

Research paper

Body mass index in obsessive-compulsive disorder

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ABSTRACT

Background: Psychiatric disorders are associated with overweight/obesity. Obsessive-compulsive disorder (OCD) may be an exception, as anecdotal evidence suggests lower BMI in OCD. Additionally, depression is associated with elevated BMI, but effects of comorbid secondary depression are unknown. The aim of the present study was to assess BMI and risk for overweight/obesity in OCD and to assess the effect of comorbid depression on BMI.

Methods: BMI, demographics, and clinical status were assessed in large samples of individuals with OCD, anxiety disorders, depressive disorders, comorbid anxiety/depressive disorders, and non-clinical controls (NCC).

Results: Although no initial differences were found between the samples on BMI, the non-depressed OCD subsample had significantly lower BMI and risk for overweight/obesity compared to all other clinical samples. NCC were nearly twice as likely to be overweight compared to non-depressed OCD.

Limitations: Eating disorders were excluded in the OCD sample, but BMI < 17 was used as an exclusion criterion in the clinical control groups in lieu of screening for Anorexia. Group differences on demographics were controlled for. Recruitment methodology differed between samples.

Conclusions: OCD is associated with significantly lower rates of obesity and overweight, but this relationship was not found when comorbid depression was present. This suggests that the purer the phenotype of OCD, the more substantial protective factor against overweight/obesity emerges compared to other clinical samples and NCC. An OCD-specific reward/anhedonia model, previously offered to elucidate lower smoking rates in OCD, may account for lower BMI in OCD. These results warrant careful clinical attention to the negative impact of comorbid depression on OCD that spans from increasing risk for obesity and cigarette smoking, to hindering treatment response.

1. Introduction

Obesity and overweight are associated with major health risks and premature mortality (Garvey et al., 2016; Rodriguez-Monforte et al., 2016). Compared to the general population, psychiatric disorders, including mood and (to a lesser degree) anxiety disorders, were found to be associated with increased rates of overweight and obesity (Petry et al., 2008; Simon et al., 2006). In particular, depression has been consistently associated with overweight and obesity, and longitudinal studies reveal a bidirectional association where obesity was found to be a risk factor for depression, and conversely, depression was a risk factor for obesity (Luppino et al., 2010). In fact, whereas psychotropic

medications such as serotonin agonists, lithium, and neuroleptic medications were also found to further increase long-term risk for obesity (Deng, 2013; Lee et al., 2016), there are indications that independent medication effects on weight gain may be masked by depression status, offering evidence that depression is the primary risk factor (Gibson-Smith et al., 2016).

Obsessive-compulsive disorder (OCD) may be uniquely associated with reduced BMI, beyond the association with anorexia nervosa. However, evidence is anecdotal, and results from a limited number of investigations are mixed (Albert et al., 2013; Drummond et al., 2011; Henninghausen et al., 1999; Subramaniam et al., 2013). For example, a large study from Singapore found that OCD may be associated with

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Table 1
Characteristics of the entire OCD sample and OCD-noDep subsample vs. clinical and non-psychiatric control samples.

	OCD (<i>n</i> = 316) M(SD)/%	OCD-noDep (<i>n</i> = 132) M(SD)/%	Anx (<i>n</i> = 227) M(SD)/%	Dep (<i>n</i> = 303) M(SD)/%	Anx + Dep (<i>n</i> = 789) M(SD)/%	Controls (<i>n</i> = 432) M(SD)/%	<i>F</i> / <i>X</i> ²	<i>F</i> / <i>X</i> ²
Age	36.86 (11.05)	36.76 (11.46)	40.46 (13.52)	40.53 (12.55)	41.23 (12.05)	39.32 (14.85)	^a 7.09***	^b 4.12**
Education (years)	12.73 (3.19)	12.93 (3.16)	12.21 (3.38)	12.08 (3.31)	11.28 (3.24)	12.83 (3.13)	^a 21.19***	^b 19.96***
Sex (% female)	52.20%	50.0%	63.60%	61.70%	68.20%	61.30%	^a 25.74***	^b 19.29*
<i>Medications</i>								
SSRIs	42.7%	36.4%	13.6%	22.4%	31.5%	0%		
Other antidepressants	8.2%	4.5%	3.1%	9.9%	11.6%	0%		
Neuroleptics	15.5%	15.9%	–	–	–	0%		
Benzodiazepines	14.2%	9.1%	18%	15.5%	29.4%	0%		
Any psychotropic medication	64.9%	54.5%	55.7%	68.6%	76.3%	0%		

OCD, total obsessive-compulsive disorder sample; OCD-noDep, OCD subsample without comorbid depression; Anx, anxiety disorders sample; Dep, depression sample; Anx + Dep, comorbid anxiety and depressive disorders sample. Controls, non-clinical controls; For all medication types, status represent medication use in the past two weeks at time of assessment.

