

Development of Disordered Eating Behaviors and Comorbid Depressive Symptoms in Adolescence: Neural and Psychopathological Predictors

Supplemental Information

Table of Contents:

Disordered eating behaviors	2
Binge-eating or purging (BoP)	3
DEB developers without any DEB at age 14	4
Medication-free participants	4
Propensity score matching	4
Voxel-based morphometry (VBM) analysis	5
Supplemental Results	6
Results in girls only	6
Results in medication-free participants.....	6
DEB developers without any DEB at age 14	7
Development of dieting with relaxed criteria	8
Supplemental Tables.....	9
Supplemental Figures	15
Supplemental References.....	19

Supplemental Methods

Disordered eating behaviors

Disordered eating behaviors were identified based on the DAWBA section P: 'Dieting, weight and body shape' questionnaire.

Binge-eating: Responding "Yes" to the following question: "sometimes people lose control over what they eat, and then they eat a very large amount of food in a short time. For example, they may open the fridge and eat as much as they can find – eating and eating until they feel physically ill. This usually happens when people are by themselves. Does this happen to you?" (question 15).

Purging: Responding "Yes" to: "Have you ever deliberately made yourself vomit (throw up)?" (question 1c), or giving a response scoring above zero to any of the two following questions. "Over the last three months, have you done any of the following to avoid putting on weight: Making yourself vomit (throw up) (question 18f) or taking pills or medicines in order to lose weight?" (question 18g). Scores for question 18 are "No" = 0, "I try to but I'm not allowed" = 1, "A little" = 2, "A lot" = 3).

Dieting: Responding "A lot" to any of the following questions: "Over the last three months, have you done any of the following to avoid putting on weight: eating less at meals (question 18a); skipping meals (question 18b) or going without food for long periods, e.g. all day or most of the day (question 18c)". "No" = 0, "I try to but I'm not allowed" = 1, "A little" = 2, "A lot" = 3.

Defining dieting behaviors with relaxed criteria: The dieting developers in the main text were defined as participants who did not report dieting behaviors (score = 0) at age 14 but developed dieting symptoms (score = 3) at ages 16 or 19. Using this definition, the group size of dieting developers (N=60) was smaller than the binge-eating developers (N=115) and purging developers (N=155). This small group size may limit the statistical power of identifying significant risk factors. Therefore, we relaxed the criteria for defining dieting developers as reporting a score for dieting “above or equal 2” at ages 16 or 19 and thus identified a larger group for dieting developers (N=217). We re-ran the psychopathological and structural brain associations with development of dieting with the relaxed criteria and presented results in the Supplemental Results.

Binge-eating or purging (BoP)

We defined groups based on Bartholdy *et al.* (2019) (1) who combined individuals reporting binge-eating or purging symptoms together. We report these as “binge-eating or purging (BoP)” in the manuscript. “BoP developers” were defined as those who did not report binge-eating or purging at age 14 but developed either one or both of these symptoms at ages 16 or 19. We also defined “BoP Maintainers” as individuals who reported binge-eating or purging at all 3 ages (N=39; 94.9% females) and “BoP Recoverers” as those who reported binge-eating or purging symptoms at age 14 only (29; 89.7% females). Controls (“non-BOP”) for these groups were matched for sex and acquisition site and comprised participants who didn’t report binge-eating or purging at any age (Table S1).

DEB developers without any DEB at age 14

We considered each DEB separately when we defined the developer groups in the main text. Although the binge-eating developers were free of binge-eating symptoms at age 14, they might have purging or dieting symptoms at the same age. To remove the confounding effect of comorbid DBEs at age 14, we re-defined the developers to be those who did not report any DEB any age 14. Accordingly, control groups (“non-DEBs”) were those who did not report any DEB at any age (Table S1, S2). To note that at ages 16 and 19, the developers were not constrained with a single DEB symptom due to group sizes. We used these groups in post-hoc tests to demonstrate that significant associations still held true after excluding comorbid DEB symptoms at age 14.

Medication-free participants

We repeated our analyses in medication-free participants only, to demonstrate that our findings were not affected by medication status. Medication status was assessed with the Timeline Followback Interview (2), asking participants for how many days they took prescription medicine during the past 30 days. Participants were excluded if they reported taking medication (i.e., answer > 0). Participants excluded from each group were as follows: 5 binge-eating developers, 11 non-bingers, 6 purging developers, 17 non-purgers, 2 dieting developers, 7 non-dieters, 8 BoP developers, 2 BoP maintainers, 10 non-BoP, 6 any DEB developers and 10 non-DEB.

