Personality Changes in Adult Subjects With Major Depressive Disorder or Obsessive-Compulsive Disorder Treated With Paroxetine

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Background: Human and animal studies point to 3 dimensions of personality that change during pharmacotherapy with a selective serotonin reuptake inhibitor (SSRI). Specifically, harm avoidance has been found to decrease, social dominance has been found to increase, and hostility in social situations has been found to decrease with SSRI treatment. We sought to determine personality changes in subjects with either major depressive disorder (MDD) or obsessive-compulsive disorder (OCD) treated with paroxetine. We also sought to determine whether or not these personality changes were associated with disease state (MDD vs. OCD) or treatment response (responders vs. nonresponders).

Method: Thirty-seven subjects diagnosed with either MDD or OCD (according to DSM-IV criteria) completed the Cattell 16 Personality Factor Inventory (16-PF) before and after treatment with paroxetine. Treatment response was defined as a Clinical Global Impressions-Improvement rating of "much" or "very much" improved and a drop in Hamilton Rating Scale for Depression score of at least 50% for MDD or Yale-Brown Obsessive Compulsive Scale score of at least 30% for OCD.

Results: No significant differences were found between subjects with MDD and OCD in personality change with treatment. In the whole group, treatment responders had a greater decrease than nonresponders in 16-PF factors relating to harm avoidance. An increase in social dominance factors and a decrease in factors relating to hostility in social situations were found, but these changes were not significantly different between responders and nonresponders.

Conclusion: These findings indicate that certain personality dimensions change with SSRI treatment and that some of these changes are independent of clinical treatment response.

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Substantial evidence shows that personality traits remain stable during adulthood.[1–4] However, a growing body of literature suggests that treatment with selective serotonin reuptake inhibitors (SSRIs) can change such traits.

Three dimensions of personality appear to change with administration of an SSRI, namely, harm avoidance, social dominance, and hostility in social situations. The first of these dimensions, harm avoidance, was originally described by Cloninger[5] as a tendency to respond intensely to signals of aversive stimuli, thereby learning to inhibit behavior to avoid punishment, novelty, and frustration. Subjects with high harm avoidance scores (as measured with the Tridimensional Personality Questionnaire [TPQ][5]) are described as fearful, tense, and slow to recuperate from stress. Harm avoidance has been found to decrease in subjects with major depressive disorder (MDD),[6] obsessive-compulsive disorder (OCD),[7] and generalized anxiety disorder[8] who respond to treatment with SSRIs or other antidepressants.

The second dimension, social dominance, refers to the rank of an animal in its group, with more dominant animals winning over more subordinate animals in competitive encounters. Social dominance has been linked to serotonergic neurotransmission in animals. This characteristic has been found to increase with both central serotonin injections[9] and administration of serotonin-enhancing medications, including an SSRI,[10] and to decrease with medications that decrease serotonergic function.[10] Anecdotal reports of increased social confidence

Table 1. Clinical Variables of Study Population[a]

	Men		Women		Age (y)		Paroxetine Dosage (mg/d)		Time Between Ratings (wk)	
Treatment Group	N	%	N	%	Mean	SD	Mean	SD	Mean	SD
MDD responders	9	60.0	6	40.0	39.5	11.7	34.0	10.6	10.2	3.3
OCD responders	5	62.5	3	37.5	40.5	11.6	40.0	9.3	10.1	2.0
MDD nonresponders	4	80.0	1	20.0	33.4	4.9	34.0	8.9	9.0	3.6
OCD nonresponders	5	55.6	4	44.4	39.8	15.8	38.9	14.5	10.3	2.8

[a]Abbreviations: MDD = major depressive disorder, OCD = obsessive-compulsive disorder.

in depressed subjects taking SSRIs[11] strengthen this connection.

