher body mass index (BMI) and other measures of obesity.

Previous neuroimaging studies have highlighted the putative role of the prefrontal cortex and dopamine-dependent fronto-striatal circuits in dysfunctional self-regulation which could underlie both substance-related and addictive disorders and pathological eating behavior (García-García et al., 2014). For example, positron emission tomography studies reported lower dopamine D2/D3 striatal receptor binding both in participants with substance-related and addictive disorders (Volkow, Wang, Fowler, & Telang, 2008) and in morbidly obese individuals (Wang et al., 2001). Indeed, in response to anticipated receipt of (rewarding) food, participants with food addiction showed altered reward-related brain activity in the dorsolateral and orbito-frontal cortex and in the caudate nucleus (Gearhardt et al., 2011).

Regarding structural variation in addictive disorders, several studies reported lower gray matter volume (GMV) in the inferior and superior frontal cortex, orbitofrontal cortex and medial occipital gyrus that discriminated stimulant-dependent individuals from nondependent controls (Ersche et al., 2012; Moreno-López et al., 2012). Lower GMV in middle and orbitofrontal areas also had a prognostic value in predicting alcohol dependence relapse after 12 months (Durazzo et al., 2011).

Similarly, obesity has been consistently associated with reduced GMV and lower cortical thickness in (pre)frontal cortex, temporal lobe and bilateral cerebellum (García-García et al., 2018; Kharabian Masouleh et al., 2016). Several studies in middle- to aged populations raised the hypothesis that the observed gray matter volume loss is mainly a consequence of adverse metabolic factors related to obesity (Willette & Kapogiannis, 2015). Low-grade inflammation and dysregulated glucose metabolism, for example, may trigger damage to nervous tissue and contribute to accelerated brain aging and an increased risk for dementia associated with obesity (Beydoun, Beydoun, & Wang, 2008). Another line of research suggests that altered gray matter structure in brain regions that govern aspects of eating behavior may represent a risk factor for weight gain and obesity (Opel et al., 2017; Yokum et al., 2011).

Taken together, according to the food addiction model, addictive-like eating behavior is one of multiple factors that contribute to obesity. Akin neurobiological mechanisms might underlie both substance-related and addictive disorders and obesity (García-García et al., 2014; Volkow et al., 2013) and possibly account for impulsive and compulsive behaviors in these disorders (Michaud, Vainik, García-García, & Dagher, 2017). Both addictive disorder and obesity are associated with alterations in gray matter structure, however, structural variation related to food addiction remains largely unexplored.

Therefore, we aimed to determine the relation of self-reported symptoms of food addiction with BMI and brain morphology in a large population-based cohort. We hypothesized that symptoms of food addiction were associated with structural alterations in fronto-striatal brain areas. In an exploratory approach, we conducted further analyses regarding anthropometric, eating behavior and personality measures. Here, we aimed to confirm our analyses by using alternative measures of obesity, such as the amount of visceral body fat assessed by abdominal MRI, instead of BMI. As previous studies proposed that certain maladaptive eating behaviors, such as disinhibited eating, correlated with

food addiction (Vainik, Neseliler, Konstabel, Fellows, & Dagher, 2015), we hypothesized that symptoms of food addiction related to these measures in our cohort. Food addiction symptoms have also been associated with negative emotionality (Markus, Rogers, Brouns, & Schepers, 2017) and we therefore investigated whether predisposing factors like personality factors or chronic stress would predict food addiction symptom scores in our sample (Gerlach, Herpertz, & Loeber, 2014; Torres & Nowson, 2007). We additionally assessed obesity-related differences in brain structure and compared the evidence for the involvement of BMI and symptoms of food addiction in selected regions of interest using a Bayesian statistical approach.

2 | METHODS

2.1 | Participants

All participants were enrolled in the “Health Study for the Leipzig Research Centre for Civilization Diseases” (LIFE-Adult) study (Loeffler et al., 2015). The Ethics Committee of the Medical Faculty of the University of Leipzig approved the study protocol and all participants provided written informed consent. We selected adult participants from the neuroimaging cohort ($n = 2,637$) with available head MRI and without history of neurological or psychiatric disease such as stroke, cancer, epilepsy, multiple sclerosis, and Parkinson's disease. We restricted the age range to younger and middle-aged participants (20–59 years old) to avoid overestimation of aging-related effects in the brain among participants older than 60 years (Storsve et al., 2014). Included participants did not take central nervous system agents and had complete data for the primary covariates Yale Food Addiction Scale (YFAS) and body mass index (BMI). Due to potential links between food addiction and depression (Flint et al., 2014), participants were excluded if they reported major depressive disorder in the last 12 months or scored >21 in the CES-D (Center for Epidemiological Studies-Depression) (Radloff, 1977). In total, 625 participants met inclusion criteria, and were included into the main analysis (see Figure 1; Table 1). Out of these, $n = 444$ underwent abdominal MRI

FIGURE 1 Flowchart showing the inclusion/exclusion criteria and variables of interest of the current study [Color figure can be viewed at wileyonlinelibrary.com]

and $n > 423$ completed further questionnaires assessing eating behavior and personality.

2.2 | Food addiction questionnaire

We measured symptoms of food addiction using the Yale Food Addiction scale (YFAS) (Gearhardt et al., 2009). This questionnaire applied the DSM-IV criteria for substance dependence to eating behavior. We selected the continuous food addiction symptom score ranging from 0 to 7 as the primary variable of interest in our analyses as only 6% of the population meet criteria for manifest food addiction (Flint et al., 2014), and food addiction, like other psychopathological traits, might be better represented in a continuum (Table 1) (Kozak & Cuthbert, 2016).

2.3 | Head magnetic resonance imaging

Anatomical T1 images were acquired using a 3 Tesla Siemens Verio MRI scanner (Siemens Healthcare, Erlangen, Germany) with a 3D MPRAGE protocol and the following parameters: inversion time, 900 ms; repetition time, 2,300 ms; echo time, 2.98 ms; flip angle, 9°; field of view, $256 \times 240 \times 176 \text{ mm}^3$; voxel size, $1 \times 1 \times 1 \text{ mm}^3$.

Cortical thickness was estimated using Freesurfer's standard pipeline recon-all (version 5.3.0) (Dale, Fischl, & Sereno, 1999). Cortical thickness data was smoothed with a Gaussian kernel of 10 mm full-width at half maximum on the fsaverage template. All images were visually checked for misplaced tissue boundaries and 56 images (~10%) were manually corrected. Three participants had to be excluded due to motion-related scan artifacts and segmentation errors.

