Serotonin Function, Personality-Trait Variations, and Childhood Abuse in Women With Bulimia-Spectrum Eating Disorders

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Background: Across populations, findings associate impulsivity, behavioral disinhibition, or hostility with reduced central serotonin (5-hydroxytryptamine: 5-HT) activity and increased likelihood of childhood abuse. Inconsistently, findings associate compulsivity, behavioral inhibition, or anxiousness with elevated 5-HT neurotransmission. We explored relationships among measures of 5-HT system functioning, behavioral inhibition/disinhibition, and childhood abuse in women with bulimia-spectrum eating syndromes.

Method: In 73 bulimic (body mass index [kg/m^2] under 30, binge eating at least once weekly) and 50 normal-eater control women, we obtained indices of platelet paroxetine binding and 5-HT agonist (*m*-CPP)-stimulated neuroendocrine responses. Cluster analysis was used to classify the bulimic women according to 5-HT "profiles." Resulting groups were then compared on symptom and trait measures.

Results: Measures of paroxetine-binding density (B_{max}) and affinity (K_d) contributed significantly ($p < .001$ and $p < .02$, respectively) to a classification of bulimic women into groups with "low density/high affinity" (N = 52) or "high density/low affinity" (N = 21) binding. The 5-HT based classification did not predict eating-symptom severity. However, the "high density" pattern was associated with increased perfectionism and compulsivity, reduced risk of childhood sexual abuse, and (to some extent) reduced probability of borderline personality disorder.

Discussion: In women with bulimic syndromes, serotonergic factors, personality-trait variations, and developmental typologies converge in principled fashion. Our findings corroborate (with neurobiological evidence) the concept of underregulated and overregulated subtypes within the bulimic population.

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Manipulations that impede central serotonin (5-hydroxytryptamine: 5-HT) neurotransmission often precipitate "binge-like" eating.[1] Consistent with such effects, bulimia nervosa patients are found to display blunted neuroendocrine responses to 5-HT precursors and agonists,[2–4] reduced platelet binding of 5-HT uptake inhibitors,[2,5,6] reduced central 5-HT reuptake,[7] reduced baseline prolactin levels,[1,3] and (when binge eating at high frequency) decreased cerebrospinal fluid (CSF) levels of the 5-HT metabolite, 5-hydroxyindoleacetic acid (5-HIAA).[8] All of these effects could indicate impaired 5-HT neurotransmission.

Dieting and binge eating can promote secondary reductions in brain 5-HT activity[1,9] and might explain reduced 5-HT tone in bulimia nervosa. However, in personality-disordered individuals, studies document associations between impulsive aggressiveness or self-destructiveness and reduced density (B_{max}) of platelet binding sites for serotonin reuptake inhibitors.[11,12] In parallel, our group noted correspondence (in women with bulimic syndromes) between (1) severity of self-reported impulsivity and reduction in density of sites for platelet paroxetine binding[2] and (2) history of self-destructive behavior and blunting of 5-HT stimulated neuroendocrine responses.[4] Likewise, Waller and colleagues[10] observed self-reportedly hostile bulimics to show smaller neuroendocrine responses following buspirone (presumed to be a

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5-HT_{1A} agonist) than nonhostile bulimics. As "hostile/impulsive" characteristics are present in roughly one third of bulimia nervosa sufferers,[13–15] such traits could partly explain propensities in the population toward reduced 5-HT activity.

Assuming the preceding to be so, we became interested in studying the serotonergic implications of another spectrum of personality traits that is common in individuals with bulimic syndromes—exemplified by compulsivity or perfectionism.[13–15] Interest in such personality variations follows from findings showing inconsistent association between compulsive behavior and high 5-HT tone (corroborated by some,[16,17] but not other[18] studies) and the theory that impulsivity and compulsivity may represent opposite poles of a continuum ranging from low to high 5-HT activation.[16,17] In the present study, we tested the concept that, in women with bulimia-spectrum eating disorders, compulsive personality traits might correspond to elevated, and impulsive traits to reduced, 5-HT activity. Our study addressed a second, related question: Some findings indicate that adult survivors of childhood abuse manifest the combination of impulsivity and reduced 5-HT tone. For instance, studies have associated borderline personality disorder (for which behavioral dysregulation is pathognomonic) with exposure to childhood sexual abuse[19] and propensity toward reduced 5-HT activity.[20] In parallel, studies have linked "borderline" or "impulsive" characteristics in bulimia nervosa with history of sexual abuse[21,22] and with reduced 5-HT activity.[21] As such relationships imply that impulsivity, childhood abuse, and 5-HT function may be interrelated in bulimia nervosa, we rounded out our study by adding childhood-abuse measures.

