Use of Factor-Analyzed Symptom Dimensions to Predict Outcome With Serotonin Reuptake Inhibitors and Placebo in the Treatment of Obsessive-Compulsive Disorder

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Objective: No consistent predictors of outcome have been identified for the pharmacotherapy of obsessive-compulsive disorder (OCD). Recent factor analytic studies have identified meaningful symptom dimensions that may be related to response to serotonin reuptake inhibitors and other treatments. **Method:** A total of 354 outpatients with primary OCD were administered the Yale-Brown Obsessive Compulsive Scale Symptom Checklist, and its 13 main symptom categories were factor analyzed by using principal components analysis. The identified symptom dimensions were then entered into multiple regression models as outcome predictors of response to serotonin reuptake inhibitors and placebo response in a group of 150 nondepressed subjects who completed six double-blind, placebo-controlled trials with a serotonin reuptake inhibitor (clomipramine, fluvoxamine, fluoxetine, sertraline, and paroxetine). Eighty-four patients received a serotonin reuptake inhibitor and 66, placebo. **Results:** The principal components analysis identified five factors that explained 65.5% of variance in outcome: symmetry/ordering, hoarding, contamination/cleaning, aggressive/checking, and sexual/religious obsessions. Serotonin reuptake inhibitors were significantly superior to placebo on all outcome measures. Initial severity of OCD was related to greater posttreatment severity of OCD. Higher scores on the hoarding dimension predicted poorer outcome following treatment with serotonin reuptake inhibitors, after control for baseline severity. No predictors of placebo response were identified. Exclusion of clomipramine did not modify the overall results, suggesting a cross-serotonin reuptake inhibitor effect. **Conclusions:** The identified symptom dimensions are largely congruent with those identified in earlier reports. Patients with OCD vary in their response to treatment with serotonin reuptake inhibitors. The presence of hoarding obsessions and compulsions is associated with poorer response to serotonin reuptake inhibitors.

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The efficacy of both exposure therapy and serotonin reuptake inhibitor antidepressant treatment in obsessive-compulsive disorder (OCD) has been well established in placebo-controlled studies. Although many have benefited from those treatments, 10% to 40% of patients do not respond to an adequate trial (1, 2). However, the existing literature on reliable predictors of treatment outcome in OCD is sparse and inconsistent. The predominance of compulsive symptoms, cleaning rituals, earlier age at onset, longer illness duration, and chronic course was found to be associated with poor response to serotonin reuptake inhibitors in some studies (3–5). In two retrospective studies, the presence of schizotypal personality was a negative outcome predictor for pharmacological (6) and behavioral (7) treatments. The presence of schizotypal, avoidant, and borderline personality disorders predicted poorer treatment outcome with clomipramine (8). However, in one study the presence of a personality disorder was not related to improvement with fluoxetine (9). Similarly, others found that the presence of various personality disorders was not related to outcome with behavior therapy (10).

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TABLE 1. Baseline Demographic and Clinical Characteristics of 150 Patients With OCD Who Participated in Six Placebo-

Variable	Jenike et al., 1989 (23)			Jenike et al., 1990 (24)			Tollefson et al., 1994 (25)			Jenike et al., 1997 (13)		
Drug	Clomipramine, 200–300 mg/day			Fluvoxamine, up to 300 mg/day			Fluoxetine, 20, 40, 60 mg/day			Fluoxetine, up to 80 mg/day		
	N			*N*			*N*			*N*		
Patients who completed the study	27			34			18			37		
Drug	13			15			14[a]			18		
Placebo	14			19			4			19		
Sex												
Male	12			16			8			20		
Female	15			18			10			17		
	Mean	*SD*	*Range*	*Mean*	*SD*	*Range*	*Mean*	*SD*	*Range*	*Mean*	*SD*	*Range*
Age (years)	39.4	10.5	24–63	34.8	10.8	19–68	32.5	9.9	19–50	36.0	12.9	20–67
Age at onset (years)	21.7	9.7	9–51	17.9	10.6	3–54	—	—	—	—	—	—
Yale-Brown Obsessive Compulsive Scale score												
Total	25.7	5.1	17–35	22.5	4.9	8–31	23.5	4.1	16–29	19.9	5.0	9–28
Obsessions	12.4	2.9	5–17	11.1	2.4	5–16	11.1	3.1	5–16	9.5	3.3	0–15
Compulsions	13.3	3.1	7–18	11.3	3.5	0–16	12.3	2.9	8–15	10.4	3.6	0–15
NIMH OCD scale score	9.4	1.2	8–12	8.8	1.6	7–12	—	—	—	7.6	0.9	5–10
Hamilton depression scale score[c]	4.8	2.5	0–10	8.3	5.8	0–19	5.9	3.8	1–13	6.7	3.6	1–15

[a] Four patients had 60 mg/day, four had 40 mg/day, and six had 20 mg/day.
[b] Eleven patients had 60 mg/day, six had 40 mg/day, and six had 20 mg/day.
[c] Based on 17-item scale.