Subcortical volumes for thalamus, caudate, putamen, pallidum, accumbens, hippocampus, and amygdala were obtained from automated labeling. For each subcortical structure, we extracted the volume for the right and left hemispheres separately and divided it by the total intracranial volume to account for head size. Two participants were identified as outliers and excluded due to enlarged ventricles and subcortical hyperintensities.

2.4 | Obesity-related variables

We used four anthropometric measures to characterize obesity (Amato, Guarnotta, & Giordano, 2013): (i) body mass index (BMI), (ii) waist-to-hip ratio (WHR), (iii) subcutaneous adipose tissue divided by height (SCAT), and (iv) visceral adipose tissue divided by height (VAT).

BMI was used as a main measure to reflect obesity, since it is widely reported in studies in the field. WHR was recorded since it is considered to reflect visceral fat deposition (Amato et al., 2013). In addition, a subgroup of participants ($n = 444$) underwent an abdominal T1-weighted MRI scan (Raschpichler et al., 2013). This acquisition covered the abdominal region starting 10 cm proximal and ending 10 cm distal from the umbilicus with a slice thickness of 5 cm. Sequence parameters can be found in the appendix. The subcutaneous and the visceral adipose tissues were quantified by means of semi-automated image segmentations and normalized by height (Raschpichler et al., 2013).

2.5 | Other eating behavior and personality questionnaires

We additionally characterized eating behavior by means of the Three Factor Eating Questionnaire (TFEQ) (Stunkard & Messick, 1985) which provides three measures of human eating behavior: (a) cognitive restraint of eating, (b) disinhibited eating, and (c) hunger. General personality traits were assessed with the short version of the NEO-FFI questionnaire, which provides measures for neuroticism, extraversion, openness, agreeableness, and conscientiousness (Körner et al., 2008).

Chronic stress was assessed with the screening scale of chronic stress (SSCS) from the Trierer Inventar zum Chronischen Stress (TICS) (Schulz, Schlotz, & Becker, 2004). CES-D (Center for Epidemiological Studies-Depression) scores were used for exclusion ($\text{CES-D} > 21$) and to control for subthreshold depressive symptoms (Radloff, 1977).

2.6 | Statistical analysis

For all statistical analyses, we used log-transformed values of the YFAS symptom score and the obesity-related variables (except WHR) to ensure normal distribution of regression residuals.

2.7 | Linear regression analysis of food addiction, obesity and personality measures

We used multiple regressions to explore associations between YFAS symptom score and the variables of interest (a) measures of obesity (b) eating behavior and personality, controlling for age, sex (with males as reference category) and BMI. Analyses were performed in R version 3.2.3.

2.8 | Cortical thickness and subcortical volume analysis

First, we performed a whole-brain analysis to detect associations of YFAS symptom score, BMI and cortical thickness using Freesurfer's `mri_glmfit`. In Model 1, we included YFAS symptom score, age and sex, in Model 2, we included BMI, age and sex and in Model 3 we assessed both YFAS symptom score, BMI, age, and sex.

Clusterwise correction for multiple comparisons based on pre-computed Monte-Carlo simulation was performed (cluster-forming threshold $p = 0.0001$, familywise error [FWE] corrected $p < 0.05$).

We applied the same statistical models in R (version 3.2.3) to analyze differences in subcortical volumes. Here, we accounted for multiple testing using Bonferroni correction ($\alpha_{BF} = 0.05/14 = 0.0036$) for the 14 regions of interest (7 per hemisphere).

2.9 | Region of interest analysis using Bayes factor

In order to understand the contribution of BMI and YFAS symptom score to fronto-striatal structural differences in more detail, we performed Bayes factor analysis using (orbito)frontal cortex and nucleus accumbens as ROIs. Here, we aimed to weight the evidence for a contribution of food addiction symptom scores, BMI or a combination of both to structural differences in brain regions within the reward network which were also previously related to food addiction (Maayan et al., 2011) and obesity (García-García et al., 2018; Opel et al., 2017).

TABLE 1 Demographic characteristics and psychological measures of the sample (n = 625, sex distribution: 344 men and 281 women)

	n	Minimum	Maximum	Mean	Std. deviation
Age (years)	625	20	59	40.6	10.8
Food addiction symptom score (YFAS)	625	0	5	1.4	0.9
Depression scores (CES-D)	625	0	21	8.4	4.6
BMI (kg/m ²)	625	17.7	55.4	25.7	4.5
Weight groups (underweight/normal weight/overweight/obese)	3/307/222/93				
WHR	625	0.64	1.17	0.89	0.09
VAT (mm ³ /cm)	444	0.7	42.4	10.1	7.5
SCAT (mm ³ /cm)	444	1.36	88.8	21.6	12.1
Cognitive restraint (TFEQ, 0–21)	623	0	20	6.4	4.2
Disinhibited eating (TFEQ, 0–16)	623	0	15	4.4	2.7
Hunger (TFEQ, 0–14)	623	0	13	3.6	2.7
Neuroticism (NEOFFI, 0–4)	435	0	3.7	1.4	0.7
Extraversion (NEOFFI, 0–4)	435	0.8	3.8	2.4	0.5
Openness (NEOFFI, 0–4)	435	0.7	3.7	2.3	0.6
Agreeableness (NEOFFI, 0–4)	435	0.8	4.0	2.9	0.6
Conscientiousness (NEOFFI, 0–4)	435	1.5	4.0	3.1	0.5
Screening scale of chronic stress (TICS, range 0–48)	423	0	37	13.9	7.1

Note. BMI: body mass index; SCAT: subcutaneous adipose tissue; VAT: visceral adipose tissue; WHR: waist-to-hip ratio.

Bayes factors (BF) quantify how likely the data are to occur under the assumption of one model compared to another (Kass & Raftery, 1995). More precisely, the Bayes factor BF_{12} is calculated as the ratio of the likelihood of the data given Model 1 over the likelihood of the data given Model 2. According to (Kass & Raftery, 1995), a BF_{12} between 3 and 20 indicates positive evidence for Model 1 over Model 2, a BF_{12} between 20 and 150 indicates strong, and a $BF_{12} > 150$ indicates very strong evidence for Model 1 over Model 2.

Here, we first compared Model 1 (including age, sex and YFAS symptom score) and Model 2 (including age, sex, and BMI) to a null model including only age and sex. If this comparison yielded positive evidence for either BMI or YFAS symptom score (defined as a Bayes Factor > 3 , Kass & Raftery, 1995), we additionally compared the models including YFAS symptom score and BMI alone (adjusted for age and sex, Model 1 vs. Model 2), and the model including BMI along with YFAS symptom score to the model including BMI alone (adjusted for age and sex, Model 3 vs. Model 2). To assess the collinearity of age, BMI and YFAS symptom score, we calculated the variance inflation factor (VIF) with the package “car” 2.1-3 in R.