METHOD

Participants

Participation in this institutional ethics board–approved study, conducted from February 1998 to February 2003, was by informed consent. Women with bulimia-spectrum disorders (N = 86) were recruited through a specialized Eating Disorders Program for adults, using the following criteria: female, aged 17 to 50 years, body mass index (BMI: kg/m^2) under 30, binge eating at least once weekly, and not pregnant, anorexic, or on psychoactive medication therapy (in the last 6 weeks). Eating disorder symptoms were confirmed using the Eating Disorders Examination (EDE).[23] We excluded 7 recruits due to ECG abnormalities or other medical conditions that would contraindicate endocrine challenge, 1 due to amphetamine abuse revealed by an enzyme-multiplied immunoassay technique (EMIT) urine screen, and another due to cannabinoid abuse. In 4 more cases, a vein could not be obtained for blood draws. We thus completed full assays in 73 women, 59 (80.8%) of whom met DSM-IV[24] criteria for bulimia nervosa–purging subtype, 6 (8.2%) for bulimia nervosa–nonpurging subtype, and 8 (11.0%) for a "subclinical" bulimia nervosa–purging type (binge eating once versus twice weekly). We felt diagnostic variations to be acceptable, given studies identifying negligible differences on psychopathologic indices between individuals who binge or purge at threshold versus subthreshold levels,[25,26] or whose calorie consumption suggests "subjective" versus "objective" binges.[27] Mean ± SD age was 25.15 (± 6.30) years and BMI was 21.93 (± 2.45).

Healthy women, recruited through university classes or newspaper advertisements (to approximate the student/nonstudent ratio among bulimics), were aged 18 to 40 years and had relatively normal BMIs (over 18 and under 30). Candidates passed an initial structured telephone screening (designed for this study) that assessed past or present eating disorders, periods of intense weight concerns or marked intentional weight loss, binge eating, purging, medical problems, history of mental-health problems (e.g., depression, anxiety, substance abuse) and treatments, pregnancy, lactation, menstrual status, and use of psychoactive/serotonergic medications. A second screening tier excluded individuals according to findings of structured diagnostic interviews (described below) and physical examinations (that included routine blood work and ECG). This stage eliminated 11 people with eating or weight concerns, 6 with major depression or an anxiety disorder, 1 reporting regular substance abuse, 2 reporting a history of suicidality, and 5 more who ultimately showed ECG or other medical abnormalities. Finally, in 5 cases, needed blood samples could not be obtained. After exclusions, we obtained data on 50 control cases. The control sample had a mean age of 22.82 (± 5.11) years and a BMI of 21.98 (± 1.99). According to t tests, bulimic and control groups did not differ on BMI. Although bulimics were, on average, slightly older than controls ($t = –2.17$, $df = 121$, $p < .04$), main comparisons of interest were performed within bulimic subjects, between groups showing similar mean ages.

Measures

Eating disorder symptoms. We assessed eating disorder symptoms using the Eating Disorders Examination (EDE),[23] a structured interview estimating presence and severity of criterion eating disorder symptoms (e.g., frequency of binge/purge behaviors). Interrater reliability and internal consistency of the EDE are excellent. An additional estimate of eating-symptom severity was obtained using the well-known Eating Attitudes Test (EAT-26).[28] Finally, we applied the body dissatisfaction subscale from the Eating Disorders Inventory-2 (EDI-2).[29] This scale evinces excellent internal consistency and provides a well-validated index of body-image problems. (The EDI-2 was introduced partway through this study and was completed, therefore, by only 63 bulimic and 42

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normal-eater women.) To reflect nutritional status, we computed BMI (kg/m^2).