The symptoms of OCD are heterogeneous, so that any given patient with this diagnosis may present with only one or, more commonly, many of these symptoms (11). Studies are, however, conflicting about whether any particular subtype of OCD is easier to treat or more likely to benefit from a particular treatment. For instance, there is some evidence that OCD patients with comorbid chronic tic disorders, and possibly those with concurrent psychotic spectrum disorders, are more likely to require the addition of a neuroleptic medication to treatment with a serotonin reuptake inhibitor (12). Recently, Jenike et al. (13) reported that monoamine oxidase inhibitors (MAOIs) may be preferentially useful for the treatment of symmetry and unusual somatic obsessions. Similarly, the presence of symmetry obsessions, ordering compulsions, and hoarding rituals predicted better response in refractory patients treated with cingulotomy (14). Patients with cleaning and checking symptoms may respond best to exposure methods, but other subgroups, such as patients with ordering compulsions, hoarding rituals, or obsessional slowness, have rarely been included in trials of behavior therapy (15). Some studies have suggested that patients with washing symptoms may do better with exposure therapy (16, 17) and worse with serotonin reuptake inhibitors (3, 5). Checking rituals predicted poorer outcome in some behavior therapy studies (16, 18), but others have found no differences in treatment response between patients with washing and checking symptoms (19). In addition, anecdotal evidence suggests that patients with predominantly obsessive symptoms (ruminations) might respond better to medication and worse to conventional behavioral techniques, but no empirical evidence is available.

Baer (20) has proposed searching for OCD symptom dimensions, which may be present in varying degrees and combinations in any given patient, rather than categorizing patients into mutually exclusive subgroups. His factor-analytic results, later replicated in a larger independent sample (21), confirmed the multidimensional and heterogeneous nature of OCD and suggested that the identified symptom dimensions may prove useful in future research into the etiopathogenesis, genetics, and treatment outcome, overcoming the limitations of the categorical approach of earlier studies (22). The elucidation of a putative relationship between symptom dimensions and treatment response addresses an important aspect of treatment specificity by characterizing the type of patients for whom a treatment is more appropriate and might, eventually, help to reduce the percentage of treatment failures.

In an effort to replicate and extend the findings of previous studies (20, 21), we factor analyzed data on the Yale-Brown Obsessive Compulsive Scale Symptom Checklist from a large patient group (N=354). The identified dimensions were then used as predictors of outcome in a subgroup of 150 patients who had completed six placebo-controlled trials with a serotonin reuptake inhibitor. Our research questions were as follows: 1) What symptom dimensions best summarize the heterogeneous phenomenology of OCD? 2) How are those dimensions related to variables such as sex, age at onset, and comorbidity with chronic tic disorders? 3) How are those dimensions related to treatment outcome with serotonin reuptake inhibitors? and 4) Are there any significant predictors of placebo response?

Controlled Trials With Serotonin Reuptake Inhibitors

Jenike et al., 1990 (26)	Jenike et al., 1991 (unpublished data)			Total		
Sertraline, 200 mg/day	Paroxetine, 20, 40, 60 mg/day					
Value	*N*			*N*		
1	33			150		
1	23[b]			84		
0	10			66		
0	30			86		
1	3			64		
Mean	*Mean*	*SD*	*Range*	*Mean*	*SD*	*Range*
49	41.6	14.5	18–73	37.4	12.2	18–73
8	28.1	15.0	1–58	19.2	13.9	1–58
23	23.2	5.5	16–36	22.7	5.3	8–36
9	11.7	3.5	1–19	11.0	3.2	0–19
14	11.5	3.7	0–18	11.6	3.4	0–18
10	8.9	1.3	7–12	8.6	1.4	5–12
8	5.0	2.9	0–11	6.3	4.1	0–19

METHOD

Patients

Three hundred fifty-four ambulatory outpatients with a primary diagnosis of OCD, seen at the OCD clinic of the Massachusetts General Hospital, were included in the principal components analysis. Of those, 181 patients had participated in several placebo-controlled drug trials, 72 were part of the DSM-IV field trial, and 101 were obtained through chart review. Participants consisted of 190 men (53.7%) and 164 women (46.3%); the mean age was 36.2 years (SD=12.3, range=18–76). All subjects had had symptoms of OCD for at least 1 year; mean age at onset was 15.5 years (SD=10.6). Mean scores on the Yale-Brown Obsessive Compulsive Scale were as follows: total, 21.8 (SD=6.3); obsessions subscale, 10.9 (SD=3.5); and compulsions subscale, 11.0 (SD=4.0). Data comparability analyses showed no differences in sex distribution, age, age at onset, Yale-Brown total score, and Yale-Brown obsessions subscale score. However, the patients who had participated in drug trials scored significantly higher than the chart review patients on the Yale-Brown compulsions subscale (Mann-Whitney U=7429.5, p=0.008). The diagnosis of OCD was confirmed in all cases by an experienced psychiatrist or psychologist through use of a structured diagnostic interview. Coexisting axis I disorders such as depression were not excluded, provided that obsessive-compulsive symptoms predated the onset of the coexisting conditions.