Propensity score matching

Each developer group was matched with the corresponding asymptomatic group for sex and acquisition site, by using the propensity score matching method implemented in the Matchit

toolbox (3). Based on sex and acquisition site, a logit model was used to estimate the propensity score (i.e., the probability of being in the DEB developer group) for each participant. The nearest-neighbour method was used to select participants (without replacement) from the asymptomatic group to match the propensity score of each participant in the DEB developer group. Each individual in the binge eating developer group was matched with 4 in the non-binge eating group (1:4 matching); the ratio was 1:3 for the purging developers vs. non-purging groups, and 1:5 for the dieting developers vs. non-dieting groups. These ratios were chosen in order to make the most use of the control group samples. Covariate balances after matching were examined using standardized differences (Supplementary Figure 1), which equals the difference of the mean values between two groups divided by the pooled standard deviation. A standardized difference less than 0.1 would indicate a negligible difference between the two groups (4).

Voxel-based morphometry (VBM) analysis

Voxel-based morphometry (VBM) analysis was carried out by using the VBM8 toolbox (<http://www.neuro.uni-jena.de/vbm/>) in SPM8. The raw T1 images were segmented into gray matter, white matter and cerebrospinal fluid images, and then normalized to the standard Montreal Neurological Institute (MNI) space by using the DARTEL toolbox (5). The normalized gray matter images were modulated by the Jacobian determinant derived from the spatial normalization, and then smoothed with an isotropic Gaussian kernel of 8mm full width at half maximum (FWHM). Intracranial volumes (ICV, in mm³) were estimated by VBM8 as the sum of the gray matter, white matter and cerebrospinal fluid volume.

Supplemental Results

Results in girls only

We tested whether the significant associations with DEBs in both sexes could remain significant in girls only. Consistent with the results in both sexes, emotional problems at age 14 were significantly associated with development of binge-eating in girls (OR = 1.28, $p = 0.028$), while CD and ADHD symptoms were significant predictors for the development of purging (OR = 1.39, $p = 1.4E-03$ for CD symptoms; OR = 1.39, $p = 2.6E-03$ for ADHD symptoms) and BoP behaviors (OR = 1.38, $p = 8.8E-04$ for CD symptoms; OR = 1.37, $p = 1.7E-03$ for ADHD symptoms). CD symptoms were also significantly associated with maintenance of BoP (OR = 1.78, $p = 1.6E-04$). However, CD symptoms were no more significantly associated with “any DEB development” when considering girls only (OR = 1.23, $p = 0.10$), although a trend was noted. The whole-brain associations were not significant in girls only.

Results in medication-free participants

Analyses on psychopathological predictors demonstrated that the significant associations presented in the main text remained significant in medication-free participants. In more detail, emotional problems were significantly associated with the development of binge-eating (OR = 1.30, $p = 0.014$), while CD and ADHD symptoms were significantly associated with the development of purging (OR = 1.37, $p = 6.4E-04$ for CD symptoms; OR = 1.34, $p = 2.6E-03$ for ADHD symptoms) and BoP (OR = 1.35, $p = 6.6E-04$ for CD symptoms; OR = 1.28, $p = 6.6E-03$ for ADHD symptoms). CD symptoms were also significant predictors of maintenance of BoP (OR = 1.57, $p = 4.3E-03$) and development of any DEB (OR = 1.36, $p = 8.5E-03$).

The significant VBM associations with DEBs presented in the main text remained significant in medication-free participants. Whole brain VBM analyses showed that higher gray matter volumes in the right putamen and globus pallidus were associated with the development of binge-eating. The development of purging was associated with lower gray matter volumes in medial OFC, gyrus rectus, the dorsomedial prefrontal cortex, the anterior and middle cingulate cortex and the left dorsolateral prefrontal cortex. Similarly, the development of BoP was associated with lower gray matter volumes in medial OFC, gyrus rectus, the dorsomedial prefrontal cortex, the anterior and middle cingulate cortex (Figure S3).

DEB developers without any DEB at age 14

To rule out the possibility that the above associations could reflect the presence of other DEBs at age 14, we redefined groups, ensuring that DEB developers were free of any DEB at age 14 ($n=75$ and $n=59$, for purging and binge-eating developers, respectively; Supplemental Table S1) and repeated our analyses. The associations between emotional problems and the development of binge-eating ($OR = 1.41$, $p = 0.019$), and associations between CD and ADHD symptoms and the development of purging ($OR = 1.48$, $p = 1.6E-03$ for CD symptoms; $OR = 1.41$, $p = 9.8E-03$ for ADHD symptoms) remained significant after excluding individuals who reported any DEB at age 14 from the analyses.

Whole brain analyses showed that lower GMVs in a cluster comprised of the mOFC, ACC and dorsomedial PFC were associated with purging development in participants free of any DEB at age 14 (Supplemental Figure S4, Table S7). For binge-eating developers without any DEB at age 14, no significant associations were found on the whole brain level.