As for the third factor, enhanced serotonergic neurotransmission has been found to decrease hostility and aggression[12–17] and to increase social affiliative behavior in both animals[18] and healthy human volunteers.[19] In one of these studies,[19] medically and psychiatrically healthy volunteers were given the SSRI paroxetine (20 mg/day) or placebo for 4 weeks. Subjects were rated for hostility levels and social affiliative behavior during a videotape of them performing a standardized dyadic puzzle task. Subjects treated with paroxetine had both a decrease in overall hostility and an increase in social affiliative behavior when compared with subjects treated with placebo.

On the basis of these prior reports, we sought to determine whether personality dimensions would change from pretreatment to posttreatment with the SSRI paroxetine in subjects with either MDD or OCD. We chose the Cattell 16 Personality Factor Inventory (16-PF) Form A questionnaire[20] to measure personality traits because of its short- and long-term reliability (dependability and stability, respectively) and because it was designed to measure stable personality traits (factors on this scale have a correlation over a 2-month period of 0.78).[21] The 16 "source traits" from this inventory were derived from strict factor analysis and have been robustly validated in many studies.[21,22] Although the number and nature of factors needed to describe personality are matters of intense debate,[22–29] the original structure of the 16-PF has been repeatedly supported.[22] In addition, personality changes have been documented with the 16-PF during other forms of intervention, such as treatment for hyperthyroidism[30] and assertiveness training.[31]

Given prior reports of a decrease in harm avoidance with SSRIs, we hypothesized that factor C scores on the 16-PF (affected by feelings vs. emotionally stable) would increase, with SSRI-treated subjects becoming more emotionally stable, and that scores on factors O (placid vs. apprehensive) and Q4 (relaxed vs. tense) would decrease, with SSRI-treated subjects becoming more placid and relaxed. On the basis of the association between increased social dominance and enhanced serotonergic activity, we hypothesized that factors E (humble vs. assertive) and H (shy vs. bold) scores would increase, with subjects becoming more assertive and bold with SSRI treatment. Given the increases in social affiliative behavior and decreases in hostility seen with SSRI treatment in previous studies, we hypothesized that factor A scores (reserved vs. outgoing) would increase, with subjects becoming more outgoing, and factor L scores (trusting vs. suspicious) would decrease, with subjects becoming more trusting with treatment. Factor L was included here because the questions that comprise this factor relate to whether one approaches social situations with a trusting or suspicious and hostile manner.

METHOD

Subjects, Treatment, and Rating Scales

This study was approved by the University of California at Los Angeles Office for the Protection of Research Subjects. Subjects gave informed consent after the procedures and potential side effects of paroxetine were fully explained.

Thirty-seven patients with either MDD (N = 20) or OCD (N = 17) completed the 16-PF before and after 8 to 12 weeks of open-label treatment with paroxetine (target dose = 40 mg/day). Subjects were instructed to complete the 16-PF with reference to their current personality traits. Clinical aspects of treatment are summarized in Table 1. Subjects were enrolled in this study after clinical evaluation and confirmation of diagnoses by administration of the Schedule for Affective Disorders and Schizophrenia-Lifetime version[32] by a rater blind to assigned diagnosis. Subjects met DSM-IV criteria for either MDD or OCD with no comorbid Axis I diagnoses (including substance abuse) and no concurrent medical conditions. All subjects were free from psychotropic medications for at least 2 weeks (and at least 5 weeks for fluoxetine) before starting the study.

No psychotropic medications were allowed during the study period other than paroxetine, and compliance was monitored by patient report during weekly medication visits with the treating psychiatrist (A.L.B. or S.S.). Symptom severity was assessed with the Hamilton Rating Scale for Depression (HAM-D),[33] the Hamilton Rating Scale for Anxiety (HAM-A),[34] and the Yale-Brown Obsessive Compulsive Scale (Y-BOCS).[35,36] Clinical improvement was recorded after treatment using the Clinical Global Impressions-Improvement scale (CGI-I).[37]

Means and standard deviations were calculated and examined for the 16-PF factors of interest. Clinical response was defined as a CGI-I score of "much" or "very much" improved and a drop in HAM-D score of 50% or greater for subjects with MDD or a drop in Y-BOCS score of 30% or greater for subjects with OCD. These thresholds were chosen on the basis of prior clinical studies that used these values.[38–40] Percentage changes in rating scale scores were calculated by subtracting the posttreatment score from the pretreatment score and dividing by the pretreatment score.