Of the patients who had participated in drug trials, 150 had completed them and were eligible for the predictors analysis. They had participated in five published double-blind, placebo-controlled trials with a serotonin reuptake inhibitor—clomipramine (23), fluvoxamine (24), fluoxetine (13, 25), and sertraline (26)—and in a sixth, unpublished study with paroxetine (M.A. Jenike et al., 1991). Since some patients had participated in more than one of those trials, only the first study they had participated in was retained. All patients underwent a physical examination and gave a complete medical and psychiatric history, as well as written informed consent, before entering those trials. No patient met criteria for major depression according to clinical interview, and each patient had a baseline score of less than 20 on the 17-item Hamilton Depression Rating Scale (27). Patients with a history of other axis I psychiatric disorders within 1 year and pregnant or lactating women were excluded from these trials. More details can be obtained in the original publications. Pretreatment demographic and clinical data for this subgroup are shown in table 1.

Clinical Measures

For the direct assessment of OCD symptoms we used the Yale-Brown Obsessive Compulsive Scale symptom checklist, which provides more than 50 examples of obsessions and compulsions and also includes a target symptom list of the four most prominent symptoms for each patient. The major outcome measures were the 10-item clinician-rated Yale-Brown Obsessive Compulsive scale (28, 29) and the National Institute of Mental Health (NIMH) OCD scale (30). In addition, the 17-item Hamilton depression scale (27) was administered. History of chronic motor and vocal tic disorders was available from all patients in the DSM-IV field trial and chart review (N=173) and was assessed with the modules designed for that purpose in the DSM-IV field trial.

Analyses

Principal components analysis was performed by using pooled data from the three different data sources (N=354), following the original methodology of Baer (20). Briefly, for each of the 13 major symptom categories of the Yale-Brown symptom checklist, if a patient did not endorse any of the specific symptoms under that heading, then that category was assigned a score of 0. If a patient endorsed at least one of the specific symptoms but did not consider it a principal problem, that category was assigned a score of 1. If a patient identified at least one of the specific symptoms as a principal or major problem, that category was assigned a score of 2. Thus, a score of 0, 1, or 2 was assigned to each of the seven major obsessive symptom categories and to each of the six major compulsive categories (miscellaneous obsessions and compulsions were excluded because each contained many heterogeneous symptoms). This method ensured that all 13 categories would have equal representation, regardless of how many specific symptom examples were provided under each. In the principal components analysis, criteria for retention of factors were eigenvalue greater than 1 (Kaiser's criterion), interpretability of the factors, and Cattell's Scree test. The initial factor solutions were followed with a Varimax rotation in order to facilitate their interpretation. The relationship between the rotated OCD factors and the miscellaneous obsessions and compulsions, severity of OCD symptoms, demographic variables, and comorbid diagnoses was studied by means of multiple correlation analyses, chi-square tests, one-way analyses of variance, and Mann-Whitney U tests. For multiple correlations, the conservative Bonferroni significance criterion was adopted to control for type I error.

Efficacy and predictors analyses were conducted by using pooled data from the six trials with serotonin reuptake inhibitors (N=150; N=84 for drug group; N=66 for placebo group). Since clomipramine is not classified as a selective serotonin reuptake inhibitor (SSRI), analyses were repeated excluding this study (N=27) in order to ascertain whether results were generalizable to all serotonin reuptake inhibitor medications (N=123; N=71 for drug group; N=52 for placebo group). Analyses included all patients who had at least one measurement after the baseline visit (end-point-carried-forward method). The primary analyses were multiple linear regressions with the posttreatment scores on each outcome scale (Yale-Brown scale, NIMH OCD scale) as dependent variables. The baseline Yale-Brown scale scores were forced first into the equations as a covariate in order to control for symptom severity (31). For predictors analyses, scores on each OCD factor were then entered into the equations. Separate regression models were tested for the drug and placebo groups. The stepwise method was used. A two-tailed significance level of 0.05 was set. All statistical analyses were conducted by using the SPSS statistical package (version 6.0).

TABLE 2. Frequencies of the Major Symptom Categories of the Yale-Brown Obsessive Compulsive Checklist Among 354 Patients With OCD

	All Patients (N=354)						Patients Receiving Serotonin Reuptake Inhibitors (N=150)					
	Present Symptom[a]		Major Symptom[b]		Total		Present Symptom[a]		Major Symptom[b]		Total	
Symptom Category	N	%	N	%	N	%	N	%	N	%	N	%
Obsessions												
Aggressive	156	44.1	90	25.4	246	69.5	60	40.0	54	36.0	114	76.0
Contamination	125	35.3	83	23.4	208	58.7	38	25.3	53	35.3	91	60.6
Sexual	52	14.7	16	4.5	68	19.2	16	10.7	11	7.3	27	18.0
Hoarding	63	17.8	14	4.0	77	21.8	22	14.7	8	5.3	30	20.0
Religious	78	22.0	17	4.8	95	26.8	17	11.3	16	10.7	30	22.0
Symmetry	126	35.6	33	9.3	159	44.9	53	35.3	23	15.3	76	50.6
Somatic	81	22.9	22	6.2	103	29.1	16	10.7	13	8.7	29	19.4
Compulsions												
Cleaning	123	34.7	89	25.2	212	59.9	33	22.0	60	40.0	93	62.0
Checking	151	42.7	102	28.8	253	71.5	51	34.0	62	41.3	113	75.3
Repeating	149	42.1	27	7.6	176	49.7	48	32.0	21	14.0	69	46.0
Counting	104	29.4	21	5.9	125	35.3	50	33.3	18	12.0	68	45.3
Ordering	102	28.8	19	5.4	121	34.2	40	26.7	16	10.7	56	37.4
Hoarding	57	16.1	16	4.5	73	20.6	16	10.7	10	6.7	26	17.4

[a] At least one symptom in the category not considered principal.
[b] At least one symptom in the category considered principal.