Development of dieting with relaxed criteria

We identified a larger group of dieting developers (N=217, 70% girls) after relaxing the criteria for defining dieting behaviors. They were matched with 217 non-dieters (70% girls) for sex and acquisition site. Whole brain VBM analyses did not identify any anatomical structure significantly associated with the development of dieting, even with this more relaxed inclusion criteria. Analyses of psychopathological predictors of dieting development, revealed that conduct problems at age 14 were significantly associated with development of dieting (OR = 1.27, $p = 0.013$). Associations with the other psychopathological predictors were not significant ($ps > 0.1$).

Supplemental Tables

Table S1. Demographics for each case and control group.

group	before matching				after matching			
	all	boy	girl	%girl	all	boy	girl	%girl
binge-eating developers	115	24	91	79.1	115	24	91	79.1
non-bingers	897	456	441	49.2	460	96	364	79.1
Total	1012	480	532		575	120	455	
purging developers	155	39	116	74.8	155	39	116	74.8
non-purgers	850	435	415	48.8	465	117	348	74.8
Total	1005	474	531		620	156	464	
dieting developers	60	23	37	61.7	60	23	37	61.7
non-dieters	548	348	200	36.5	300	115	185	61.7
Total	608	371	237		360	138	222	
any DEB developers	138	54	84	60.9	138	54	84	60.9
non-DEB	525	335	190	36.2	276	114	162	58.7
Total	663	389	274		414	168	246	
BoP developers	204	53	151	74.0	204	53	151	74.0
non-BoP	778	424	354	45.5	408	106	302	74.0
Total	982	477	505		612	159	453	
BoP maintainers	39	2	37	94.9	39	2	37	94.9
non-BoP	778	424	354	45.5	312	16	296	94.9
Total	817	426	391		351	18	333	
BoP recoverers	29	3	26	89.7	29	3	26	89.7
non-BoP	778	424	354	45.5	232	24	208	89.7
Total	807	427	380		261	27	234	
binge-eating developers without any DEB at age 14	59	17	42	71.2	59	17	42	71.2
non-DEB	525	335	190	36.2	236	79	157	66.5
Total	584	352	232		295	96	199	
purging developers without any DEB at age 14	75	28	47	62.7	75	28	47	62.7
non-DEB	525	335	190	36.2	300	128	172	57.3
Total	600	363	237		375	156	219	
dieting developers without any DEB at age 14	59	23	36	61.0	59	23	36	61.0
non-DEB	525	335	190	36.2	295	119	176	59.7
Total	584	358	226		354	142	212	

BoP, binge-eating or purging. non-DEB, no any DEB at any age.

Table S2. Psychopathology scores at age 14 and BMI in each sex- and site- matched group (means and standard deviations in parentheses).

	conduct problems	emotional symptoms	hyper-activity/inattention	peer problems	BMI at age 14	BMI z-score at age 14*	BMI at age 19
binge-eating developers	2.23 (1.57)	3.39 (1.80)	4.23 (1.98)	1.92 (1.64)	21.16 (2.75)	0.35 (0.81)	22.90 (3.68)
non-bingers	1.86 (1.31)	2.83 (2.04)	3.73 (2.06)	1.58 (1.47)	20.76 (3.32)	0.17 (0.94)	22.52 (4.05)
purging developers	2.28 (1.43)	3.27 (2.00)	4.41 (1.93)	1.66 (1.56)	21.18 (2.88)	0.36 (0.77)	23.11 (4.10)
non-purgers	1.78 (1.28)	2.88 (2.08)	3.81 (2.09)	1.69 (1.55)	20.47 (3.34)	0.08 (0.96)	22.68 (4.26)
dieting developers	2.00 (1.52)	2.70 (2.01)	3.98 (1.83)	1.83 (1.38)	22.27 (3.65)	0.62 (0.80)	23.77 (3.84)
non-dieters	1.74 (1.31)	2.39 (1.90)	3.70 (2.13)	1.57 (1.41)	19.55 (2.77)	-0.17 (0.92)	21.63 (3.56)
any DEB developers	2.04 (1.48)	2.67 (1.86)	4.17 (1.81)	1.74 (1.42)	21.29 (3.25)	0.37 (0.85)	23.22 (3.86)
non-DEB	1.66 (1.26)	2.44 (1.93)	3.74 (2.26)	1.57 (1.55)	19.35 (2.59)	-0.24 (0.95)	21.64 (3.31)
binge-eating developers without any DEB at age 14	2.07 (1.56)	3.20 (1.81)	4.31 (1.79)	1.86 (1.56)	20.86 (2.77)	0.26 (0.85)	22.78 (3.55)
non-DEB	1.67 (1.20)	2.53 (1.95)	3.83 (2.22)	1.49 (1.40)	19.53 (2.78)	-0.19 (0.95)	21.73 (3.64)
purging developers without any DEB at age 14	2.20 (1.55)	2.53 (1.78)	4.39 (1.90)	1.60 (1.54)	20.96 (3.05)	0.29 (0.83)	22.51 (3.56)
non-DEB	1.66 (1.22)	2.38 (1.90)	3.68 (2.20)	1.62 (1.46)	19.42 (2.59)	-0.21 (0.93)	21.61 (3.39)
dieting developers without any DEB at age 14	1.95 (1.48)	2.61 (1.90)	3.92 (1.76)	1.85 (1.39)	22.30 (3.67)	0.62 (0.81)	23.73 (3.61)
non-DEB	1.77 (1.35)	2.32 (1.91)	3.79 (2.22)	1.52 (1.42)	19.30 (2.59)	-0.25 (0.91)	21.25 (3.19)