^a Omnibus test between the OCD, Anx, Dep, Anx + Dep, and controls.

^b Omnibus test between the OCD-noDep, Anx, Dep, Anx + Dep, and controls. Total *n* = 2069; overall: mean age, *M* = 39.98, *SD* = 12.85, 62.9% females.

* *p* < 0.05.

** *p* < 0.001.

*** *p* < 0.0001.

elevated risk of underweight (Subramaniam et al., 2013). These findings mirror trends where adolescents with OCD exhibited lower BMI compared to matched controls (Henninghausen et al., 1999), and that the prevalence of OCD among obese individuals is low compared to most major disorders (Husky et al., 2018). On the other hand, other studies have found an association between OCD and increased rates of metabolic syndrome, and even high rates of overweight (Albert et al., 2013; Drummond et al., 2011). However these latter studies suffer from some methodological limitations, including the use of highly selective samples (e.g., inpatients with severe OCD which would further entail multiple comorbidities), reliance on subjective self-reported weight and height, inclusion of patients where OCD is not necessarily the primary disorder, and lack of exclusion criteria or control for eating disorders or medications. Thus, there is a need for a direct examination of BMI in OCD, while addressing the limitations of past studies.

The current study sought to address this gap in the literature by directly investigating overweight and obesity in OCD while addressing past limitation. In addition, this study sought to examine factors that may account for the inconsistencies in the literature (i.e., type of comorbidities and psychotropic medication) through the use of data from two large-scale Dutch consortia. BMI of individuals with OCD was compared to that of large samples of individuals with primary depression, primary anxiety, comorbid anxiety and depression and non-clinical controls (NCC). We hypothesized that individuals with OCD would demonstrate lower BMI and obesity rates compared to individuals with anxiety or depression and that no differences would be observed compared with NCC. Additionally, we hypothesized that comorbid depression and medication status would moderate this effect, accounting for inconsistencies in previous research.

2. Methods

2.1. Participants

Data were drawn from two large Dutch multicenter clinical consortiums. The OCD data was obtained from the Netherlands Obsessive Compulsive Disorder Association (NOCDA) study (Schuurmans et al., 2012). The NOCDA consortium is an ongoing naturalistic cohort study of patients with a lifetime diagnosis of OCD referred to one of seven participating mental health care centers for evaluation and treatment. The NOCDA includes individuals 18 years or older that are fluent in Dutch. OCD, as well as other comorbidities, were determined using the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I; First et al., 2002). Detailed methodological information regarding the

NOCDA consortium can be found elsewhere (Schuurmans et al., 2012).

Importantly, lifetime diagnosis of a comorbid eating disorder served as an exclusion criterion in the present study for the NOCDA sample (as assessed using the SCID). In the present study we included only participants fulfilling criteria for current (i.e., one-month prevalence), primary DSM-IV OCD (*N* = 316). Demographic information is presented in Table 1. The OCD sample had a moderate degree of severity as assessed by Yale-Brown Obsessive Compulsive Scale (Y-BOCS; *M* = 20.7, *SD* = 7.01), and 205 participants (65%) of the sample were medicated (SSRIs: 42.7%; Tricyclic antidepressants: 8.2%; Neuroleptics: 15.5%; and Benzodiazepines: 14.2%). Lifetime comorbid disorders included depression (54%, *n* = 171), social anxiety disorder (22%, *n* = 70), panic Disorder (18%, *n* = 57), specific phobia (10.1%, *n* = 32), generalized anxiety disorder (9.8%, *n* = 31), dysthymia (6.3%, *n* = 20), schizophrenia or psychotic disorder (5.1%, *n* = 16), post-traumatic stress disorder (3.2%, *n* = 10), and bipolar disorder (3.2%, *n* = 10).