RESULTS

Frequencies of the major symptom categories of the Yale-Brown symptom checklist in our study group are listed in table 2. As would be expected on the basis of previous studies (32), the most frequent specific categories included obsessions about harm, contamination, and symmetry, as well as checking, cleaning, and repeating compulsions.

The principal components analysis yielded a five-factor solution. The five factors accounted for 65.5% of the total variance and were named as follows: symmetry/ordering, hoarding, contamination/cleaning, aggressive/checking, and sexual/religious obsessions. The first factor accounted for 19% of the variance and included symmetry obsessions and ordering, counting, and repeating compulsions; loadings ranged from 0.41 to 0.82. The hoarding factor accounted for 13.8% of the variance and included hoarding obsessions and compulsions, both with a loading of 0.90. The third factor (12.7% of the variance) included contamination obsessions and cleaning/washing compulsions. Both symptom categories had a loading of 0.91 on this factor. The aggressive/checking factor explained a 10.4% of the variance and included aggressive obsessions and checking compulsions, with loadings over 0.82. The fifth factor accounted for 9.7% of the total variance. Sexual and religious obsessions had strong loadings (>0.71) on this factor. The five-factor solution is highly congruent with other factor-analytic studies following a comparable methodology (table 3).

After Bonferroni correction for 55 tests (0.05/55= 0.0009), the symmetry/ordering dimension was robustly associated with the compulsive need to know (r=0.20; for this and the following correlations, N= 354, p<0.0009), fear of not saying the right thing (r= 0.24), lucky numbers (r=0.25), and touching compulsions (r=0.20). The need to know was also associated with higher scores on hoarding (r=0.22). Fear of saying certain things (r=0.22), intrusive images (r=0.24) and sounds (r=0.20), lucky numbers (r=0.23), colors with special significance (r=0.20), and the need to tell, ask, or confess (r=0.28) were all positively associated with higher scores on sexual/religious obsessions.

After correction for multiple tests (0.05/15=0.003), the symmetry/ordering dimension was significantly correlated with Yale-Brown scale total score (r=0.16, N=354, p<0.003) and compulsions subscale score (r= 0.22, N=354, p<0.003) but not with obsessions subscale score (r=0.04, N=354). The contamination/cleaning dimension was also significantly correlated with Yale-Brown scale total score (r=0.20, N=354, p< 0.003) and compulsions subscale score (r=0.23, N= 354, p<0.003) but not with obsessions subscale score (r=0.10, N=354).

Men (N=190) scored significantly higher than women (N=164) on symmetry/ordering (men: mean= 0.12, SD=1.09; women: mean=–0.14, SD=0.85) (Mann-Whitney U=13598.5, p=0.03). Women scored higher than men on contamination/cleaning (men: mean=–0.09, SD=1.00; women: mean=0.10, SD=0.99) (Mann-Whitney U=13642.5, p=0.04) and aggressive/ checking (men: mean=–0.11, SD=0.96; women: mean= 0.12, SD=1.03) (Mann-Whitney U=13429.5, p=0.02).

For the 172 patients for whom age at onset was available, it was significantly negatively correlated with symmetry/ordering (r=–0.16, N=172, p=0.02), aggressive/checking (r=–0.18, N=172, p=0.01), and sexual/ religious obsessions (r=–0.21, N=172, p=0.005). In analyses by gender, age at onset was correlated with symmetry/ordering only in men (r=–0.26, N=90, p=

TABLE 3. Comparison of Three Independent Studies That Factor Analyzed Patients' Ratings on the Yale-Brown Obsessive Compulsive Scale Symptom Checklist

Study and Factor	Percent of Variance	Symptom Checklist Category
Baer, 1994 (N=107) (20)		
Symmetry/hoarding	20.7	Obsessions: symmetry, hoarding; compulsions: hoarding, ordering, repeating, counting
Contamination/checking	16.0	Obsessions: contamination, somatic; compulsions: cleaning, checking
Pure obsessions	11.3	Obsessions: sexual, religious, aggressive
Leckman et al., 1997 (N=292) (21)		
Obsessions and checking	30.1	Obsessions: aggressive, sexual, religious, somatic; compulsions: checking
Symmetry and ordering	13.8	Obsessions: symmetry; compulsions: repeating, counting, ordering
Cleanliness and washing	10.2	Obsessions: contamination; compulsions: cleaning
Hoarding	8.5	Obsessions: hoarding; compulsions: hoarding
Present study, 1999 (N=354)		
Symmetry/ordering	19.0	Obsessions: symmetry; compulsions: repeating, counting, ordering
Hoarding	13.8	Obsessions: hoarding; compulsions: hoarding
Contamination/cleaning	12.7	Obsessions: contamination; compulsions: cleaning
Aggressive/checking	10.4	Obsessions: aggressive; compulsions: checking
Sexual/religious obsessions	9.7	Obsessions: sexual, religious