We extracted individual cortical thickness values based on the Desikan-Killiany parcellation in Freesurfer for lateral OFC and medial OFC, rostral and superior frontal cortex on both hemispheres. Nucleus accumbens volume was normalized by the total intracranial volume.

We used the package “BayesFactor” version 0.9.12 in R version 3.2.3 to calculate and compare Bayes factors.

3 | RESULTS

3.1 | Sample characteristics

The items of the YFAS showed an acceptable internal consistency in the current sample of 625 healthy adults (Cronbach's $\alpha = 0.78$). YFAS symptom score was not significantly associated with age, sex or

FIGURE 2 Relations between age (a), sex (b), CES-D depression score (c) and YFAS symptom scores in the investigated sample, visualized on the raw data. YFAS: Yale food addiction scale; CES-D: Center for Epidemiological Studies-Depression [Color figure can be viewed at wileyonlinelibrary.com]

FIGURE 3 Association of YFAS symptom score (log-transformed) and (a) body mass index (BMI, log-transformed); (b) waist-to-hip ratio (WHR); (c) subcutaneous adipose tissue (SCAT, log-transformed); and (d) visceral adipose tissue (VAT, log-transformed). The regression coefficient B and confidence interval (C.I.) are based on the multiple regression analysis accounting for age and sex [Color figure can be viewed at wileyonlinelibrary.com]

depression scores (all $p > 0.05$) (see Figure 2). Fifty-six participants (8.9%) showed three or more symptoms of food addiction. Among those, eight participants (1.3%) fulfilled the diagnosis criteria for food addiction and additionally reported clinical impairment or distress (Gearhardt et al., 2009).

3.2 | Food addiction symptoms and obesity-related measurements

YFAS symptom score predicted BMI and WHR in the multiple regression analyses independent of age and sex. In the subgroup of participants with MRI-based measures of abdominal fat ($n = 444$), we also found that YFAS symptom score was positively associated with SCAT but not VAT (see Figure 3; Table 2).

3.3 | Relationship between food addiction symptoms, eating behavior and personality

In the multiple regression analyses, YFAS symptom scores explained variance in disinhibited eating (TFEQ), hunger (TFEQ), neuroticism (NEO-FFI) and chronic stress (TICS) after accounting for the effect of age, sex and BMI. In the four analyses, the directionality of the relation was positive (see Figure 4; Table 3).

3.4 | Food addiction symptoms, BMI and cortical thickness

There was no statistically significant association of YFAS symptom score and cortical thickness using Model 1 (adjusting for age and sex) and Model 3 (additionally adjusting for BMI) (whole-brain FWE-corrected all $p_{\text{cluster}} > 0.05$).

Model 2 revealed significant associations of BMI and cortical thickness adjusting for age and sex. Higher BMI was associated with cortical thinning in right lateral orbitofrontal cortex (OFC), rostral

TABLE 2 Multiple regression analyses predicting different obesity-related measurements as a function of age, sex, and YFAS symptom score. B/beta represent unstandardized/standardized regression coefficients

	Adj. R^2	B	C.I.	β	p
BMI					
Model	0.22				<0.001
Age		0.0027	[0.0022, 0.0032]	0.41	<0.001
Sex		-0.03	[-0.04, -0.02]	-0.18	<0.001
YFAS symptom score		0.08	[0.04, 0.11]	0.16	<0.001
WHR					
Model	0.51				<0.001
Age		0.0035	[0.003, 0.0039]	0.42	<0.001
Sex		-0.10	[-0.11, -0.09]	-0.56	<0.001
YFAS symptom score		0.06	[0.03, 0.09]	0.10	<0.001
SCAT					
Model	0.23				<0.001
Age		0.0082	[0.0065, 0.01]	0.39	<0.001
Sex		0.13	[0.09, 0.17]	0.27	<0.001
YFAS symptom score		0.22	[0.10, 0.35]	0.15	<0.001
VAT					
Model	0.54				<0.001
Age		0.019	[0.018, 0.022]	0.63	<0.001
Sex		-0.25	[-0.29, -0.21]	-0.36	<0.001
YFAS symptom score		0.09	[-0.05, 0.24]	0.041	0.19

FIGURE 4 Association of YFAS symptom score (log-transformed) and (a) body mass index (BMI, log-transformed); (b) waist-to-hip ratio (WHR); (c) subcutaneous adipose tissue (SCAT, log-transformed); and (d) visceral adipose tissue (VAT, log-transformed). The regression coefficient B and confidence interval (C.I.) are based on the multiple regression analysis accounting for age and sex [Color figure can be viewed at wileyonlinelibrary.com]

middle frontal, parahippocampal, isthmus cingulate and left lateral occipital cortex and middle and superior temporal cortex (see Figure 5, Supporting Information Table S1). When adjusting for YFAS

symptom score (Model 3), all clusters except for the cluster in the isthmus cingulate remained significantly associated with BMI (see Supporting Information Table S1).

TABLE 3 Multiple regression analyses predicting different eating behavior and personality measurements as a function of age, sex, YFAS symptom score, and BMI. Significant coefficients ($p < 0.05$) are shown in bold. B/beta represent unstandardized/standardized regression coefficients

	Adj. R^2	B	C.I.	β	p
Dependent variable: disinhibited eating (TFEQ)					
Model	0.19				<0.001
Age		-0.068	[-0.088, -0.049]	-0.27	<0.001
Sex		1.16	[0.77, 1.56]	0.22	<0.001
YFAS symptom score		2.8	[1.5, 4.1]	0.16	<0.001
Body mass index		13.9	[10.8, 16.9]	0.37	<0.001
Dependent variable: hunger (TFEQ)					
Model	0.073				<0.001
Age		-0.051	[-0.072, -0.03]	-0.20	<0.001
Sex		0.31	[-0.11, 0.73]	0.057	0.15
YFAS symptom score		3.2	[1.8, 4.5]	0.18	<0.001
Body mass index		5.4	[2.2, 8.7]	0.14	0.0012
Dependent variable: neuroticism (NEOFFI)					
Model	0.073				<0.001
Age		-0.006	[-0.013, 0.001]	-0.091	0.076
Sex		0.28	[0.16, 0.42]	0.21	<0.001
YFAS symptom score		0.72	[0.3, 1.14]	0.16	<0.001
Body mass index		-0.2	[-1.21, 0.81]	-0.02	0.69
Dependent variable: screening scale for chronic stress (TICS)					
Model 1	0.035				<0.001
Age		-0.006	[-0.08, 0.07]	-0.009	0.86
Sex		1.3	[-0.07, 2.7]	0.091	0.061
YFAS symptom score		8.3	[3.9, 12.7]	0.18	0.002
Body mass index		-4.1	[-14.7, 6.6]	-0.041	0.45