Data for the three non-OCD clinical samples and the non-psychiatric control samples were drawn from the Netherlands Study of Depression and Anxiety (NESDA; Penninx et al., 2008). NESDA is a multicenter study designed to examine the long-term course and consequences of depressive and anxiety disorders. Detailed methodological information regarding the NESDA consortium can be found elsewhere (Penninx et al., 2008). In brief, a total of 2981 NESDA participants were recruited from various settings, including from the community, primary care centers, and specialized mental health centers. Across recruitment settings, uniform inclusion and exclusion criteria were used. Inclusion criteria included age of 18 to 65 years, as well as a diagnosis of dysthymia, major depressive disorder, generalized anxiety disorder, panic disorder, social phobia, or agoraphobia. Exclusion criteria included not being fluent in Dutch and diagnosis of any other psychiatric disorders (e.g., OCD, psychotic disorder, bipolar disorder).

From the baseline sample we selected those persons with BMI data and further excluded NCC that were taking psychotropic medications at the time of assessment. In addition, Since the NESDA consortium did not screen for eating disorders, participants with clinical levels of low BMI were excluded (BMI < 17, *n* = 7; American Psychiatric Association, 2013). The final NESDA samples included a current anxiety disorder sample (Anx, *n* = 227), a current depression sample (Dep, *n* = 303), current comorbid Anx + Dep sample (*n* = 789), and NCC with no lifetime history of psychiatric disorders (*n* = 432). The Anx sample included 127 medicated participants (55.7%), the Dep sample included 208 medicated participants (68.6%), and the Anx + Dep sample included 603 medicated participants (76.3%). The Composite Interview Diagnostic Instrument (CIDI) – Lifetime Version 2.1

(Wittchen, 1994) was used for clinical screening in the NEDSA samples using the DSM-IV algorithms. All participants signed an informed consent in accordance with the declaration of Helsinki.

2.2. Measures

2.2.1. Weight assessment

At baseline, weight and height were measured by trained clinical research staff at a study site (Penninx et al., 2008). BMI was then calculated for each participant. In accordance with the World Health Organization definition, BMI categories were defined as follows: underweight BMI = 17.0–18.49, normal weight = 18.5–24.99, overweight = 25.0–29.99, and obesity \geq 30.

2.2.2. OCD symptom severity

In the OCD sample, symptom severity was assessed using the Yale-Brown Obsessive-Compulsive Scale (Goodman et al., 1989), a gold standard clinician-administered structured interview which was administered by trained licensed clinicians.

2.3. Statistical analysis

All analyses were carried out using IBM SPSS 20. Group differences in demographic variables were examined using univariate analyses of variance (ANOVA), and χ^2 tests. Since years of education, gender ratio, and age, differed significantly between the groups (see Section 3.1), these variables were used as covariates in subsequent analyses. Subsequently, univariate analyses of covariance (ANCOVA) planned contrasts were conducted, comparing mean BMI between the OCD sample and each of the other samples. To examine the risk of obesity and overweight, a series of logistic regressions were employed where each control sample was used as the reference group. Age and gender were entered as covariates across these logistic regressions, and education included in the model when relevant.

In order to assess the impact of depression and medication status on BMI within the OCD group, we conducted a linear regression analysis of potential moderators of BMI within the OCD group. In this model, the dependent variable was BMI, and predictors included demographic (age, and gender) and clinical (OCD symptom severity, OCD age of onset, medication status, and comorbid depression) variable. Given the other variables in the model, comorbid depression – but not medication use – was a significant predictor of BMI in the OCD sample (see Section 3.1). In order to further investigate the role of comorbid depression as a predictor of overweight and obesity in OCD, a similar series of logistic regressions were conducted for the subsample of OCD patients without comorbid depression.

3. Results

3.1. Demographic and clinical variables

An overall significant difference for age was found between the groups [$F(4, 2064) = 7.094, p < 0.000, \eta^2 = 0.014$] (Table 1). Post-

hoc analyses revealed that the OCD group's mean age was significantly lower than the other groups (M_{DIF} ranging from 2.5 to 4.4 years, all p 's < 0.01). In addition, the Anx + Dep group had a higher mean age compared to the control group ($M_{DIF} = 1.9$ years, $p = 0.013$). An overall significant difference was further found on years of education [$F(4, 2064) = 21.194, p < 0.0001, \eta^2 = 0.039$]. Post-hoc analyses revealed that the Anx + Dep group had significantly lower mean years of education compared to all groups (M_{DIF} ranging from 0.8 to 1.55 years, all p 's < 0.0001). Furthermore, the control group had a significantly higher mean years of education compared to the Dep, Anx, and Anx + Dep groups ($M_{DIF} = 0.63, \text{ and } 1.55$ years, $p = 0.018, \text{ and } p < 0.0001, \text{ respectively}$), and the Dep group had lower mean years of education compared to the OCD group ($M_{DIF} = 0.65, p = 0.013$). A significant difference was also found between the groups on gender proportions ($\chi^2(4) = 25.742, p < 0.0001$). In light of these differences, all subsequent between-group comparisons included age, education, and gender as covariates.