TABLE 4. Symptom Dimensions That Predicted Outcome With Serotonin Reuptake Inhibitors (SRIs) and Placebo for Patients With OCD[a]

Dependent Variable and Treatment Condition	Variables in Equation	SRI[b] Patient Group (N=150)			SSRI[c] Patient Group (N=123)		
		Beta	R^2 Change	p	Beta	R^2 Change	p
Posttreatment Yale-Brown Obsessive Compulsive Scale total							
Drug	1: baseline scale score	0.47	0.30	<0.001	0.49	0.36	<0.001
	2: hoarding	0.25	0.36	0.007	0.30	0.44	0.002
Placebo	1: baseline scale score	0.63	0.40	<0.001	0.65	0.42	<0.001
Posttreatment NIMH OCD scale							
Drug	1: baseline scale score	0.25	0.09	0.03	0.37	0.18	0.003
	2: hoarding	0.31	0.18	0.006	0.26	0.25	0.03
Placebo	1: baseline scale score	0.58	0.34	<0.001	0.69	0.48	<0.001

[a] For clarity, only significant predictors are shown.
[b] Includes clomipramine.
[c] Excludes clomipramine.

0.01) and with aggressive/checking (r=–0.25, N=82, p=0.01) and sexual/religious obsessions (r=–0.31, N=82, p=0.004) only in women.

Forty-six (26.6%) of 173 patients met criteria for a lifetime history of chronic motor or vocal tic disorders or both. They were compared with the 127 patients without that diagnosis on all demographic and clinical variables. Male patients were significantly more frequent in the tic group (N=30 [65.2%] of 46) than in the nontic group (N=59 [46.5%] of 127) (χ^2=4.76, df=1, p=0.03). Groups did not differ on age. Patients with comorbid tic disorders had a significantly earlier age at onset (tic group: mean=12.51, SD=7.95; nontic group: mean=16.90, SD=10.10) (F=4.05, df=1, 90, p=0.04) and scored higher on the Yale-Brown scale total (tic group: mean=23.65, SD=6.89; nontic group: mean=20.89, SD=6.57) (F=5.77, df=1, 171, p=0.01) and compulsions subscale (tic group: mean=11.73, SD=4.25; nontic group: mean=10.08, SD=4.32) (F=4.98, df=1, 171, p=0.02). Patients with tics scored significantly higher on symmetry/ordering (tic group: mean=0.02, SD=0.83; nontic group: mean=–0.36, SD=0.81) (F=7.52, df=1, 171, p=0.006). Separately by gender, men with tics scored significantly higher on symmetry/ordering (tic group: mean=0.12, SD=0.89; nontic group: mean=–0.34, SD=0.85) (F=5.89, df=1, 87, p=0.02). Women with tics scored significantly higher than women without tics on the Yale-Brown total (tic group: mean=24.81, SD=6.93; nontic group: mean=20.67, SD=6.37) (F=5.28, df=1, 82, p=0.02) and obsessions subscale (tic group: mean=12.68, SD=3.36; nontic group: mean=10.44, SD=3.61) (F=5.12, df=1, 82, p=0.03).

Patients treated with serotonin reuptake inhibitors were significantly improved after treatment on all measures as compared to placebo-treated patients, after adjustment for initial severity scores (Yale-Brown scale: beta=0.19, R^2=0.35, p=0.004; NIMH scale: beta=0.23, R^2=0.21, p=0.001). This pattern was also observed after the exclusion of the clomipramine study (Yale-Brown scale: beta=0.23, R^2=0.39, p=0.001; NIMH scale: beta=0.15, R^2=0.29, p=0.05).

Regression analyses showed that severity at baseline predicted posttreatment severity for drug and placebo conditions on all clinical measures. After control for symptom severity, higher scores on the hoarding dimension predicted poorer outcome at posttreatment on all outcome measures. No predictors of placebo response were obtained. Exclusion of clomipramine recipients did not modify the overall results, suggesting a cross-serotonin reuptake inhibitor effect. Table 4 shows the beta coefficients and the proportion of vari-

ance in the dependent variables accounted for by the independent variables (R^2 change).

DISCUSSION

To our knowledge, this is the first study to report a relationship between factor-analyzed symptom dimensions and response to serotonin reuptake inhibitors in OCD. Previous research had failed in the attempt to relate OCD symptom subtypes to clinical and demographic variables and to treatment outcome with serotonin reuptake inhibitors. The five dimensions obtained in the present study are consistent with prior factor-analytic research that used a similar methodology (20, 20) and were found to be differentially related to sex, age at onset, comorbid tic-related disorders, and response to serotonin reuptake inhibitors.