Trait and mood characteristics. To reflect impulsivity, we used the Barratt Impulsivity Scale (BIS, version 10),[30] a 30-item scale showing good internal consistency and correspondence with behavioral tests of response disinhibition. We also applied selected subscales from the Dimensional Assessment of Personality Pathology-Basic Questionnaire (DAPP-BQ),[31] which taps such traits as compulsivity (characterized by orderliness, conscientiousness, and hypervigilance), sensation seeking (defined by recklessness, impulsivity, and hyperactivity), restricted expression (involving proneness to low self-disclosure and restricted affective expression), and affective instability (implying mood lability, overreactivity, and irritability). The DAPP has been carefully developed using factor-analytic techniques applied to responses on expert-generated symptom items of various clinical groups. Subscales evince solid internal consistency and discriminant validity. To complement the personality assessment, we included the perfectionism subscale from the EDI-2 (in the subset of cases described above). This scale evinces excellent internal consistency, 1-week and 1-year test-retest reliability, and ability to discriminate eating- and non–eating-disordered populations. Finally, to measure depression, we used the Center for Epidemiological Studies Depression (CES-D) scale,[32] a 20-item self-report scale showing good content and concurrent and discriminant validity.

Borderline personality disorder. The borderline personality disorder construct was assessed using the Structured Clinical Interview for DSM-IV Axis-II Disorders.[33] For present purposes, we excluded the borderline personality disorder criterion referring to overeating. Data collection took place over a roughly 4-year period. During roughly the first 2 years of the study, we obtained a kappa of .80 (representing 91.7% agreement) for a borderline personality disorder/non–borderline personality disorder distinction in a subset of 12 interviews selected quasi-randomly to represent borderline and nonborderline cases. A similar test conducted using 26 quasi-randomly selected interviews from the second 2 years of the study yielded a kappa of .91 (and percent agreement of 96.2%).

To screen for psychiatric comorbidity, we used a computerized version of the Diagnostic Interview Schedule, Version IV (DIS4)[34] to guide face-to-face clinical interviews. This DSM-IV version of the NIMH Diagnostic Interview Schedule evinces satisfactory sensitivity for various Axis I entities (depression/dysthymia and phobic, panic, and generalized anxiety disorders), but lesser sensitivity for obsessive-compulsive and drug use/dependence disorders. Reported kappa values reflecting correspondence with traditional diagnostic interview methods are high, and obtained disorder prevalences correspond to expected values.[34]

Childhood abuse. The Childhood Trauma Interview (CTI)[35] is a roughly 30-minute structured interview designed to elicit and characterize experiences of childhood physical, sexual, and emotional abuse. The interview quantifies severity of various forms of abuse and establishes perpetrators' and subjects' ages when abuse occurred. Interrater reliability, construct validity, and convergent validity for indices reflecting the nature, severity, frequency, and duration of traumata are reportedly very good. In the present study, we utilized severity and age indices to isolate experiences of nonambiguous physical or sexual maltreatment occurring at or below age 14, according to criteria described elsewhere.[21]

Scale translation. Given a bilingual population, French translations of scales were required. Elsewhere, we have described the preparation, application, and validation of French translations of scales used.[4,21]

Measures of serotonin function. As serotonin promotes prolactin secretion from the pituitary, it is conventional to draw inferences about central 5-HT functioning from 5-HT–induced alterations in plasma prolactin.[36] The partial 5-HT agonist meta-chlorophenylpiperazine (*m*-CPP) binds with highest affinity to $5\text{-}HT_{2C}$ receptors and lesser affinity to $5\text{-}HT_{1A}$ and α_2-noradrenergic receptors; hence, *m*-CPP is believed to constitute a fairly specific 5-HT probe. Similarly, binding of 5-HT reuptake inhibitors to platelet membranes is believed to model some aspects of central (presynaptic) 5-HT transporter function.[37] In keeping with this belief, studies using platelet imipramine binding[5] or [^{3}H]-paroxetine binding[2,6] have shown reduced transporter density (B_{max}), but not altered affinity (K_d), in bulimic women. The pertinence of such findings to central processes is suggested by photon emission tomography studies showing reduced 5-HT transporter (reuptake) availability in bulimia nervosa.[7] Blood samples to support paroxetine-binding measurements were obtained from all participants in our study. Serial measurements for prolactin response after *m*-CPP were obtained from a subset of 63 bulimic and 43 control individuals.