FIGURE 5 Higher BMI was associated with lower cortical thickness in the right lateral OFC, rostral middle frontal cortex, parahippocampal, isthmus cingulate and left lateral occipital, middle and superior temporal cortex after correcting for age and sex. The color bar represents the $\log_{10}(p)$ values at each vertex projected onto the Freesurfer average brain [Color figure can be viewed at wileyonlinelibrary.com]

3.5 | Food addiction symptoms, BMI and subcortical gray matter volumes

No significant correlations between YFAS symptom scores and subcortical volumes emerged after age, sex (Model 1) and age, sex and BMI correction (Model 3) (corrected for multiple comparisons, all $p > 0.0036$). BMI was significantly positively associated with increased left accumbens volume after correction for multiple comparisons (Model 2: standardized $\beta = 0.15$, $p < 0.001$, Model 3: standardized $\beta = 0.14$, $p = 0.002$) (see Table 4).

3.6 | Bayesian model comparison

For the predefined regions of interest (right and left medial and lateral OFC, superior frontal and rostral middle frontal cortex, nucleus accumbens), we compared the evidence for models including age, sex and (a) YFAS symptom score (Model 1) (b) BMI (Model 2) and (c) BMI and YFAS symptom score (Model 3) using Bayes factors (see Table 5).

The variance inflation factors of age, BMI, and YFAS were 1.22, 1.29, and 1.03, respectively.

For the right medial OFC, the analysis provided evidence in favor of Model 2 including BMI, age, and sex compared to the null model including only age and sex ($BF_{20} = 266$) and compared to Model 1 including YFAS symptom score, age and sex ($BF_{10} = 52$). There was no difference between Model 2 and Model 3 including both BMI and YFAS symptom score, as well as age and sex ($BF_{32} = 0.86$).

In case of the right lateral OFC, there was very strong evidence for Model 2 including BMI, age and sex ($BF_{20} = 1997$). Strong evidence also suggested Model 1 including YFAS, age and sex ($BF_{10} = 107$), however when comparing the age and sex-adjusted Model 2 with Model 1, Model 2 including BMI was preferred ($BF_{21} = 18$). Positive evidence suggested including both YFAS and BMI in Model 3 compared to Model 2 including only BMI ($BF_{32} = 11$).

For right superior frontal, rostral middle frontal cortex and nucleus accumbens, the null hypothesis was preferred over age and sex-adjusted Models 1 and 2 including BMI or YFAS symptom score (all BF of comparison against null $< 1/3$).

Regarding the left hemisphere, no positive evidence for an association of BMI or YFAS symptom score and OFC or frontal cortical thickness was found (all BF of comparisons against null $< 1/3$). In line with the linear regression, a Bayes factor of 48 suggested strong evidence for an association of BMI and left nucleus accumbens volume which was more likely than Model 1 including YFAS symptom score alone ($BF_{21} = 28$). Including both BMI and YFAS in Model 3 yielded a model that was equally likely than Model 2 ($BF_{32} = 1.16$).

4 | DISCUSSION

YFAS symptom score explained inter-individual variance in obesity measures, uncontrolled eating behavior and negative emotionality in a population-based cohort of 625 participants. Higher BMI was independently associated with reduced cortical thickness in right prefrontal, orbitofrontal, parahippocampal, left temporal and occipital cortex and increased left nucleus accumbens volume. In a whole brain approach, YFAS symptom score was not significantly associated with cortical thickness. Yet, a hypothesis-driven Bayes factor ROI analyses suggested a small contribution of YFAS symptom score to the cortical thickness of right lateral OFC, in addition to BMI.

4.1 | Neural correlates of symptoms of food addiction and BMI

In this well-powered analysis, we found no statistically significant association of YFAS symptom score and cortical thickness on a whole-brain level. Similarly, subcortical volumes were not associated

TABLE 4 Multiple regression analyses predicting subcortical volumes using Model 1 (age, sex, YFAS symptom score), Model 2 (age, sex, BMI), and Model 3 (age, sex, BMI, YFAS symptom score)

	R^2	β	p
Dependent variable: left putamen			
Model	0.13		<0.001
Age		−0.37	<0.001
Sex		0.035	0.54
Model 1/3: YFAS symptom score		0.078/0.068	0.03/0.07
Model 2/3: body mass index		0.073/0.059	0.08/0.16
Dependent variable: left thalamus			
Model	0.004		0.17
Dependent variable: left caudate			
Model	0.086		<0.001
Age		−0.27	<0.001
Sex		0.13	0.02
YFAS symptom score (Model 1/3)		0.005/0.006	0.89/0.87
Body mass index (Model 2/3)		−0.008/−0.09	0.84/0.83
Dependent variable: left accumbens			
Model	0.09		<0.001
Age		−0.32	<0.001
Sex		0.13	0.001
YFAS symptom score (Model 1/3)		0.08/0.06	0.02/0.09
Body mass index (Model 2/3)		0.15/0.13	<0.001/0.002
Dependent variable: left amygdala			
Model	<0.001		0.74
Dependent variable: left pallidum			
Model	0.023		0.002
Age		−0.11	0.008
Sex		0.08	0.04
YFAS symptom score (Model 1/3)		0.07/0.07	0.08/0.08
Body mass index (Model 2/3)		0.007/−0.006	0.9/0.9
Dependent variable: left hippocampus			
Model	0.042		<0.001
Age		−0.0028	0.95
Sex		0.19	<0.001
YFAS symptom score (Model 1/3)		0.021/0.034	0.59/0.39
Body mass index (Model 2/3)		−0.073/−0.08	0.09/0.07
Dependent variable: right putamen			
Model	0.19		<0.001
Age		−0.45	<0.001
Sex		0.05	0.19
YFAS symptom score (Model 1/3)		0.05/0.05	0.15/0.16
Body mass index (Model 2/3)		0.015/0.005	0.7/0.9

(Continues)

TABLE 4 (Continued)