In order to assess the potential impact of clinical and demographic variables within the OCD group, we conducted a linear regression analysis within the OCD sample, where BMI was the dependent variable, and age, gender, age of onset, symptom severity (Y-BOCS), comorbid depression, and medication status were predictors. Results of this analysis revealed a significant model ($F = 2.93, p = 0.009$). However, only comorbid depression was found to be a significant predictor of BMI within the OCD group, controlling for all other variables in the model ($t = 2.38, p = 0.018$). Notably, when comorbid depression was entered into the model, medication status was rendered non-significant. Corroborating the results of this analysis, we controlled for age and gender in a univariate ANCOVA comparing BMI in medicated ($M = 25.24, SD = 5.21$) versus non-medicated ($M = 23.85, SD = 4.35$) OCD participants, and found a significant difference between the subgroups [$F(3, 312) = 4.64, p = 0.032$]. However, this effect was rendered non-significant when comorbid depression was entered as a second covariate [$F(4, 311) = 2.44, p = 0.120$]. Finally, controlling for age and gender, an ANCOVA analysis revealed that OCD with comorbid depression had a significantly higher BMI ($M = 25.39, SD = 5.24; F(3, 312) = 8.47, p = 0.004$) compared to the non-depressed OCD subsample ($M = 23.73, SD = 4.32$).

3.2. Overweight and obesity analyses

3.2.1. BMI group comparisons

Planned comparisons between the OCD group and each of the Anx, Dep, Anx + Dep, and NCC (while controlling for age, gender, and education) on the average BMI score yielded no significant differences (all p 's > 0.05 ; see Table 2). Notably, only the OCD and control groups had a mean BMI lower than the overweight threshold (i.e., BMI < 25). A series of logistic regressions assessing the risk for overweight alone (while adjusting for age, gender, and education) revealed elevated risk for overweight associated with all groups compared to OCD (OR range 1.06–1.33), albeit these OR were not significant (see Table 3). The same analyses were conducted for risk of obesity only, with elevated risk for obesity found to be associated with the Dep, Anx, and Anx + Dep

Table 2

BMI comparisons of the entire OCD and non-depressed OCD subsample vs. clinical and non-psychiatric control samples.

	OCD (n = 316) M(SD)	OCD-noDep (n = 132) M(SD)	Anx (n = 227) M(SD)	F^1	F^2	Dep (n = 303) M(SD)	F^1	F^2	Anx + Dep (n = 789) M(SD)	F^1	F^2	Controls (n = 432) M(SD)	F^1	F^2
BMI	24.75 (4.96)	23.88 (4.36)	25.17 (4.81)	0.48	4.08*	25.57 (4.84)	0.61	5.27*	26.04 (5.46)	2.02	7.08**	24.80 (4.56)	0.12	3.25

OCD, obsessive-compulsive disorder sample; OCD-noDep, non-depressed OCD subsample; Anx, anxiety disorders sample; Dep, depression sample; Anx + Dep, comorbid anxiety and depressive disorders sample; Controls, non-clinical controls; F^1 , omnibus coefficient with the entire OCD sample; F^2 , omnibus coefficient with the OCD-noDep subsample.

* $p < 0.05$.

** $p < 0.001$.

Table 3
Odds ratios assessing risk for overweight, obesity, or both for each control group versus the OCD sample or the non-depressed OCD subsample.