* BMI is transformed to age- and sex-adjusted z-scores based on the Centre for Disease Control and Prevention Growth Chart (6). non-DEB, no any DEB at any age.

Table S3. Associations between the development of DEBs and the development of depression and anxiety.

development of mental health symptoms	development of DEB	OR	95% CI	P
Depression development	binge-eating	4.55	2.92-7.15	3.1E-11
	purging	2.14	1.42-3.20	3.0E-04
	dieting	4.43	2.47-7.93	1.1E-06
	BoP	3.08	2.13-4.45	3.9E-09
	any DEB	4.53	2.87-7.16	1.4E-10
Generalized anxiety development	binge-eating	3.47	2.24-5.35	5.5E-08
	purging	2.02	1.31-3.06	1.7E-03
	dieting	4.25	2.16-8.11	5.4E-05
	BoP	2.63	1.78-3.87	1.7E-06
	any DEB	3.60	2.12-6.08	3.0E-06

The p-values shown in bold survived the Holm-Bonferroni correction for 10 tests. Control variables were sex, acquisition site and the mental health symptom (i.e., depression or anxiety) at age 14.

Table S4. Psychopathological associations with binge-eating or purging (BoP).

	SDQ subscales at age 14	Without controlling for BMI			Controlling for BMI		
		OR	95% CI	P	OR	95%CI	P
BoP Developers vs. non-BoP	conduct problems	1.40	1.18-1.66	1.0E-04	1.37	1.16-1.64	2.7E-04
	emotional symptoms	1.24	1.05-1.48	0.012			
	hyperactivity/inattention	1.28	1.08-1.53	4.7E-03	1.30	1.09-1.55	3.8E-03
	peer problems	1.12	0.951-1.33	0.18			
BoP Maintainers vs. non-BoP	conduct problems	1.69	1.26-2.28	5.8E-04	1.62	1.20-2.20	1.5E-03
	emotional symptoms	1.46	1.06-2.00	0.019			
	hyperactivity/inattention	1.32	0.94-1.86	0.10			
	peer problems	0.99	0.69-1.37	0.94			
BoP Recoverers vs. non-BoP	conduct problems	1.68	1.14-2.50	0.0087			
	emotional symptoms	1.30	0.88-1.90	0.17			
	hyperactivity/inattention	1.49	1.00-2.26	0.054			
	peer problems	1.32	0.91-1.87	0.12			

The p values shown in bold survived the Holm-Bonferroni correction, correcting for 12 tests (without controlling for BMI). Significant associations were further controlled for BMI. BoP, binge-eating or purging. non-BoP, no binge-eating or purging at any age.

Table S5. Psychopathological predictors for the development of any DEB

	SDQ subscales at age 14	Without controlling for BMI			Controlling for BMI		
		OR	95% CI	P	OR	95%CI	P
Any DEB developers vs. non-DEB	conduct problems	1.36	1.10-1.68	3.9E-03	1.42	1.13-1.78	2.4E-03
	emotional symptoms	1.13	0.92-1.39	0.25			
	hyperactivity/inattention	1.23	1.00-1.52	0.051			
	peer problems	1.12	0.91-1.37	0.27			

The p-values shown in bold survived the Holm-Bonferroni correction for 4 tests (without controlling for BMI). Significant associations were further controlled for BMI. DEB: disordered eating behavior. Control variables were sex and acquisition site. non-DEB, no any DEB at any age.

Table S6. Gray matter volumes at age 14 associating with the DEB development, CD and ADHD symptoms