The first dimension was named symmetry/ordering and had high factor loadings from symmetry obsessions and ordering, counting, and repeating compulsions. As in previous studies (20, 21), patients with comorbid tic disorders scored significantly higher on this factor. As many as 27% of the patients met criteria for a lifetime history of chronic motor or vocal tics or both; this finding is consistent with previous research (33). These patients had an earlier age at onset, and most were men. In fact, analyses by gender revealed that only male patients with tics scored significantly higher on symmetry/ordering. Scores on this dimension were correlated with total score on the Yale-Brown scale and the compulsions subscale score but not with the obsessions subscale score. Similarly, Holzer and associates compared the phenomenological features of 35 OCD patients with comorbid tics to 35 age- and sex-matched OCD patients without tics and found that patients with tics had more touching, tapping, rubbing, blinking, and staring rituals and fewer cleaning rituals but did not differ on obsessions (34). This tic-like factor corresponds to Janet's classic description of patients who were tormented by an inner sense of imperfection and felt that their actions were never completely achieved to their satisfaction (35). This feeling of incompleteness is also experienced by patients with Tourette's syndrome and trichotillomania (32). It also corresponds to the form of OCD that is thought to be genetically related to Tourette's syndrome, as family and genetic data have suggested (36). McDougle and associates found that serotonin reuptake inhibitor monotherapy was less effective in OCD patients with comorbid chronic tics than in those without tics (37) and that those patients may benefit from the combination of a serotonin reuptake inhibitor and a dopamine antagonist (12). In light of these findings, it would be expected that symmetry/ordering symptoms would be related to poorer outcome with serotonin reuptake inhibitors. Nonetheless, in the current study, this dimension was unrelated to treatment outcome. A putative explanation is that comorbid tic disorders were entry exclusion criteria for the studies included in our predictors analysis.

The second factor, termed "hoarding," had high factor loadings from hoarding/saving obsessions and hoarding compulsions. Baer's original factor analysis (20) grouped this factor with symmetry/ordering. In fact, correlation analysis showed that these two factors were the most intimately linked. Hoarding symptoms were present in as many as 20% of the patients and were a major problem for about 5% of them, as previously reported (32). Different accounts of the hoarding phenomenon in OCD are evident. First, hoarding has been seen as an abnormal personality characteristic, and it constituted a diagnostic criterion for obsessive-compulsive personality disorder in DSM-III-R. Second, from an ethological perspective, hoarding symptoms can be regarded as inappropriately released fixed-action patterns (38). Third, hoarding can be conceptualized as the consequence of dysfunctional beliefs formed by prior learning experiences (39).

Hoarding obsessions and compulsions predicted poor response to serotonin reuptake inhibitors, regardless of the outcome measure used or the inclusion of the clomipramine trial. In our principal components analysis, somatic obsessions also loaded on this factor (loading=0.35) but were not listed because we set 0.40 as the cutoff point. This is especially interesting in light of the results of the study by Jenike et al., in which symmetry, hoarding, ordering, and unusual somatic obsessions were significantly more common in patients who responded to phenelzine than in those who responded to fluoxetine (13). Moreover, one study found that presence of symmetry obsessions, ordering compulsions, and hoarding rituals predicted better response in patients treated with cingulotomy (14). Therefore, hoarding, and perhaps somatic obsessions, which predicted poor outcome with serotonin reuptake inhibitors in this study, might better respond to alternative treatments such as MAOIs or cingulotomy. This statement is speculative and requires further examination.

Factors 3 and 4 correspond to the classic contamination and checking dimensions of the Maudsley Obsessional Compulsive Inventory (40) and, as in previous studies (32), were the most frequent symptoms in our group. Finally, the sexual/religious obsessions dimension corresponds to the pure obsessions factor in Baer's study (20). These OCD symptoms are usually termed "pure obsessional disorder" when they appear in isolation (32).

The rationale for a dimensional model of OCD, according to which certain symptom dimensions—that, in most cases, coexist in the same patient—are differentially related to demographic and clinical characteristics and treatment response, reflects the existing contemporary neurobiological models for the disorder (22). It has been hypothesized that the heterogeneous phenomenology of OCD could be mediated by neuroanatomically different structures (41). The striatum has a well-described topographic organization with re-

spect to its afferent cortical connections and connections to other subcortical structures, as well as cytoarchitecture and neurotransmitters (42). According to the model, the symptoms of OCD would parallel the topography of dysfunction within the corticostriatal network. The extent and location of the dysfunction would determine the heterogeneous clinical picture of OCD. This would explain, for example, why different symptoms can occur either alone or in combination with others in any given patient, the relationship between certain symptoms and comorbid diagnoses, and the differential treatment response. The model still has to explain why the clinical manifestations of OCD change over time, as suggested by Rettew et al. (43) in the only published study directly addressing this issue. These authors followed up 79 children and adolescents with OCD over 2 to 7 years and found that none maintained the same constellation of symptoms from initial assessment to follow-up. Analogous data have yet to be published for adults with OCD.