	R^2	β	p
Dependent variable: right thalamus			
Model	0.04		<0.001
Age		−0.21	<0.001
Sex		−0.02	0.56
YFAS symptom score (Model 1/3)		0.08/0.08	0.05/0.05
Body mass index (Model 2/3)		0.008/−0.007	0.9/0.9
Dependent variable: right caudate			
Model	0.09		<0.001
Age		−0.28	<0.001
Sex		0.15	<0.001
YFAS symptom score (Model 1/3)		−0.013/−0.015	0.7/0.7
Body mass index (Model 2/3)		0.012/0.015	0.8/0.7
Dependent variable: right accumbens			
Model	0.10		<0.001
Age		−0.28	<0.001
Sex		0.17	<0.001
YFAS symptom score (Model 1/3)		0.04/0.04	0.3/0.3
Body mass index (Model 2/3)		0.02/0.02	0.8/0.8
Dependent variable: right amygdala			
Model	0.005		0.14
Dependent variable: right pallidum			
Model	0.03		<0.001
Age		−0.13	0.001
Sex		−0.02	0.49
YFAS symptom score (Model 1/3)		−0.04/−0.02	0.3/0.5
Body mass index (Model 2/3)		−0.09/−0.09	0.03/0.05
Dependent variable: right hippocampus			
Model	0.037		<0.001
Age		−0.01	0.81
Sex		0.20	<0.001
Food addiction (Model 1/3)		0.011/0.012	0.78/0.75
Body mass index (Model 2/3)		−0.010/−0.012	0.82/0.77

Note. Adjusted R^2 and standardized regression coefficient (β) of age and sex are given for Model 3. If the overall fit was not significant regression coefficients are not shown. Regression coefficients for YFAS symptom score/BMI derived from Model 3 are underlined. Significant coefficients ($p < 0.0036$) are shown in bold.

with YFAS symptom score. Regarding obesity, our analysis largely confirmed previous findings of BMI-associated reduced gray matter volume/cortical thickness. We replicated consistently reported lower gray matter volume in the right medial prefrontal cortex related to obesity, more specifically in its rostral subdivision and the orbitofrontal cortex (García-García et al., 2018). BMI was also associated with reduced cortical thickness in right parahippocampal, left temporal and

TABLE 5 Results from the Bayesian model comparison between the Yale food addiction scale (YFAS) symptom score and body mass index (BMI) for gray matter volume/cortical thickness in predefined regions of interest

		Bayes factors				
		YFAS vs. null (Model 1): BF ₁₀	BMI vs. null (Model 2): BF ₂₀	Model 1 vs. 2 comparison: BF ₂₁	BMI + YFAS vs. null (Model 3): BF ₃₀	Model 2 vs. 3 comparison: BF ₃₂
Rh	Medial OFC	5	266	Favors Model 2: 52	309	Equal support: 0.86
	Lateral OFC	107	1997	Favors Model 2: 18	21,898	Favors Model 3: 11
	Superior frontal	0.14	0.59			
	Rostral middlefrontal	0.28	2			
	Nucleus accumbens	0.15	0.24			
Lh	Medial OFC	0.33	0.38			
	Lateral OFC	0.28	2.57			
	Superior frontal	0.11	0.51			
	Rostral middle frontal	0.11	0.2			
	Nucleus accumbens	48	1.69	Favors Model 2: 28	29	Equal support: 1.6

Note. Bayes factors indicating strong evidence (BF >20) are shown in bold. lh: left hemisphere; OFC: orbitofrontal cortex; rh: right hemisphere.

lateral occipital regions. We found a small positive association of BMI and increased left accumbens volume. This finding is in line with other studies (Coveleskie et al., 2015; Horstmann et al., 2011; Veit et al., 2014) and might reflect previously reported differences in reward processing in obesity (García-García et al., 2014; Horstmann, Fenske, & Hankir, 2015). Yet, volumetric differences in nucleus accumbens in relation to eating behavior or obesity seem to be less consistent than functional alterations (de Groot et al., 2015) and therefore require further investigation. All findings related to BMI remained essentially unaltered after adjusting for YFAS symptom score. This indicates that addictive-like eating behavior does not account for the major part of structural differences related to obesity in the general population.

Accordingly, the model comparison using Bayes factors indicated that BMI rather than YFAS symptom score explained cortical thinning in frontal regions of the right hemisphere, and increased volume of the left nucleus accumbens. For the right lateral OFC, the data however supported a model including YFAS symptom score alone, though this was 20 times less likely. Yet, positive evidence indicated that both BMI and YFAS symptom score might be associated with cortical thinning in this region. These—compared to the whole-brain analysis—somewhat conflicting findings should be interpreted cautiously. On the one hand, the evidence based on Bayes factors in the ROI analysis still seems rather moderate, rendering a definite conclusion about the association of YFAS symptom score and OFC thickness difficult. On the other hand, a smaller effect size of YFAS symptom score compared to BMI or other factors such as age and sex, as well as the collinearity of BMI and YFAS symptom score, might have masked a significant effect of food addiction symptoms.

The OFC is a cardinal structure in our understanding of impulsive- and/or compulsive-related behavior (Burguière, Monteiro, Feng, & Graybiel, 2013; Zeeb, Floresco, & Winstanley, 2010). Structural alterations in the OFC have been associated with impaired ability for goal-directed behavior and impulsivity (Reber et al., 2017) and several studies reported diminished cortical thickness or GMV in the OFC of individuals with substance-related disorders (Durazzo et al., 2011; Ersche et al., 2012).

More specific to overeating behaviors, reduced OFC gray matter volume and thickness have been related to less restrained eating (Su,

Jackson, Wei, Qiu, & Chen, 2017) and unhealthy food choice (Cohen, Yates, Duong, & Convit, 2011), although one study reported larger OFC volume in binge-eating disorder patients compared to healthy controls (Schäfer, Vaitl, & Schienle, 2010). First evidence suggests that individual differences in OFC thickness partly mediate the genetic risk for obesity (Opel et al., 2017), possibly by provoking, or failing to inhibit, impulsive and compulsive (eating) behavior. Subsequent intake of high fat diet, weight gain and adverse metabolic consequences of obesity, such as increased low-grade inflammation or progressive insulin resistance, might further harm brain tissue (Corlier et al., 2018; Dingess, Darling, Kurt Dolence, Culver, & Brown, 2017; Shaw, Nettersheim, Sachdev, Anstey, & Cherbuin, 2017; Thompson et al., 2017). In this vicious cycle, structural damage to frontal brain regions would contribute to more impulsive and compulsive eating behavior, and lead to even more weight gain or reduced dieting success (DelParigi et al., 2007; Schmidt et al., 2018).