	cluster		peak				
	p (FWE-corrected)	#voxels	T	x	y	z	Anatomical location
DEBs: controlling for sex and sites							
binge eating developers > non-bingers	0.010	1469	4.23	17	8	0	R. Globus pallidus
			3.81	27	-2	2	R. Putamen
purging developers < non-purgers	1.0E-08	8335	4.71	-17	47	15	L. Dorsolateral PFC
			4.60	-8	47	24	L. Dorsomedial PFC
			4.56	-11	35	-12	L. Medial OFC
			4.05	-2	21	35	L. MCC
			4.03	5	39	21	R. ACC
			3.84	0	41	12	L. ACC
			3.35	5	38	-17	R. Gyrus rectus
BoP < non-BoP	2.0E-07	6380	5.41	-11	32	-12	L. Medial OFC
			4.51	-12	29	32	L. Dorsomedial PFC
			4.35	-12	18	38	L. MCC
			4.23	-3	53	-3	L. ACC
			3.86	8	36	-20	R. Gyrus rectus
DEBs: controlling for sex, sites and BMI							
binge eating developers > non-bingers	0.013	1347	4.19	17	8	0	R. Globus pallidus
			3.75	26	20	0	R. Putamen
purging developers < non-purgers	7.3E-08	7144	4.61	-17	47	15	L. Dorsolateral PFC
			4.51	-11	35	-12	L. Medial OFC

			4.45	-8	47	24	L. Dorsomedial PFC
			4.04	-12	29	30	L. ACC
			3.96	-2	21	35	L. MCC
			3.82	5	39	21	R. ACC
			3.26	5	38	-17	R. Gyrus rectus
BoP < non-BoP	2.6E-06	5006	5.28	-11	32	-12	L. Medial OFC
			4.34	-15	45	14	L. ACC
			4.23	-9	45	27	L. Dorsaomedial PFC
			4.15	-12	17	39	L. MCC
			4.06	-3	53	-3	L. ACC
			3.61	8	36	-18	R. Gyrus rectus
CD & ADHD symptoms: controlling for sex and sites							
CD symptoms	6.3E-03	1561	3.87	8	23	-12	R. Medial OFC
			3.74	0	33	9	L. Anterior cingulate cortex
	0.028	1071	5.32	-18	9	48	L. Superior & middle frontal gyrus
ADHD symptoms	4.31E-07	5911	4.81	0	57	-24	L. Gyrus rectus
			4.40	21	53	-23	R. Anterior orbital gyrus
			4.34	33	38	-8	R. IFG, pars orbitalis
			4.18	3	66	2	R. SFG, medial part
			3.87	-26	32	-23	L. Anterior orbital gyrus
			3.76	15	44	-15	R. Medial OFC
			3.12	-18	53	-21	L. Medial OFC

Results were thresholded with voxel-level $p < 0.001$ (uncorrected) and cluster-level $p < 0.05$ (FWE corrected). BoP, binge-eating or purging; OFC, orbitofrontal cortex; PFC, prefrontal cortex; MCC, middle cingulate cortex; ACC, anterior cingulate cortex, IFG, inferior frontal gyrus; SFG, superior frontal gyrus.

Table S7. Gray matter volumes at age 14 associating with the development of purging in participants who didn't report any DEB at age 14

	cluster		peak				
	p (FWE-corrected)	#voxels	T	x	y	z	Anatomical location
purging developers (without any DEB at age 14) < non-DEB	0.0014	2218	3.99	-2	39	5	L. ACC
			3.83	-8	33	-12	L. Medial OFC
			3.62	-12	27	32	L. Dorsomedial PFC
			3.22	14	36	5	R. ACC
			12	47	3	12	R. Dorsomedial PFC

Results were thresholded with voxel-level $p < 0.001$ (uncorrected) and cluster-level $p < 0.05$ (FWE corrected). Control variables were sex, site and total intracranial volume. OFC, orbitofrontal cortex; PFC, prefrontal cortex; MCC, middle cingulate cortex; ACC, anterior cingulate cortex; non-DEB, no any DEB at any age.

Table S8. Gray matter volumes at age 14 associate with the development of depressive symptoms.

	cluster		peak				
	p (FWE-corrected)	#voxels	T	x	y	z	Anatomical location
Depression developers < no-depressive symptoms	5.5E-03	1709	4.83	-45	26	24	L. Dorsolateral PFC
	1.8E-06	5501	4.62	0	9	44	SMA
			4.46	15	42	27	R. SFG
			4.26	0	59	-2	Medial OFC
			4.21	0	-6	48	L. MCC
			4.15	3	53	20	Dorsomedial PFC
			3.85	14	11	35	R. MCC
			3.54	-14	41	5	L. ACC
			3.51	-29	62	3	L. Lateral OFC

Results were thresholded with voxel-level $p < 0.001$ (uncorrected) and cluster-level $p < 0.05$ (FWE corrected). Control variables were sex, site, total intracranial volume and depressive symptoms at age 14. OFC, orbitofrontal cortex; PFC, prefrontal cortex; SMA, supplementary motor area; SFG, superior frontal gyrus; MCC, middle cingulate cortex; ACC, anterior cingulate cortex.