		Overweight			Obesity			Overweight + Obesity		
		OR	CI 95%	p	OR	CI 95%	p	OR	CI 95%	p
OCD	Anx	1.06	0.78–1.62	0.783	1.17	0.69–1.99	0.552	1.13	0.76–1.65	0.498
	Dep	1.33	0.89–1.98	0.166	1.37	0.85–2.22	0.200	1.28	0.90–1.81	0.174
	Anx + Dep	1.16	0.83–1.62	0.395	1.25	0.83–1.87	0.282	1.17	0.87–1.56	0.294
	Controls	1.23	0.86–1.76	0.251	0.86	0.53–1.36	0.528	1.08	0.79–1.47	0.646
OCD-noDep	Anx	1.48	0.86–2.56	0.162	1.38	0.69–2.90	0.365	1.42	0.88–2.30	0.155
	Dep	2.07	1.18–3.56	0.011	1.42	1.02–1.99	0.430	1.40	1.11–1.78	0.005
	Anx + Dep	1.74	1.06–2.86	0.029	1.83	0.98–3.40	0.060	1.20	1.05–1.39	0.010
	Controls	1.97	1.18–3.29	0.010	1.39	0.66–1.98	0.320	1.70	1.10–2.64	0.016

OCD, entire obsessive-compulsive disorder sample; OCD-noDep, non-depressed OCD subsample; Anx, anxiety disorders sample; Dep, depression sample; Anx + Dep, comorbid anxiety and depressive disorders sample; Controls, non-clinical controls; OR, odds ratio; all odd ratios are computed with OCD or OCD-noDep as the reference group with weight category as a dependent variable contrasted with normal weight.

samples compared to the OCD group (OR range 1.17–1.37), with the exception of the control group (OR = 0.86). However, these ORs were not significant. A third series of logistic regression assessed the risk of overweight and obesity (i.e., BMI > 25). All ORs indicated higher risk for overweight and obesity across control groups compared to the OCD group (OR range 1.08–1.28), albeit these ORs were not significant (see Table 3).

3.2.2. Non-depressed OCD

Planned comparisons between the subgroup of OCD participants without depression (OCD-noDep, n = 132) and the clinical and NCC samples are presented in Table 2. BMI comparisons between the OCD-noDep, and the Anx, Dep, Anx + Dep, and control groups on the average BMI score yielded a significantly elevated BMI in the Anx group (BMI = 25.17, p = 0.048), Dep group (BMI = 25.6, p = 0.017), the Anx + Dep group (BMI = 26.04, p = 0.008) compared to the OCD-noDep group (BMI = 23.9). No significant differences were found between the OCD and Anx groups or the control groups. Table 3 depicts a series of logistic regressions adjusted for age, gender, and education. The regression models assessing OR for overweight only across control samples compared to the non-depressed OCD subsample revealed significantly elevated risk associated with the Dep (OR = 2.07), the Anx + Dep (OR = 1.74), and the control groups (OR = 1.97). This finding suggests that compared to non-depressed OCD patients, non-clinical controls are approximately twice as likely to be overweight. Compared to the OCD-noDep group, elevated OR (although non-significant) was found for the Anx group as well (OR = 1.48).

Similar analyses were conducted for the risk for obesity only (See Table 3.). Elevated ORs were found for all groups, albeit non-significant (OR range 1.38–1.83), suggesting higher risk of obesity in all groups compared to non-depressed OCD patients. Finally, a similar series of logistic regressions were conducted for the risk of being either overweight or obese. Results showed significant risk for the Dep (OR = 1.97), the Anx + Dep (OR = 1.77), and the NCC (OR = 1.71) samples. An elevated, non-significant risk was found for the Anx sample (OR = 1.39). For a graphical depiction of the prevalence of overweight and obesity across samples, see Fig. 1.

3.3. Medications

Although comorbid depression was found to mask medication status in the OCD sample, we sought to examine the association between individual medication classes and BMI within the OCD group. We conducted four MANOVAs comparing participants with OCD that were taking either SSRIs, tricyclic antidepressants (TCAs), benzodiazepines, and neuroleptics at the time of testing, versus participants that were not taking these medications. In all four MANCOVA models, we controlled for age, education, gender, symptom severity (Total Y-BOCS score) and age of onset. Results indicated that there were no significant differences on BMI between OCD participants taking or not taking benzodiazepines and TCAs (Benzodiazepines: F(1,275) = 0.002, p = 0.963, TCAs: F(1,275) = 1.225, p = 0.269,), and effect sizes were small to null (Cohen's d = 0.01; and d = 0.23; for benzodiazepines and TCAs respectively). Significantly higher BMI was found among OCD