Blood sampling. Participants were required to have been free of prescribed psychoactive medications for at least 6 weeks. Except for 4 cases in whom menses were absent, all participants were tested in follicular phase (5 to 14 days following start of last menses). Amenorrheic individuals had relatively normal BMIs (mean = 20.31, range, 18.6–22.1) and were evenly distributed (2 per group) across "high" or "low" 5-HT activity groups. This factor could not, therefore, have confounded findings. We did not treat oral contraceptive use as an exclusion criterion, but did control statistically for its potential effects. Samples were drawn after an overnight fast (begun at 11 p.m.). Participants were asked to refrain from alcohol, exercise, or street drugs for 48 hours prior to testing and from binge eating for 24 hours. A urine screen for

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Table 1. Values for Bulimic and Control Participants on Variables Reflecting Eating Symptoms, Psychological Traits, and Neurobiological Findings[a]

	Bulimic Women		Control Women			
Variable	Mean (SD)	N	Mean (SD)	N	t	(df)
Binge episodes/mo (past 3 mo)	33.03 (30.31)	73	0.00 (0.00)	50	...	
Binge days/mo (past 3 mo)	17.22 (7.22)	73	0.00 (0.00)	50	...	
Vomiting episodes/mo (past 3 mo; vomiters only)	53.64 (65.28)	63	0.00 (0.00)	50	...	
EAT-26	39.24 (12.46)	71	3.49 (4.01)	49	–19.39	(118)**
CES-D total	29.18 (12.70)	70	8.95 (6.85)	50	–10.24	(118)**
Impulsivity	70.90 (9.51)	71	61.53 (8.49)	50	–5.51	(119)**
Compulsivity	3.47 (0.90)	69	3.02 (0.75)	50	–2.91	(117)*
Perfectionism	9.74 (5.00)	63	3.86 (3.53)	42	–6.60	(103)**
Paroxetine binding:B_{max} (fmol/mg)	546.33 (268.03)	73	1061.50 (509.00)	50	7.30	(121)**
K_d (nM)	0.16 (0.16)	73	0.22 (0.27)	50	1.58	(121) NS
Area under the curve prolactin	39.44 (19.41)	63	53.23 (25.77)	43	3.14	(104)*
Baseline prolactin (ng/mL)	7.41 (2.99)	63	10.74 (5.39)	43	4.08	(104)**

[a]Occasional missing values are indicated by Ns and dfs.
*$p \leq .01$.
**$p \leq .001$.
Abbreviations: CES-D = Center for Epidemiological Studies-Depression, EAT-26 = Eating Attitudes Test, NS = nonsignificant.

illicit drug use (Syva EMIT kit, manufactured by Syva, Cupertino, Calif., or Adaltis, San Diego, Calif.) was also applied. Given known seasonal variations on *m*-CPP–stimulated prolactin release[38] and paroxetine binding,[39] we used covariance techniques to control for possible seasonal influences. Effects of seasonal variations were tested using 3 "dummy codes" to contrast summer values to each of the remaining seasons. The specific procedure applied is described in detail elsewhere.[21] Similarly, our specific sampling and laboratory procedures are detailed elsewhere.[2,6,21]