Taken together, even though an association of reduced OFC thickness and addictive-like eating behavior seems plausible and is somewhat supported by the data, the current cross-sectional study provides evidence for a negative association of BMI and (orbito)frontal cortex thickness, largely independent of symptoms of food addiction. Future studies investigating the neurobiological mechanisms underlying food addiction and obesity should therefore acquire longitudinal data, include more sensitive assessments of addictive-like or uncontrolled eating behavior (Vainik et al., 2015) and investigate brain function, rather than structure, related to these eating behaviors, for example using task-based functional MRI.

4.2 | Symptoms of food addiction related to obesity and personality

Although the percentage of participants with high YFAS symptom score is low in general populations (Pedram et al., 2013), addictive-like processes might contribute to the high prevalence of obesity in modern societies. A previous study, for instance, reported that participants tend to experience food addiction symptoms in relation to high-fat and sweet or savory foods (Markus et al., 2017). This result suggests that homeostatic mechanisms might be overwritten in favor of hedonic or

habit-based eating. Such ingestive behavior might ultimately lead to weight gain. In line with these observations, we obtained modest but consistent positive correlations between the YFAS symptom score and different measures of obesity. Further, our findings of linear relationships between YFAS symptom scores and obesity measures highlight that “food addiction” per se might rather be regarded as a dimensional trait which, like other psychopathological traits, might not fit traditional 1 versus 0 (“all or none”) diagnostic categories (Kozak & Cuthbert, 2016). Our results support a certain collinearity between obesity and food addiction (Pedram et al., 2013). Thus, taking into account individual tendencies for addictive-like eating behaviors might inform clinical approaches targeting trans-diagnostic symptoms of addictive behaviors, such as heightened impulsivity or compulsivity.

In the present study, higher YFAS symptom score was also associated with increased scores in disinhibited eating and hunger, two scales that reflect overeating and subjective food cravings, respectively. It is indeed possible that symptoms of food addiction, disinhibited eating and hunger are partly overlapping scales, since they all do represent hyperphagia and loss of control over eating. In fact, some authors have suggested that different eating-related questionnaires tend to capture individual variations in “uncontrolled eating”, a dimension reflecting decreased self-control over eating (Vainik et al., 2015).

We additionally observed that YFAS symptom score predicted neuroticism, a personality trait linked with increased sensitivity to punishment and for negative emotionality (Körner et al., 2008). This result is in line with previous findings suggesting that increases in depressive symptoms or emotional dysregulation significantly contribute to food addiction (Markus et al., 2017; Pivarunas & Conner, 2015). Again, the relationship between negative emotionality and symptoms of food addiction could be reciprocal. A longitudinal study on a large cohort of female adolescents observed that depressive symptoms at baseline predicted the development of overeating behavior, while overeating behavior also predicted the onset of depressive symptoms (Skinner, Haines, Austin, & Field, 2012). Note that in the current analyses, we avoided confounding of potential manifest depression by excluding participants with CES-D scores >21 and the majority of those were females. Notably, we did not observe sex differences in the YFAS symptom score, which might point to a similar prevalence of food addiction symptoms in both women and men. However, please note that we excluded participants with neurological and psychiatric disorder and focused on a healthy cohort. In this rather homogenous sample, presumable sex differences in food addiction, as seen in many psychiatric disorders (Dohrenwend & Dohrenwend, 1976), might have been masked out.

4.3 | Methodological considerations

We would like to acknowledge three important limitations of the current study. First, we assessed addictive-like eating behavior with the YFAS symptom score, which has a limited range (0–7) with relatively little variation in this population-based sample. It might therefore lack sensitivity for inter-individual differences in impulsive-compulsive eating behavior (Vainik et al., 2015). In addition, more complex associations such as interactions between BMI and food addiction symptoms might not have been detected in this sample that included only 15%

obese individuals and 9% individuals with three or more symptoms of food addiction. Second, we collected no measurement for binge eating behavior. Food addiction presents some clinical overlap with binge eating disorder, since both conditions entail loss of control over food consumption along with continued use despite adverse consequences (Vainik et al., 2015). Third, we cannot conclude on the directionality of the associations due the cross-sectional nature of our study. Strengths of our study include a large, well-characterized population-based sample with high-resolution cranial MRI, several proxies of obesity including highly sensitive MRI-derived estimates of abdominal and subcutaneous fat, extensive questionnaires, and strict controls for possible confounding effects in the statistical analyses.

4.4 | Conclusions and outlook

The present study showed no association of food addiction symptoms and cortical thickness in a whole brain analysis. ROI-based Bayesian analysis suggested that BMI and YFAS symptom score might be independently negatively associated with right lateral OFC thickness. We confirmed previous findings of BMI-related cortical thinning in frontal, temporal and occipital brain regions. Our findings indicate that symptoms of food addiction do not account for the major part of the structural differences commonly associated with obesity. Therefore, one plausible interpretation of our cross-sectional finding is that obesity-associated differences in brain morphology represent consequences of metabolic factors related to obesity, even in young to middle-aged healthy adults. Considering the overall low intensity of addictive-like eating behavior in our cohort, it is also possibly that subtle functional rather than gross structural differences in frontal or striatal brain regions drive these behaviors (Romer, Su Kang, Nikolova, Gearhardt, & Hariri, 2018). Finally, it is also possible, that a vicious cycle relates structural differences, addictive-like eating behavior and obesity. In this view, structural differences in frontal brain regions, either genetically determined or induced by obesity-related factors, might exacerbate impulsive and compulsive aspects of eating behavior, similar as in addictive disorders, and thereby lead to weight gain or reduced dieting success (DelParigi et al., 2007). Thus, strategies aiming to reduce impulsive and compulsive eating behaviors might be beneficial in the treatment of obesity.