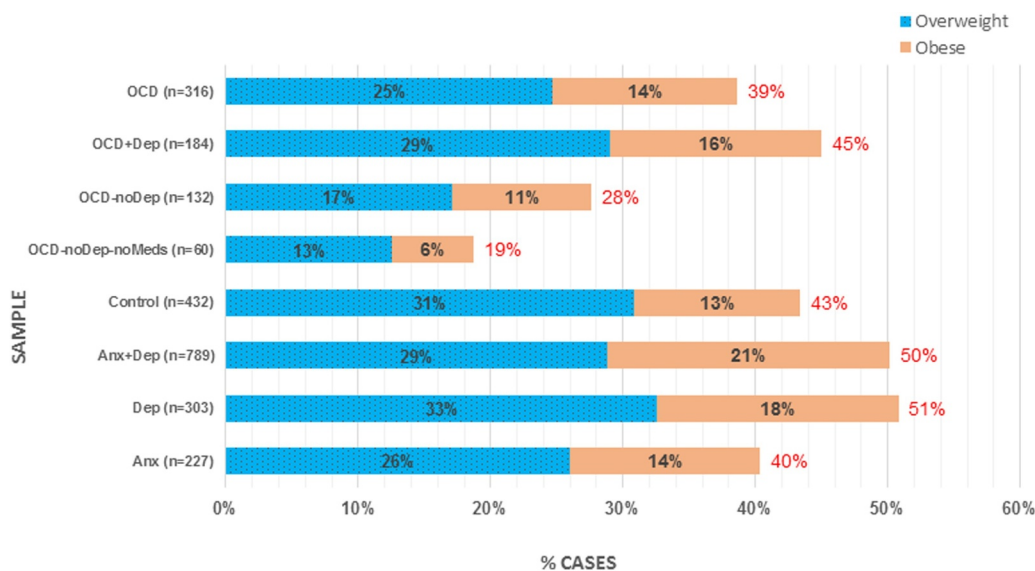


Fig. 1. Percent overweight and obese participants across clinical and non-psychiatric control samples. OCD, Obsessive-Compulsive Disorder, entire sample; OCD-noDep, non-depressed OCD subsample; OCD-noDep-noMeds, non-depressed, unmedicated OCD subsample; Control, non-psychiatric control sample; Anx, Anxiety disorders sample; Dep, Depression Sample; Anx + Dep, comorbid depressive and anxiety disorders sample. Coefficients in red font (at the top of each bar) represent total overweight and obesity percent in each sample; Total n for each sample and subsample appear in brackets.

participants who were taking SSRIs at the time of assessment ($BMI M_{DIF} = 1.35$, $F(1,275) = 4.724$, $p = 0.031$, Cohen's $d = 0.26$). A similar effect of medium magnitude was found for neuroleptics, which had the relatively largest effect size among medication types ($BMI M_{DIF} = 3.05$, $F(1,275) = 8.612$, $p = 0.004$, Cohen's $d = 0.49$). However, as noted previously the significance of medication effects were nullified when comorbid depression was entered.

3.4. Clinical correlates

No significant correlation was found between BMI and OCD symptom severity within the OCD sample, as measured by the Y-BOCS total score ($r = 0.09$, $p = 0.106$). A non-significant correlation was also found for age of onset of OCD and BMI ($r = 0.10$, $p = 0.089$), as well as for the number of comorbid conditions and BMI within the OCD group ($r = -0.026$, $p = 0.790$).

4. Discussion

The aim of the present study was to utilize large, carefully screened clinical and control samples to assess BMI in OCD, with the primary hypothesis that OCD would be associated with lower BMI and obesity rates compared to other psychiatric disorders and non-clinical controls. The secondary aim was to assess the impact of comorbid depression and psychotropic medication on BMI in individuals with OCD. Both categorical BMI analyses (odds ratio; OR) were conducted as well as dimensional (continuous BMI value) comparisons. We did not find evidence for our first hypothesis, as mean BMI comparisons yielded no significant difference between the OCD and the other four groups. Notably, only the control and OCD groups had a mean BMI lower than the overweight threshold (i.e., $BMI < 25$). Furthermore, an OR analysis for the entire OCD sample revealed trends for risk for overweight, obesity, or both, constantly greater than one across groups when compared to the OCD group. However, these results were not statistically significant.

In accordance with our second hypothesis, comorbid depression in OCD was found to strongly mediate elevated BMI. Notably, the substantial impact of depression on BMI masked the effect of medication status on BMI in the OCD sample. For example, BMI in the non-depressed OCD sample was significantly lower than all three clinical control groups, with no difference (albeit a trend) compared to the control group. Risk analyses indicated significant risk factors wherein compared to OCD-noDep, individuals in the Dep, Anx + Dep, and NCC were nearly twice as likely to be overweight. The Anx groups risk was elevated, but not significant ($OR = 1.5$). A similar picture was revealed when the risks of being obese, or overweight/obese were calculated. Risk for obesity only was elevated in all groups (OR range 1.38–1.83), albeit non-significant, presumably given the relatively small number of obese individuals. Risks for obesity and overweight combined pointed to a similar range (OR range 1.20–1.70) and were significant, apart for the Anx group. Notably, these findings were found while controlling for age, gender, and education.