RESULTS

An initial analysis contrasted bulimic and control participants on variables reflecting eating symptoms, psychological traits, and neurobiological indices (Table 1). Given "zero" values for control participants on binge and vomit frequencies, we performed no statistical tests on these variables. Compared with control women, bulimic women had significantly higher EAT-26, CES-D, impulsivity, compulsivity, and perfectionism scores. The bulimic versus control effect for B_{max} from paroxetine binding was significant in a t test (see Table 1), and also in an analysis of covariance (ANCOVA) in which "contraceptive use" and "season of testing" were entered as covariates ($F = 133.81$, $df = 1,116$; $p < .001$). The corresponding bulimic versus control comparison on K_d yielded nonsignificant results in a simple t test (see Table 1), but a statistical trend in an ANCOVA controlling contraceptive and season effects ($F = 3.13$, $df = 1,116$; $p < .08$). On measures of area-under-the-curve (AUC) prolactin, means for bulimics and controls differed on a t test (see Table 1) and in an ANCOVA that controlled for contraceptive and season effects ($F = 4.89$, $df = 1,100$; $p < .03$). Similarly, means for bulimic and control women on baseline prolactin differed on a t test (see Table 1) and in ANCOVA controlling contraceptive and season effects ($F = 6.95$, $df = 1,100$; $p < .02$). In sum, bulimic patients showed expected global reductions in 5-HT activity compared with normal eaters.

To examine the extent to which profiles of 5-HT functioning isolated distinct bulimic subgroups, we entered 4 biological parameters—those reflecting receptor density (B_{max}), receptor affinity (K_d), baseline prolactin, and AUC prolactin—into a cluster analysis treating bulimic participants only. (Ten participants were lost from this analysis due to missing prolactin values). Two variables, B_{max} ($F = 131.63$, $df = 1,61$; $p < .001$) and K_d ($F = 5.84$, $df = 1,61$; $p < .02$) contributed significantly to differentiation of cluster centers. The clustering indicated one group ($N = 43$) to be characterized by low density of binding sites (B_{max} cluster center = 407.08) and high binding affinity (K_d cluster center = .12), and another ($N = 20$), by relatively high binding with low affinity (B_{max} cluster center = 891.14; Kd cluster center = .23). B_{max} and K_d were significantly correlated in the overall sample ($r = .45$, $p < .001$), among eating-disordered participants only ($r = .39$, $p < .001$), and among controls only ($r = .47$, $p < .001$). Of course, given the nature of B_{max} and K_d values, positive correlations indicate an inverse relationship. Higher B_{max} and K_d values in the "high 5-HT reuptake density" bulimic group approached mean values obtained in our reference group of normal-eater controls (mean $B_{max} = 1061.50$; mean $K_d = .22$). (Analysis of the range of B_{max} values obtained in bulimic and nonbulimic groups suggested that we were sampling from substantially different populations. We therefore opted to treat the control participants as a single reference group, rather than attempting to cluster them into parallel high and low transporter density groups). Given that B_{max} and K_d alone contributed to the clustering, we reclassified our full sample

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Table 2. Values on Measures of Eating Symptoms and Psychopathologic Traits and Number Reaching Criterion Scores on Categorical Axis I and II Diagnoses[a]