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REFERENCES

- Amato, M., Guarnotta, V., & Giordano, C. (2013). Body composition assessment for the definition of cardiometabolic risk. *Journal of Endocrinological Investigation*, 36, 537–543.
- Beydoun, M. A., Beydoun, H. A., & Wang, Y. (2008). Obesity and central obesity as risk factors for incident dementia and its subtypes: A systematic review and meta-analysis. *Obesity Reviews*, 9, 204–218.
- Burguière, E., Monteiro, P., Feng, G., & Graybiel, A. M. (2013). Optogenetic stimulation of lateral orbitofronto-striatal pathway suppresses compulsive behaviors. *Science*, 340, 1243–1246.
- Cohen, J. I., Yates, K. F., Duong, M., & Convit, A. (2011). Obesity, orbitofrontal structure and function are associated with food choice: A cross-sectional study. *BMJ Open*, 1, e000175.
- Corlier, F., Hafzalla, G., Faskowitz, J., Kuller, L. H., Becker, J. T., Lopez, O. L., ... Braskie, M. N. (2018). Systemic inflammation as a predictor of brain aging: Contributions of physical activity, metabolic risk, and genetic risk. *NeuroImage*, 172, 118–129.
- Coveleskie, K., Gupta, A., Kilpatrick, L. A., Mayer, E. D., Ashe-McNalley, C., Stains, J., ... Mayer, E. A. (2015). Altered functional connectivity within the central reward network in overweight and obese women. *Nutrition & Diabetes*, 5, e148.
- Dale, A. M., Fischl, B., & Sereno, M. I. (1999). Cortical surface-based analysis: I. Segmentation and surface reconstruction. *Neuroimage*, 9, 179–194.
- de Groot, C., Feliuss, A., Trompet, S., de Craen, A. J. M., Blauw, G. J., van Buchem, M. A., ... van der Grond, J. (2015). Association of the fat mass and obesity-associated gene risk allele, rs9939609A, and reward-related brain structures. *Obesity*, 23, 2118–2122.
- DelParigi, A., Chen, K., Salbe, A. D., Hill, J. O., Wing, R. R., Reiman, E. M., & Tataranni, P. A. (2007). Successful dieters have increased neural activity in cortical areas involved in the control of behavior. *International Journal of Obesity*, 31, 440.
- Dingess, P. M., Darling, R. A., Kurt Dolence, E., Culver, B. W., & Brown, T. E. (2017). Exposure to a diet high in fat attenuates dendritic spine density in the medial prefrontal cortex. *Brain Structure and Function*, 222, 1077–1085.
- Dohrenwend, B. P., & Dohrenwend, B. S. (1976). Sex differences and psychiatric disorders. *American Journal of Sociology*, 81, 1447–1454.
- Durazzo, T. C., Tosun, D., Buckley, S., Gazdzinski, S., Mon, A., Fryer, S. L., & Meyerhoff, D. J. (2011). Cortical thickness, surface area, and volume of the brain reward system in alcohol dependence: Relationships to relapse and extended abstinence. *Alcoholism: Clinical and Experimental Research*, 35, 1187–1200.
- Ersche, K. D., Jones, P. S., Williams, G. B., Turton, A. J., Robbins, T. W., & Bullmore, E. T. (2012). Abnormal brain structure implicated in stimulant drug addiction. *Science*, 335, 601–604.
- Fletcher, P. C., & Kenny, P. J. (2018). Food addiction: A valid concept? *Neuropsychopharmacology*, 43, 2506–2513.
- Flint, A. J., Gearhardt, A. N., Corbin, W. R., Brownell, K. D., Field, A. E., & Rimm, E. B. (2014). Food-addiction scale measurement in 2 cohorts of middle-aged and older women. *The American Journal of Clinical Nutrition*, 99, 578–586.
- García-García, I., Horstmann, A., Jurado, M. A., Garolera, M., Chaudhry, S. J., Margulies, D. S., ... Neumann, J. (2014). Reward processing in obesity, substance addiction and non-substance addiction. *Obesity Reviews*, 15, 853–869.
- García-García, I., Michaud, A., Dadar, M., Zeighami, Y., Neseliler, S., Collins, D. L., ... Dagher, A. (2018). Neuroanatomical differences in obesity: Meta-analytic findings and their validation in an independent dataset. *International Journal of Obesity*. <https://doi.org/10.1038/s41366-018-0164-4DO>
- Gearhardt, A. N., Corbin, W. R., & Brownell, K. D. (2009). Preliminary validation of the Yale food addiction scale. *Appetite*, 52, 430–436.
- Gearhardt, A. N., Yokum, S., Orr, P. T., Stice, E., Corbin, W. R., & Brownell, K. D. (2011). Neural correlates of food addiction. *Archives of General Psychiatry*, 68, 808–816.
- Gerlach, G., Herpertz, S., & Loeber, S. (2014). Personality traits and obesity: A systematic review. *Obesity Reviews*, 16, 32–63.
- Horstmann, A., Busse, F., Mathar, D., Mueller, K., Lepsien, J., Schloegl, H., ... Pleger, B. (2011). Obesity-related differences between women and men in brain structure and goal-directed behavior. *Frontiers in Human Neuroscience*, 5, 58.
- Horstmann, A., Fenske, W. K., & Hankir, M. K. (2015). Argument for a non-linear relationship between severity of human obesity and dopaminergic tone. *Obesity Reviews*, 16, 821–830.
- Kass, R. E., & Raftery, A. E. (1995). Bayes factors. *Journal of the American Statistical Association*, 90, 773–795.
- Kharabian Masouleh, S., Arélin, K., Horstmann, A., Lampe, L., Kipping, J. A., Luck, T., et al. (2016). Higher body mass index in older adults is associated with lower gray matter volume: Implications for memory performance. *Neurobiology of Aging*, 40, 1–10.
- Körner, A., Geyer, M., Roth, M., Drapeau, M., Schmutzer, G., Albani, C., ... Brähler, E. (2008). Personality assessment with the NEO-five-factor inventory: The 30-item-short-version (NEO-FFI-30). *Psychotherapie, Psychosomatik, Medizinische Psychologie*, 58, 238–245.
- Kozak, M. J., & Cuthbert, B. N. (2016). The NIMH research domain criteria initiative: Background, issues, and pragmatics. *Psychophysiology*, 53, 286–297.
- Loeffler, M., Engel, C., Ahnert, P., Alfermann, D., Arelin, K., Baber, R., et al. (2015). The LIFE-Adult-Study: objectives and design of a population-based cohort study with 10,000 deeply phenotyped adults in Germany. *BMC Public Health*, 15, 691.
- Maayan, L., Hoogendoorn, C., Sweat, V., & Convit, A. (2011). Disinhibited Eating in Obese Adolescents Is Associated With Orbitofrontal Volume Reductions and Executive Dysfunction. *Obesity*, 19, 1382–1387.
- Markus, C. R., Rogers, P. J., Brouns, F., & Schepers, R. (2017). Eating dependence and weight gain; no human evidence for a 'sugar-addiction' model of overweight. *Appetite*, 114, 64–72.
- Michaud, A., Vainik, U., Garcia-Garcia, I., & Dagher, A. (2017). Overlapping neural Endophenotypes in addiction and obesity. *Frontiers in Endocrinology (Lausanne)*, 8, 127.
- Moreno-López, L., Catena, A., Fernández-Serrano, M. J., Delgado-Rico, E., Stamatakis, E. A., Pérez-García, M., et al. (2012). Trait impulsivity and prefrontal gray matter reductions in cocaine dependent individuals. *Drug Alcohol Depend*, 125, 208–214.
- Opel, N., Redlich, R., Kaehler, C., Grotegerd, D., Dohm, K., Heindel, W., ... Arolt, V. (2017). Prefrontal gray matter volume mediates genetic risks for obesity. *Molecular Psychiatry*, 22, 703–710.
- Pedram, P., Wadden, D., Amini, P., Gulliver, W., Randell, E., Cahill, F., ... Zhai, G. (2013). Food addiction: Its prevalence and significant association with obesity in the general population. *PLoS One*, 8, e74832.
- Pivarunas, B., & Conner, B. T. (2015). Impulsivity and emotion dysregulation as predictors of food addiction. *Eating Behaviors*, 19, 9–14.
- Radloff, L. (1977). The CES-D scale a self-report depression scale for research in the general population. *Applied Psychological Measurement*, 1, 385–401.
- Randolph, T. G. (1956). The descriptive features of food addiction. Addictive eating and drinking. *Quarterly Journal of Studies on Alcohol*, 17, 198–224.
- Raschpichler, M., Straatman, K., Schroeter, M. L., Arelin, K., Schlögl, H., Fritzsche, D., ... Stumvoll, M. (2013). Abdominal fat distribution and its relationship to brain changes: The differential effects of age on cerebellar structure and function: A cross-sectional, exploratory study. *BMJ Open*, 3, e001915.
- Reber, J., Feinstein, J. S., O'doherty, J. P., Liljeholm, M., Adolphs, R., & Tranel, D. (2017). Selective impairment of goal-directed decision-making following lesions to the human ventromedial prefrontal cortex. *Brain*, 140, 1743–1756.
- Romer, A. L., Su Kang, M., Nikolova, Y. S., Gearhardt, A. N., & Hariri, A. R. (2018). Dopamine genetic risk is related to food addiction and body mass through reduced reward-related ventral striatum activity. *Appetite*, 133, 24–31.
- Schäfer, A., Vaitl, D., & Schienle, A. (2010). Regional grey matter volume abnormalities in bulimia nervosa and binge-eating disorder. *NeuroImage*, 50, 639–643.
- Schmidt, L., Tusche, A., Manoharan, N., Hutcherson, C., Hare, T., & Plassmann, H. (2018). Neuroanatomy of the vmPFC and dlPFC predicts