Although medication status' effect on BMI was found to be masked by depression status, our results further indicate that only specific medications were associated with higher BMI in the OCD sample, even after controlling for all demographic and clinical variables, including symptom severity. Benzodiazepines and TCAs had no significant effect on BMI, but a significant small effect was found for SSRIs, and a significant medium effect was found for neuroleptics. These results are in line with previous findings that neuroleptics are associated with greater weight gain compared to SSRIs (Hasnain et al., 2012). Finally, comorbid depression was the only clinical factor with an impact on BMI among individuals with OCD. This relationship remained significant after controlling for demographic (i.e., age, education, and gender) and clinical (i.e., symptom severity, age of onset, and the number of comorbid conditions) variables.

These results highlight that, as opposed to other psychiatric disorders, individuals diagnosed with OCD do not differ from NCC in terms of BMI. Furthermore, our results underscore that compared to other clinical samples, *non-depressed OCD* participants have a lower BMI compared to both non-clinical, and psychiatric controls. The risk of being overweight is significant for clinical samples or the general population when compared to non-depressed OCD individuals. These findings may be unique to OCD, given the extant literature reporting elevated BMI and obesity in other major psychiatric disorders including affective disorders, personality disorders, some anxiety disorders, and alcohol use disorders (Petry et al., 2008; Simon et al., 2006). Our data further indicate that there were only trends, but no meaningful differences, between the OCD and Anx groups. This is in accordance with studies that show that only some anxiety disorders may be associated with a substantial risk for obesity (e.g., panic disorder), but a meta-analysis determined that no conclusive judgment could be made regarding the role of anxiety disorders as a risk factor for obesity (Garipey et al., 2010). Thus, in the context of BMI, it appears that the role of comorbid depression is meaningful for any anxiety disorder, but particularly for OCD.

Our findings regarding comparable or reduced BMI rates in OCD compared to controls are supported by evidence indicating lower BMI in OCD (Henninghausen et al., 1999; Subramaniam et al., 2013). A hypothesis that may explain these findings concerns the effects of repeated negative reinforcements resulting in alterations of positive reinforcement mechanisms (Abramovitch et al., 2015; 2014). In light of this hypothesis, our results bear a striking resemblance to the results of a previous study demonstrating lower tobacco smoking rates in OCD compared to major disorders and the general population in the United States (Abramovitch et al., 2015). Our hypothesis is further supported by findings of elevated clinical levels of anhedonia in OCD above and beyond the effects of depression levels (Abramovitch et al., 2014). The authors argue that OCD is unique in that it is associated with a vicious negative reinforcement cycle. Individuals with OCD repeatedly experience distress from obsessive thoughts, and repeatedly engage in rituals in order to alleviate their distress. This mechanism is similar to the negative reinforcement cycle seen in opiate substance addiction (Fontenelle et al., 2011). The long-term consequences of this pervasive negative reinforcement cycle among individuals diagnosed with OCD may result in a deficient ability to experience positive reinforcement/reward. Although reframing this hypothesis in the context of food-related positive reinforcement is speculative, such a mechanism has been previously proposed as a psychopathological mechanism in OCD and may apply to a host of rewarding behaviors (Abramovitch et al., 2014; Fontenelle et al., 2011), particularly in the case of nicotine in tobacco smoking in OCD (Abramovitch et al., 2015; Bejerot and Humble, 1999). Additional support for this hypothetical mechanism was recently received from two studies demonstrating aberrant connectivity between prefrontal regions, and the ventral striatum/nucleus accumbens, which is associated with reward processing (Jung et al., 2013; Xie et al., 2017).