Statistical Analysis

Changes in the 7 personality traits listed above (16-PF factors A, C, E, H, L, O, and Q4) were evaluated using a repeated-measures multivariate analysis of variance (MANOVA) with 2 within-subject factors (16-PF factor and time) and 2 between-subject factors (treatment response and diagnosis) (SPSS version 8.0). The raw data from the 16-PF were used for this analysis. On the basis of these results (presented below), we performed repeated-measures analyses of variance (ANOVAs) for each of the 7 16-PF factors of interest hypothesized to change with treatment. In these analyses, the pretreatment and posttreatment 16-PF factor scores were the repeated measures, and diagnosis (MDD vs. OCD) and treatment response (responders vs. nonresponders) were the between-subject factors. Alpha levels for these hypothesized contrasts were set at $p < .05$. Additionally, given a prior report of gender differences in personality change with clinical change,[41] we also ran the analyses for the 7 16-PF factors of interest with gender as a covariate.

To screen the remaining 9 16-PF factors, repeated-measures ANOVAs were performed for these factors in an identical way to the ANOVAs described above. However, a more stringent criterion, $p \leq .01$, was used for significance in these secondary analyses because these tests were considered exploratory.

RESULTS

Twenty-three subjects were treatment responders (15 subjects with MDD and 8 with OCD), and 14 subjects were treatment nonresponders (5 with MDD and 9 with OCD). For the total group, mean scores for 6 of the 7 16-PF factors changed in the predicted directions (see Figures 1 to 3). The exception was factor A (reserved vs. outgoing), which showed no consistent pattern of change. The overall MANOVA indicated a significant change in the 16-PF factors with time ($F = 4.61$, $df = 6,28$; $p = .002$) and a significant difference between treatment responders and nonresponders in the extent of change in the 16-PF factors with time ($F = 4.07$, $df = 6,28$; $p = .005$). This MANOVA did not indicate any significant differences in personality change between subjects with MDD and those

Figure 1. Mean Changes for Treatment Responders and Nonresponders in 16-PF Factors Relating to Harm Avoidance