	Bulimic With Low Reuptake Density		Bulimic With High Reuptake Density		Control		
Variable	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Statistic
Age	25.00 (6.02)	52	25.52 (7.10)	21	22.82 (5.11)	50	F = 2.40, df = 2,120
Binge episodes/mo (past 3 mo)	33.54 (29.09)	52	31.76 (33.88)	21	0 (0)	50	t = 0.23, df = 71; NS
Binge days/mo (past 3 mo)	17.19 (7.53)	52	17.30 (8.38)	21	0 (0)	50	t = –0.06, df = 71; NS
Vomiting episodes/mo (past 3 mo; vomiters only)	55.46 (63.84)	45	49.07 (70.46)	18	0 (0)	50	t = 0.35, df = 61; NS
EAT-26	39.39 (12.89)[b]	50	38.89 (11.64)[b]	21	3.49 (4.01)[a]	49	F = 186.48, df = 2,117***
Body dissatisfaction	17.94 (8.21)[b]	43	19.35 (7.55)[b]	20	6.49 (6.88)[a]	42	F = 31.33, df = 2,102***
Body mass index	21.89 (2.27)	52	22.04 (2.91)	21	21.98 (1.99)	50	F = 0.04, df = 2,120; NS
Barratt impulsivity	71.22 (9.58)[b]	50	70.14 (9.52)[b]	21	61.53 (8.79)[a]	50	F = 15.17, df = 2,118***
CES-D total	30.02 (11.40)[b]	49	27.24 (15.47)[b]	21	8.95 (6.85)[a]	50	F = 52.95, df = 2,117***
Affective instability	3.58 (0.87)[b]	48	3.66 (0.83)[b]	21	2.34 (0.70)[a]	50	F = 37.01, df = 2,116***
Stimulus seeking	2.92 (0.91)[b]	48	2.88 (0.87)[b]	21	2.42 (0.58)[a]	50	F = 5.56, df = 2,116**
Compulsivity	3.33 (0.92)[a]	48	3.81 (0.77)[b]	21	3.02 (0.75)[a]	50	F = 6.82, df = 2,116**
Restricted expression	3.15 (0.84)[b]	48	3.39 (0.81)[b]	21	2.28 (0.70)[a]	50	F = 22.13, df = 2,116***
Anxiousness	3.74 (0.89)[b]	48	3.94 (0.79)[b]	21	2.36 (0.86)[a]	50	F = 40.96, df = 2,116***
Self-harm	2.17 (1.06)[b]	48	2.23 (1.24)[b]	21	1.13 (0.25)[a]	50	F = 21.93, df = 2,116***
Perfectionism	8.97 (4.94)[b]	43	11.38 (4.83)[c]	20	3.86 (3.53)[a]	42	F = 24.48, df = 2,102***
	n (%)	N	n (%)	N	n (%)	N	
Panic disorder	11 (22.4)	49	5 (26.3)	19	0 (0)	49	χ^2 = 13.53, df = 2**
Generalized anxiety disorder	10 (20.4)	49	4 (21.1)	19	0 (0)	49	χ^2 = 11.47, df = 2**
Major depression	34 (69.4)	49	14 (73.7)	19	4 (8.2)	49	χ^2 = 48.24, df = 2***
Obsessive-compulsive disorder	8 (16.3)	49	4 (21.1)	19	1 (2.1)	48	χ^2 = 7.16, df = 2*
Physical abuse before age 14	35 (68.6)	51	16 (76.2)	21	17 (36.2)	47	χ^2 = 14.30, df = 2**
Sexual abuse before age 14	21 (41.2)	51	3 (14.3)	21	6 (12.8)	47	χ^2 = 12.09, df = 2**
Borderline personality disorder	17 (35.4)	48	3 (14.3)	21	0 (0)	48	χ^2 = 21.38, df = 2***

[a]F and χ^2 tests reported here are for 3-group comparisons. Results of tests implicating the 2 bulimic groups alone are reported in the text. Means with different superscript letters differ at the $p < .05$ level on Newman-Keuls tests.
*$p \leq .05$.
**$p \leq .01$.
***$p \leq .001$.
Abbreviations: CES-D = Center for Epidemiological Studies-Depression, EAT-26 = Eating Attitudes Test, NS = nonsignificant.

of 73 bulimics (for whom paroxetine binding indices were always available) into "high" (N = 52) and "low" (N = 21) 5-HT transporter density groups, applying B_{max} and K_d indices in a second cluster analysis.

We next compared "high density," "low density," and normal-control groups on variables reflecting age, eating symptoms, psychopathologic traits, lifetime history of selected Axis I entities, borderline personality disorder, and history prior to age 14 of severe childhood sexual and physical abuse (see Table 2). Bulimic/control differences were obtained on most variables. Comparisons across bulimic groups suggested, however, that the 5-HT–based classification had little bearing upon eating symptoms (monthly binge/vomit frequencies, monthly binge days, maladaptive eating attitudes shown by the EAT-26, body dissatisfaction, or BMI), but did correspond to various differences on indices of general psychopathology and child abuse. Notably, "low density" bulimics reported childhood sexual abuse (prior to age 14) more often than did their "high density" counterparts ($\chi^2 = 4.84$, df = 1, $p < .04$, in a 2×2 χ^2 test of the difference between bulimic groups only), and a trend toward more frequent borderline personality disorder ($\chi^2 = 3.17$, df = 1, $p < .10$)—but lower scores on compulsivity and perfectionism (see Table 2). Furthermore, the "high density" bulimics showed elevated compulsivity and perfectionism when compared with normal-eater controls. In other words, reduced 5-HT transporter density coincided with greater risk of sexual abuse and (as a trend) borderline personality disorder, whereas increased 5-HT density coincided with compulsivity, perfectionism, and reduced risk of childhood abuse. Other effects obtained were attributable to a bulimic/control distinction rather than the 5-HT–based classification (see Table 2).