The notion that anhedonia and deficient experience from positive reward are underlying mechanisms for lower BMI in OCD may be counterintuitive given that anhedonia and deficient reward responsiveness are hallmark findings in depression (Pizzagalli, 2014), which is strongly associated with elevated rates of obesity (Luppino et al., 2010). However, although OCD is generally associated with altered reward responsiveness (Figeo et al., 2011), there is evidence that reward deficiencies and anhedonia in OCD may be disorder-specific, and likely associated with different mechanisms than those seen in depression. First, individuals with OCD have demonstrated anhedonia beyond what would be explained by depressive symptoms (Abramovitch et al., 2014). Second, a recent imaging study demonstrated a disorder-specific alteration in nucleus accumbens-prefrontal connectivity in *non-depressed OCD* participants, when depressive severity was controlled (Jung et al., 2013). Indeed, the authors reported identifying OCD-

specific alterations at rest, as well as a disorder specific alteration in connectivity during incentive processing.

The speculative mechanism offered here in which food may be associated with reduced positive reinforcement value in individuals with OCD, requires further research. However other plausible explanations and mechanisms that warrant empirical examination include active exertion of control regarding eating behavior (e.g., “I should never surrender to temptations and eat too much”), increased exercise activities, or a preference for healthier foods. In addition, more idiosyncratic disorder-specific mechanisms may account for these findings, such as prominent contamination concerns and disgust. However, individuals diagnosed with OCD vary in the content of their obsessions and compulsions, and not all suffer from contamination concerns or disgust. In addition, individuals with primary contamination concerns usually create an ‘uncontaminated environment’ to place food and eat, which may not impact caloric intake. Nevertheless, these are speculative accounts that should be subject to empirical investigations, potentially through tracking food consumption and examining cognitions about food.

The present study has several strengths, including the utilization of large and well-screened OCD and control samples with sufficient power to examine moderators of BMI, and objective assessment of weight and height. However, this study is not without limitations. First, given the potential association between eating disorders (predominantly anorexia nervosa) and OCD, we excluded eating disorders from this sample. Nevertheless, all other comparison groups were taken from the NESDA study in which eating disorders were not screened. This limitation was addressed by excluding participants with BMI lower than 17 (the DSM cutoff for anorexia) across samples. Only seven participants out of 1751 NESDA participants were excluded under this condition, and our data indicated that their removal did not alter this study's results. In addition, the NESDA study utilized the CIDI to screen for DSM disorders, while the NOCDA utilized the SCID to screen for OCD. Although these are different measures, both are based on DSM criteria and have demonstrated very good diagnostic concordance in both OCD, depressive, and anxiety disorders (Kessler et al., 2013; Ruscio et al., 2010). Finally, the OCD sample was recruited from mental health care settings, and the NESDA samples were recruited from primary care settings, mental health care centers, as well as from the community. Nevertheless, best practices for assessor training and diagnostic procedures were employed in both cases.

5. Conclusion

Overall, we found that OCD is associated with lower rates of obesity and overweight compared to individuals with depressive and comorbid depressive and anxiety disorders, with no differences between the OCD and NCC – an unusual finding in the context of psychiatric disorders. Furthermore, individuals with OCD without comorbid depression demonstrated reduced obesity rates compared to NCC and other clinical samples. In addition, apart from comorbid depression, symptom severity and age of onset did not moderate this effect, nor did the number of comorbid conditions. Importantly, medication effects were masked by a significant effect of depression. These results suggest that individuals with purer OCD phenotype experience a stronger protective factor against overweight and obesity.

In line with previous findings concerning a unique effect of lowered tobacco smoking in OCD compared to other disorders and the general population, and the similar role comorbid depression plays in tobacco smoking in OCD (i.e., non-depressed OCD status is associated with even lowered tobacco smoking rates), we speculate that OCD-specific anhedonia, associated with a disorder-specific negative reinforcement cycle in OCD (hindering positively rewarding experiences), may account for these results. Taken together with research indicating the role of comorbid depression in hindering treatment response in OCD, we recommend that clinicians carefully assess comorbid depression in OCD

and consider the impact of this comorbidity in treatment planning. We suggest that future studies examine whether there is an explicit control element regarding food intake in OCD (e.g., active caloric restriction), as well as investigate the association between the long term negative reinforcement cycle and changes in reward responsivity and anhedonia in OCD.

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Author contributions

AA and GA conceived the study and its design, conducted the analyses, and drafted the manuscript. AC conducted statistical analyses and contributed to drafting the manuscript. PVO, BP, EG, and TB, contributed to data acquisition, and contributed to revising the manuscript critically for important intellectual content.

Conflict of interest

BP was supported by grants from the Dutch government, ministry of health (NWO/ZonMw), during the conduct of the study. AA, GA, AC, AB, EG, and PO have no financial or other conflicts of interest relevant to this manuscript.

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