Supplemental Figures

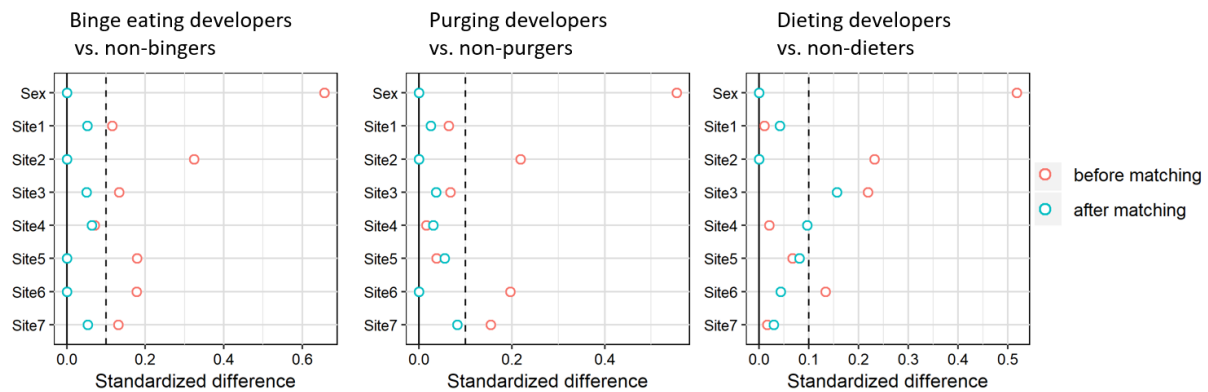


Figure S1. Covariate balance plot. Standardized differences in sex and study sites (dummy coded) between the case group and the control group are plotted before and after matching. Dashed lines represent 0.1. The cobalt package was used to create the plot (<https://github.com/ngreifer/cobalt>).

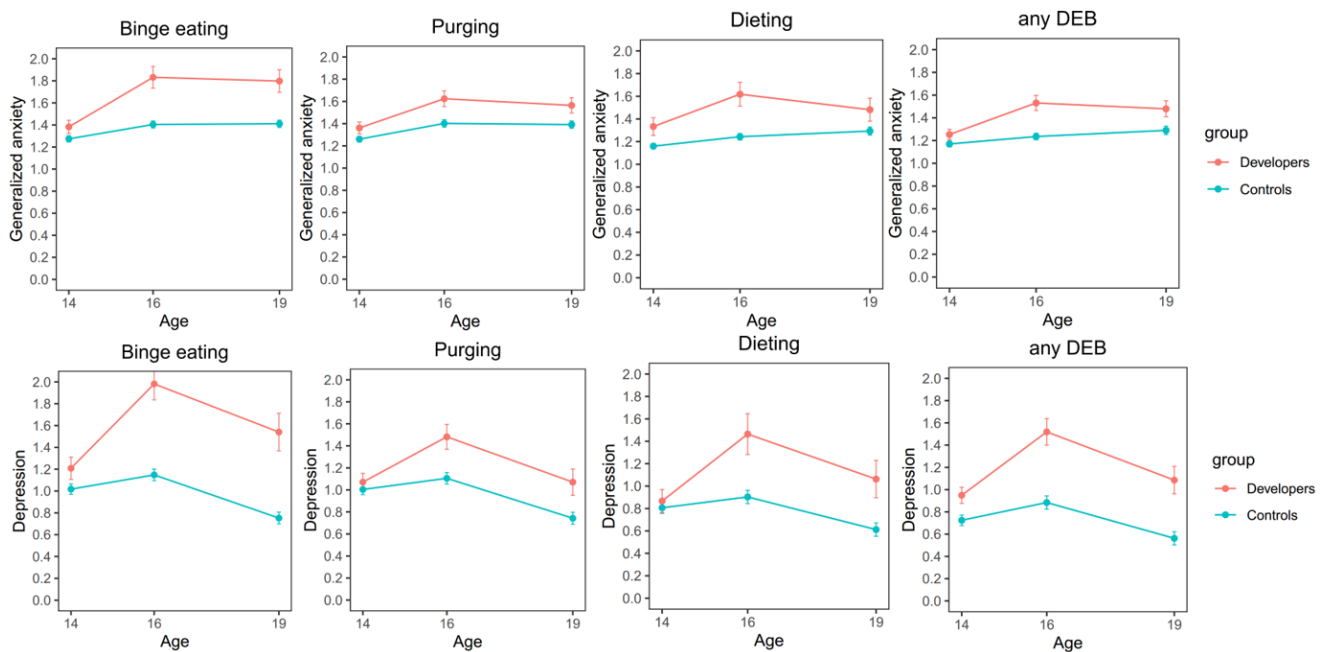


Figure S2. Computer-generated predictions (DAWBA bands) for depression and generalized anxiety (the y axis), comparing 'developers' in each DEB group to their sex- and site-matched controls. The error bars represent standard errors.