DISCUSSION

This study was structured around 2 concepts: (1) that women with bulimia-spectrum eating disorders could be grouped empirically according to indices of serotonin function and (2) that 5-HT–based classifications would covary systematically with traits of an impulsive or compulsive type and with developmental experiences (like childhood abuse). Cluster analytic findings support the first concept partially, suggesting 2 key clusters, attributable to variations in paroxetine-binding density (B_{max}) and affinity (K_d). We note that, based on significance levels obtained, the clustering results should be understood to be

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more strongly attributable to B_{max} than to K_d and imply that women suffering bulimic syndromes often evince reduced density of platelet binding sites for paroxetine—as would be consistent with previous results [2,5,6]—but sometimes show elevations. If so, the question arises: What are the implications of serotonergic variations within the population?

Findings indicating low 5-HT density in individuals with bulimic syndromes are compatible with other findings in the literature associating binge-eating with reduced activity in 5-HT mechanisms.[1–8] It is necessary to note, of course, that the finding of reduced platelet paroxetine binding is not specific to the presence of active bulimia nervosa. Rather, platelet paroxetine binding (B_{max}) is found to be low in cocaine dependency,[40] suicide attempters,[41] recent stroke,[42] self-mutilation and impulsive aggression,[11,12] and other disturbances. An implication is that reduced B_{max} cannot be unique to bulimic syndromes, but may signal presence of a generalized psychopathologic state, often having a flavor of behavioral and affective dysregulation.

Correlates of "cluster" findings. In keeping with the preceding, patients evincing the "low transporter density" profile displayed heightened propensity to childhood sexual abuse and, as a trend, borderline personality disorder. Such correlates are compatible with findings linking reduced 5-HT activity in bulimia nervosa sufferers to greater impulsivity, "borderline traits," self-mutilativeness and hostility,[2,4,10] and (in bulimic and nonbulimic women alike) exposure to childhood abuse.[20,21] Together, such findings point to an association among low 5-HT activity, behavioral and affective dysregulation, and childhood abuse. It is not evident, at this point, whether an observed connection between low 5-HT activity and abuse indicates (1) an adverse impact of abuse on 5-HT activity, (2) a serotonergic correlate of a trait (like impulsivity) that coincides with heightened risk of abuse, (3) chance co-occurrence of risk agents, some developmental and some constitutional, in maladjusted populations, or (4) activation of an underlying constitutional vulnerability (e.g., tendency to reduced 5-HT activity) by traumatic stressors (like childhood sexual abuse).

In intriguing counterpoint to the preceding, our results indicate existence of a "high 5-HT density" bulimic variant, characterized by proneness to perfectionism, compulsivity, and relatively low risk of childhood sexual abuse. This pattern is intriguing for several reasons: (1) it coincides with reported associations of a link between compulsive-spectrum traits and elevated 5-HT activity in other (non–eating-disordered) populations[16,17]; (2) it resembles findings linking heightened perfectionism and compulsivity with elevated 5-HT metabolism in recovered anorexic women[43]; and (3) it challenges the prevailing notion that binge eating arises from a generalized reduction in 5-HT tone—as we observe "high" and "low" 5-HT density variants in patients who are, otherwise, comparable as to bulimic symptoms and apparent nutritional status. This implies that 5-HT status in women with bulimic syndromes is not a simple consequence of an active eating disorder, but may correspond to other factors—notably "trait" characteristics like impulsivity and compulsivity. According to our findings, a systematic relationship is indicated between cluster, analytically derived 5-HT typologies, on the one hand, and various trait and developmental typologies, on the other.