Possible limitations of the present study need to be considered. The retrospective acquisition of information from case records is not ideal, but histories were comprehensive and followed a semistructured format. Additional prospective research on outcome predictors is required both for behavior and drug therapies. We pooled data from different SSRIs. It may be premature to conclude that differences in outcome are attributable to symptom dimensions when there has been no control for which SSRI was given to which patient. Nonetheless, power was inadequate to analyze each drug separately. Another direction for future study will be to develop a self-rated version of the symptom checklist in order to use it as a standardized instrument in OCD research. Further research on genetics, neuroimaging, and neuropsychology is warranted to confirm the differential involvement of distinct neural elements with the identified symptom dimensions. It is possible that OCD may constitute a label that researchers and clinicians use to name multiple disorders with multiple etiologies, rather than a homogeneous disease. The factor-analytic approach used in the present study and in others has identified meaningful symptom dimensions to help guide future research.

REFERENCES

1. Goodman WK, Price LH, Rasmussen SA, Delgado PL, Heninger GR, Charney DS: Efficacy of fluvoxamine in obsessive-compulsive disorder: a double-blind comparison with placebo. Arch Gen Psychiatry 1989; 46:36–44
2. Stanley MA, Turner SM: Current status of pharmacological and behavioral treatment of obsessive-compulsive disorder. Behav Ther 1995; 26:163–186
3. Alarcón RD, Libb JW, Spitler D: A predictive study of obsessive-compulsive disorder response to clomipramine. J Clin Psychopharmacol 1993; 13:210–213
4. Ackerman DL, Greenland S, Bystrytsky A, Morgenstern H, Katz RJ: Predictors of treatment response in obsessive-compulsive disorder: multivariate analyses from a multicenter trial of clomipramine. J Clin Psychopharmacol 1994; 14:247–254
5. Ravizza L, Barzega G, Bellino S, Bogetto F, Maina G: Predictors of drug treatment response in obsessive-compulsive disorder. J Clin Psychiatry 1995; 56:368–373
6. Jenike MA, Baer L, Minichiello WE, Schwartz CE, Carey RJ Jr: Concomitant obsessive-compulsive disorder and schizotypal personality disorder. Am J Psychiatry 1986; 143:530–533
7. Minichiello WE, Baer L, Jenike MA: Schizotypal personality disorder: a poor prognostic indicator for behaviour therapy in the treatment of obsessive compulsive disorder. J Anxiety Disorders 1987; 1:273–276
8. Baer L, Jenike MA, Black DW, Treece C, Rosenfeld R, Greist J: Effect of axis II diagnoses on treatment outcome with clomipramine in 55 patients with obsessive-compulsive disorder. Arch Gen Psychiatry 1992; 49:862–866
9. Jenike MA: Predictors of treatment failure, in Obsessive Compulsive Disorders: Theory and Management, 2nd ed. Edited by Jenike MA, Baer L, Minichiello WE. Chicago, Year Book Medical, 1990, pp 306–311
10. Dreessen L, Hoekstra R, Arntz A: Personality disorders do not influence the results of cognitive and behavior therapy for obsessive compulsive disorder. J Anxiety Disorders 1997; 11: 503–521
11. Rasmussen SA, Eisen JL: Clinical and epidemiological findings of significance to neuropharmacologic trials in obsessive-compulsive disorder. Psychopharmacol Bull 1988; 24: 466–470
12. McDougle CJ, Goodman, WK, Price LH: Dopamine antagonists in tic-related and psychotic spectrum obsessive compulsive disorder. J Clin Psychiatry 1994; 53(suppl 3):24–31
13. Jenike MA, Baer L, Minichiello WE, Rauch SL, Buttolph ML: Placebo-controlled trial of fluoxetine and phenelzine for obsessive-compulsive disorder. Am J Psychiatry 1997; 154: 1261–1264
14. Baer L, Rauch SL, Ballantine HT, Martuza R, Cosgrove R, Cassem E, Giriunas I, Manzo PA, Dimino C, Jenike MA: Cingulotomy for intractable obsessive compulsive disorder: prospective long-term follow-up of 18 patients. Arch Gen Psychiatry 1995; 52:384–392
15. Ball SG, Baer L, Otto MW: Symptom subtypes of obsessive-compulsive disorder in behavioral treatment studies: a quantitative review. Behav Res Ther 1996; 34:47–51
16. Rachman S, Hodgson RJ: Obsessions and Compulsions. Englewood Cliffs, NJ, Prentice-Hall, 1980
17. Buchanan AW, Ko SM, Marks IM: What predicts improvement and compliance during the behavioral treatment of obsessive compulsive disorder? Anxiety 1996; 2:22–27
18. Basoglu M, Lax T, Kasvikis Y, Marks IM: Predictors of improvement in obsessive compulsive disorder. J Anxiety Disorders 1988; 2:299–317
19. Foa EB, Goldstein A: Continuous exposure and complete response prevention in the treatment of obsessive-compulsive neurosis. Behavior Therapy 1978; 9:821–829
20. Baer L: Factor analysis of symptom subtypes of obsessive compulsive disorder and their relation to personality and tic disorders. J Clin Psychiatry 1994; 55(March suppl):18–23
21. Leckman JF, Grice DE, Boardman J, Zhang H, Vitale A, Bondi C, Alsobrook J, Peterson BS, Cohen DJ, Rasmussen SA, Goodman WK, McDougle CJ, Pauls DL: Symptoms of obsessive-compulsive disorder. Am J Psychiatry 1997; 154:911–917
22. Rauch SL, Dougherty DD, Shin LM, Alpert NM, Manzo P, Leahy L, Fischman AJ, Jenike MA, Baer L: Neural correlates of factor-analyzed OCD symptom dimensions: a PET study. CNS Spectrums 1998; 3(7):37–43
23. Jenike MA, Baer L, Summergrad P, Weilburg JB, Holland A, Seymour R: Obsessive-compulsive disorder: a double-blind, placebo-controlled trial of clomipramine in 27 patients. Am J Psychiatry 1989; 146:1328–1330
24. Jenike MA, Hyman S, Baer L, Holland A, Minichiello WE, Buttolph L, Summergrad P, Seymour R, Ricciardi J: A controlled trial of fluvoxamine in obsessive-compulsive disorder: implica-