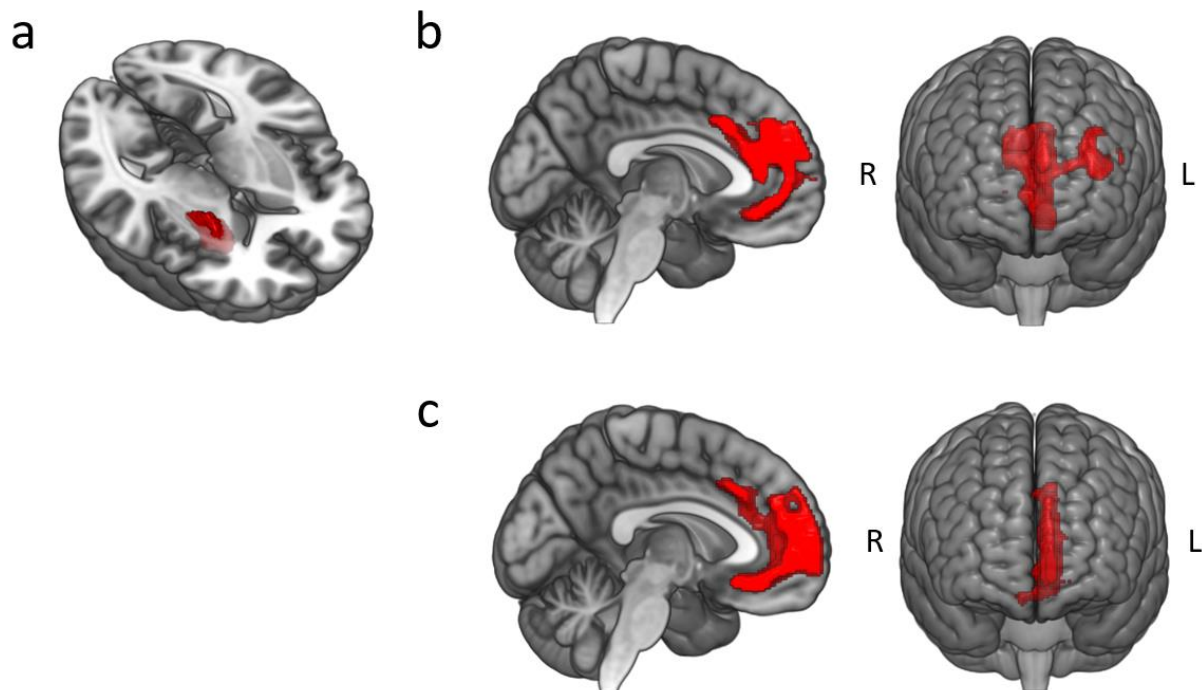


Figure S3. Structural brain associations with the development of binge-eating (a), purging (b) and BoP (c) in medication-free participants. Higher gray matter volumes in the right putamen and globus pallidus were associated with the development of binge-eating (a). The development of purging was associated with lower gray matter volumes in the medial OFC, gyrus rectus, the dorsomedial prefrontal cortex, the anterior and middle cingulate cortex and the left dorsolateral prefrontal cortex (b). The development of BoP was associated with lower gray matter volumes in the medial OFC, gyrus rectus, the dorsomedial prefrontal cortex, the anterior and middle cingulate cortex (c). Control variables included sex, acquisition site and ICV. Statistical parametric maps were thresholded at voxel-level $p < 0.001$ (uncorrected) and cluster-level $p < 0.05$ (FWE corrected).

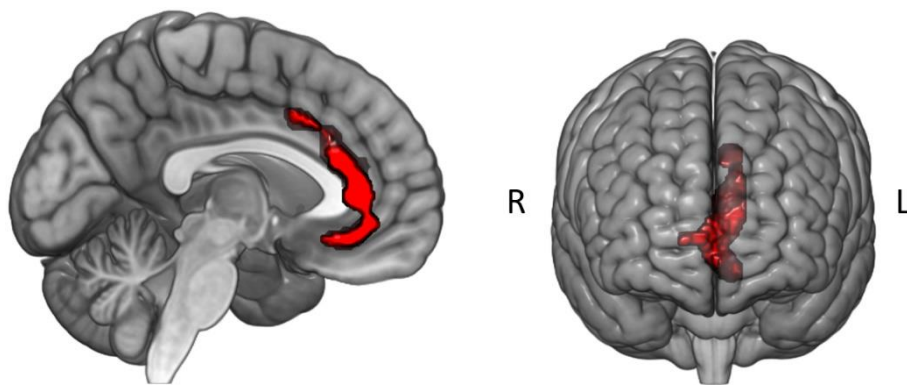


Figure S4. Structural brain associations with the development of purging in participants without any DEB at age 14. Smaller gray matter volumes in the medial OFC, the dorsomedial prefrontal cortex, the anterior and middle cingulate cortex at age 14 (without any DEB at this age) were associated with development of purging at later ages. Control variables included sex, acquisition site and ICV. Statistical parametric maps were thresholded at voxel-level $p < 0.001$ (uncorrected) and cluster-level $p < 0.05$ (FWE corrected).