- individual differences in cognitive regulation during dietary self-control across regulation strategies. *The Journal of Neuroscience*, 25, 5799–5806.
- Schulte, E. M., Joyner, M. A., Potenza, M. N., Grilo, C. M., & Gearhardt, A. N. (2015). Current considerations regarding food addiction. *Current Psychiatry Reports*, 17, 19.
- Schulz, P., Schlotz, W., & Becker, P. (2004). *Trierer Inventar zum chronischen Stress: TICS*. Göttingen, Germany: Hogrefe.
- Shaw, M. E., Nettersheim, J., Sachdev, P. S., Anstey, K. J., & Cherbuin, N. (2017). Higher fasting plasma glucose is associated with increased cortical thinning over 12 years: The PATH through life study. *Brain Topography*, 30, 408–416.
- Skinner, H. H., Haines, J., Austin, S. B., & Field, A. E. (2012). A prospective study of overeating, binge eating, and depressive symptoms among adolescent and young adult women. *The Journal of Adolescent Health*, 50, 478–483.
- Storsve, A. B., Fjell, A. M., Tamnes, C. K., Westlye, L. T., Overbye, K., Aasland, H. W., & Walhovd, K. B. (2014). Differential longitudinal changes in cortical thickness, surface area and volume across the adult life span: Regions of accelerating and decelerating change. *Journal of Neuroscience*, 34, 8488–8498.
- Stunkard, A. J., & Messick, S. (1985). The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. *Journal of Psychosomatic Research*, 29, 71–83.
- Su, Y., Jackson, T., Wei, D., Qiu, J., & Chen, H. (2017). Regional gray matter volume is associated with restrained eating in healthy Chinese young adults: Evidence from voxel-based morphometry. *Frontiers in Psychology*, 8, 443.
- Thompson, J. L., Drysdale, M., Baimel, C., Kaur, M., MacGowan, T., Pitman, K. A., & Borgland, S. L. (2017). Obesity-induced structural and neuronal plasticity in the lateral orbitofrontal cortex. *Neuropsychopharmacology*, 42, 1480.
- Torres, S. J., & Nowson, C. A. (2007). Relationship between stress, eating behavior, and obesity. *Nutrition*, 23, 887–894.
- Vainik, U., Neseliler, S., Konstabel, K., Fellows, L. K., & Dagher, A. (2015). Eating traits questionnaires as a continuum of a single concept. Uncontrolled eating. *Appetite*, 90, 229–239.
- Veit, R., Kullmann, S., Heni, M., Machann, J., Häring, H.-U., Fritsche, A., & Preissl, H. (2014). Reduced cortical thickness associated with visceral fat and BMI. *NeuroImage: Clinical*, 6, 307–311.
- Volkow, N. D., Wang, G.-J., Fowler, J. S., & Telang, F. (2008). Overlapping neuronal circuits in addiction and obesity: Evidence of systems pathology. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 363, 3191.
- Volkow, N. D., Wang, G. J., Tomasi, D., & Baler, R. D. (2013). Obesity and addiction: Neurobiological overlaps. *Obesity Reviews*, 14, 2–18.
- Wang, G.-J., Volkow, N. D., Logan, J., Pappas, N. R., Wong, C. T., Zhu, W., ... Fowler, J. S. (2001). Brain dopamine and obesity. *The Lancet*, 357, 354–357.
- Willette, A. A., & Kapogiannis, D. (2015). Does the brain shrink as the waist expands? *Ageing Research Reviews*, 20, 86–97.
- Yokum, S., Ng, J., & Stice, E. (2011). Relation of regional gray and white matter volumes to current BMI and future increases in BMI: a prospective MRI study. *International Journal of Obesity*, 36, 656–664.
- Zeeb, F. D., Floresco, S. B., & Winstanley, C. A. (2010). Contributions of the orbitofrontal cortex to impulsive choice: Interactions with basal levels of impulsivity, dopamine signalling, and reward-related cues. *Psychopharmacology*, 211, 87–98.

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