We add a note on the interpretation of findings indicating a "high 5-HT density" clustering among our bulimic women. The "higher" paroxetine-binding values obtained in this second bulimic group compare with those obtained (on average) in our normal-eater women, and could therefore imply bulimics with normal (rather than subnormal) levels of 5-HT reuptake. Alternatively, considering that dietary pressures in such actively bulimic individuals should tend to reduce 5-HT activity,[1,8,9] we speculate that these findings may actually show a suppression of supranormal 5-HT activity—a similar explanation having been proposed to explain findings indicating reduced metabolism in active cases compared with supranormal 5-HT metabolism in recovered anorexics.[43] Whether the "high transporter density" profile indicates "average" or "supranormal" 5-HT density, however, its presence calls into question the premise that bulimic syndromes must be uniformly associated with reduced 5-HT transporter function.

We add that, in the present study, we observe no relationship, as previously reported by our group,[2] between reduced B_{max} (for paroxetine binding) and heightened non-planning impulsivity (measured by the Barratt scale). We do, however, observe a significant association between high B_{max} and compulsivity (see Table 2), and a significant inverse correlation between compulsivity and non-planning impulsivity in our bulimic participants ($r = –0.36$, $p < .005$). Given these tendencies, we infer that we are observing parallel effects, but revealed in one study by a negative correlation between 5-HT reuptake density and impulsivity, and in the current study, by a positive relationship between the same index of 5-HT reuptake and compulsivity. Inconsistencies, we presume, reflect complexities of the relationship between compulsivity and impulsivity dimensions—and the probability that bulimic, impulsive, and compulsive tendencies coincide in complex ways with 5-HT dysregulation, rather than some simple unidirectional tendency toward serotonergic underactivity or overactivity.

It is also necessary to bear in mind limitations of drawing inferences about central transporter function based on a peripheral (platelet) measure of 5-HT reuptake. Aside from basic questions about the extent to which central and peripheral indices are ontogenous, many intervening variables may act upon peripheral indices, so as to cause them to come into desynchrony with central ones. Nonetheless,

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evidence from brain-imaging,[7] treatment-response,[44] and other studies do argue that platelets may (at least) represent a "proxy" for central functioning.

Conclusions. We understand our results to indicate competing trait-related serotonergic processes—some associating behavioral dysregulation and childhood abuse with hyposerotonergic status; others, behavioral overregulation with hyperserotonergic status. In indicating a systematic convergence between serotonergic factors and personality/developmental typologies in individuals with bulimic syndromes, our findings validate a distinction among sufferers based on underregulated and overregulated behavioral characteristics.[13–15] The present findings are, however, among the first to demonstrate a convergence of trait-related, developmental, and serotonergic factors that could underlie the different clusterings of bulimic individuals to which these proposals have referred. Despite areas of ambiguity, our findings suggest that "traits" are an important organizing construct in modeling eating and related pathologies. Indeed, evidence seems to suggest that traits may be central to the proper characterization of patterns of variation on developmental and biological indices within (and probably beyond) the population of eating-disordered individuals. If so, then these findings encourage various speculations concerning potential clinical implications: For example, if impulsivity (or generalized dysregulation) implies a psychopathology characterized by decreased 5-HT activity and exposure to developmental adversity, whereas compulsivity (or overregulation) implies excess 5-HT activity with lesser likelihood of developmental trauma, then these trait variations would quite likely indicate different patient subgroups, with different treatment needs. In the former, it is possible that adjunctive treatment with selective serotonin reuptake inhibitors (SSRIs), or with psychotherapeutic interventions aimed at self-regulatory deficits, will be required. In the latter, we may be witnessing effects of high anxiety or stress, but lesser constitutional propensity to serotonergic insufficiency. Studies on the prognostic and treatment implications of trait and 5-HT variations in bulimic syndromes thus seem indicated.

Drug names: amphetamine (Adderall and others), buspirone (BuSpar), paroxetine (Paxil and others).

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