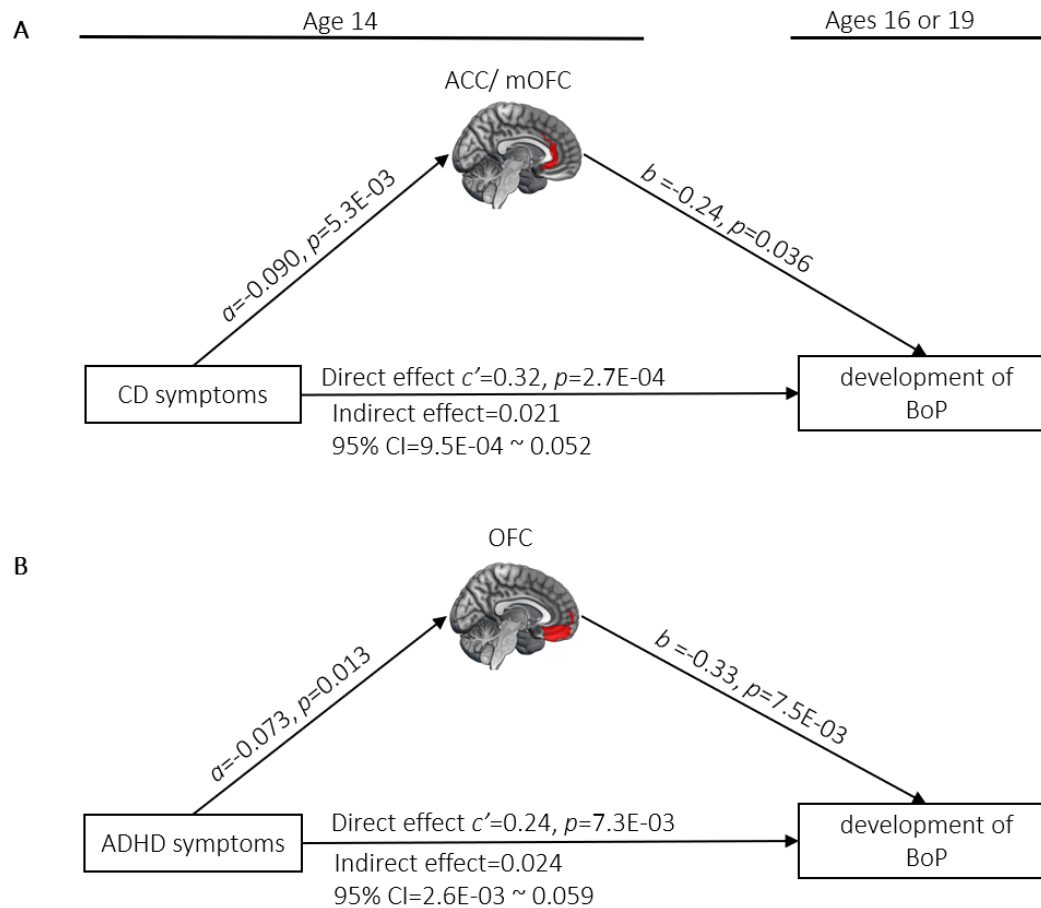


Figure S5. Results for the mediation analysis between the relationship of CD symptoms (A), ADHD symptoms (B) and the development of binge-eating or purging (BoP). The ACC/mOFC ROI linked to CD symptoms (A) and the OFC ROI linked to ADHD symptoms (B) were used as mediators. Control variables included sex, acquisition sites and the total intracranial volume. ROI: region of interest; CI: confidence interval; ACC: anterior cingulate cortex; OFC: orbitofrontal cortex.

Supplemental References

1. Bartholdy S, O'Daly OG, Campbell IC, Banaschewski T, Barker G, Bokde ALW, et al. (2019): Neural Correlates of Failed Inhibitory Control as an Early Marker of Disordered Eating in Adolescents. *Biol Psychiatry*. 85:956-965.
2. Sobell LC, Cunningham JA, Sobell MB (1996): Recovery from alcohol problems with and without treatment: prevalence in two population surveys. *Am J Public Health*. 86:966-972.
3. Ho DE, Imai K, King G, Stuart EA (2011): MatchIt: Nonparametric Preprocessing for Parametric Causal Inference. *J Stat Softw*. 42:1-28.
4. Austin PC (2011): An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. *Multivariate Behav Res*. 46:399-424.
5. Ashburner J (2007): A fast diffeomorphic image registration algorithm. *Neuroimage*. 38:95-113.
6. Flegal KM, Cole TJ (2013): Construction of LMS parameters for the Centers for Disease Control and Prevention 2000 growth charts. *National health statistics reports*.1-3.