tions for a serotonergic theory. Am J Psychiatry 1990; 147: 1209–1215
25. Tollefson GD, Rampey AH, Potvin JH, Jenike MA, Rush AJ, Dominguez RA, Koran LM, Shear MK, Goodman WK, Genduso LA: A multi-center investigation of fixed-dose fluoxetine in the treatment of obsessive-compulsive disorder. Arch Gen Psychiatry 1994; 51:559–567
26. Jenike MA, Baer L, Summergrad P, Minichiello WE, Holland A, Seymour R: Sertraline in obsessive-compulsive disorder: a double-blind comparison with placebo. Am J Psychiatry 1990; 147:923–928; correction, 147:1393
27. Hamilton M: A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56–62
28. Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, Heninger GR, Charney DS: The Yale-Brown Obsessive Compulsive Scale, I: development, use, and reliability. Arch Gen Psychiatry 1989; 46:1006–1011
29. Goodman WK, Price LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR, Charney DS: The Yale-Brown Obsessive Compulsive Scale, II: validity. Arch Gen Psychiatry 1989; 46: 1012–1016
30. Insel TR, Murphy DL, Cohen RM, Alterman L, Kilts C, Linnoila M: Obsessive-compulsive disorder: a double-blind trial of clomipramine and clorgyline. Arch Gen Psychiatry 1983; 40: 605–612
31. Cohen J, Cohen P: Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences, 2nd ed. Hillsdale, NJ, Lawrence Erlbaum Associates, 1983
32. Rasmussen SA, Eisen JL: Phenomenology of OCD: clinical subtypes, heterogeneity and coexistence, in The Psychobiology of Obsessive-Compulsive Disorder. Edited by Zohar J, Insel TR, Rasmussen SA. New York, Springer-Verlag, 1991, pp 13–43
33. Pitman RK, Green RC, Jenike MA, Mesulam MM: Clinical comparison of Tourette's disorder and obsessive-compulsive disorder. Am J Psychiatry 1987; 144:1166–1171
34. Holzer JC, Goodman WK, McDougle CJ, Baer L, Boyarsky BK, Leckman JF, Price LH: Obsessive compulsive disorder with and without a chronic tic disorder: a comparison of symptoms in 70 patients. Br J Psychiatry 1994; 164:469–473
35. Pitman RK: Pierre Janet on obsessive-compulsive disorder (1903): review and commentary. Arch Gen Psychiatry 1987; 44:226–232
36. Pauls DL, Alsobrook JP II, Goodman W, Rasmussen S, Leckman JF: A family study of obsessive-compulsive disorder. Am J Psychiatry 1995; 152:76–84
37. McDougle CJ, Goodman WK, Leckman JF, Barr LC, Heninger GR, Price LH: The efficacy of fluvoxamine in obsessive-compulsive disorder: effects of comorbid chronic tic disorder. J Clin Psychopharmacol 1993; 13:354–358
38. Swedo SE: Rituals and releasers: an ethological model of obsessive-compulsive disorder, in Obsessive Compulsive Disorder in Children and Adolescents. Edited by Rapoport JL. Washington, DC, American Psychiatric Press, 1989, pp 269–288
39. Shafran R, Tallis F: Obsessive-compulsive hoarding: a cognitive-behavioural approach. Behavioural and Cognitive Psychotherapy 1996; 24:209–221
40. Hodgson RJ, Rachman S: Obsessional-compulsive complaints. Behav Res Ther 1977; 15:389–395
41. Baxter LR, Schwartz JM, Guze BH, Szuba MP: Neuroimaging in obsessive-compulsive disorder: seeking the mediating neuroanatomy, in Obsessive Compulsive Disorders: Theory and Management, 2nd ed. Edited by Jenike MA, Baer L, Minichiello WE. Chicago, Year Book Medical, 1990, pp 167–188
42. Alexander GE, DeLong MR, Stick PL: Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu Rev Neurosci 1986; 9:357–381
43. Rettew DC, Swedo SE, Leonard HL, Lenane MC, Rapoport JL: Obsessions and compulsions across time in 79 children and adolescents with obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry 1992; 31:1050–1056