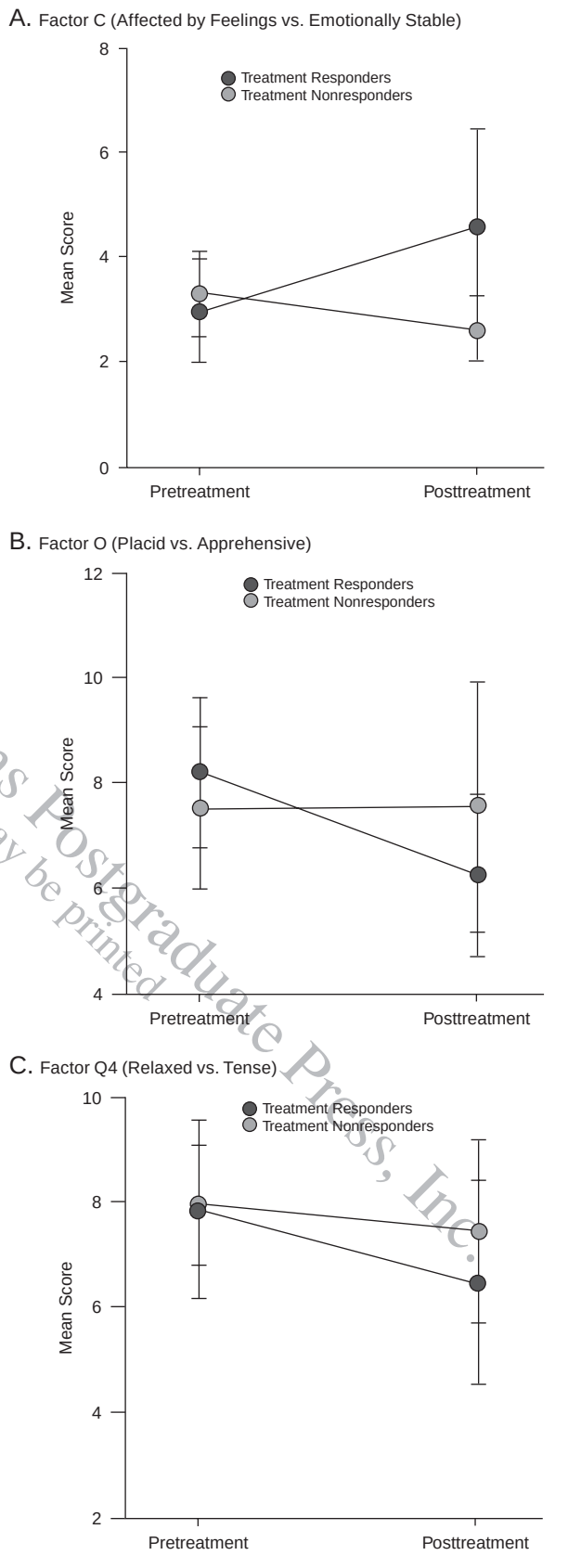


Figure 2. Mean Changes for Treatment Responders and Nonresponders in 16-PF Factors Relating to Social Dominance

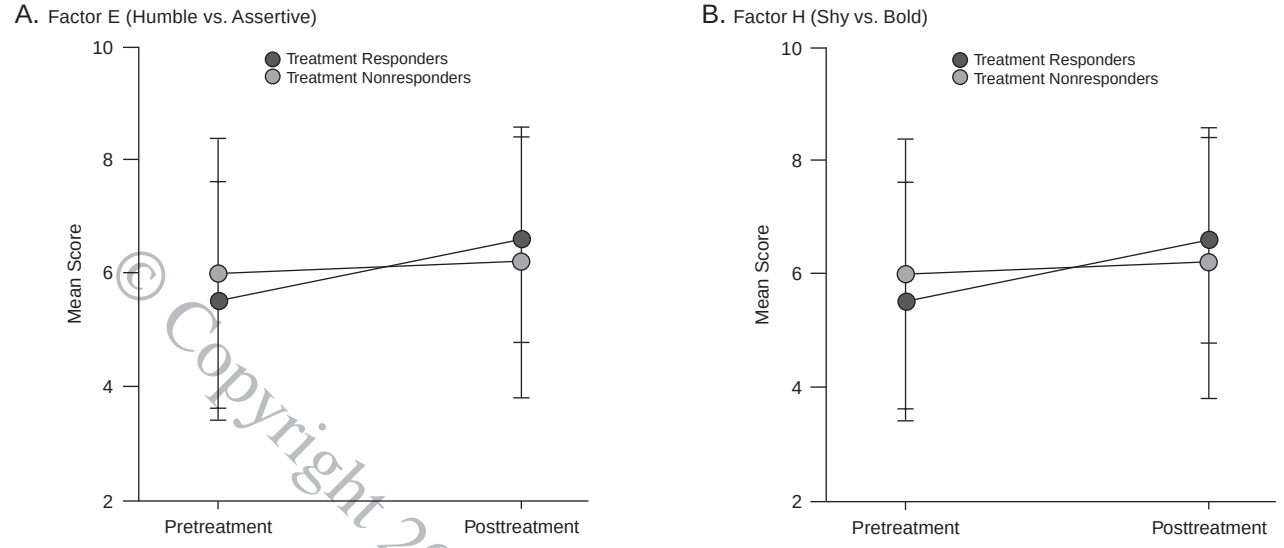
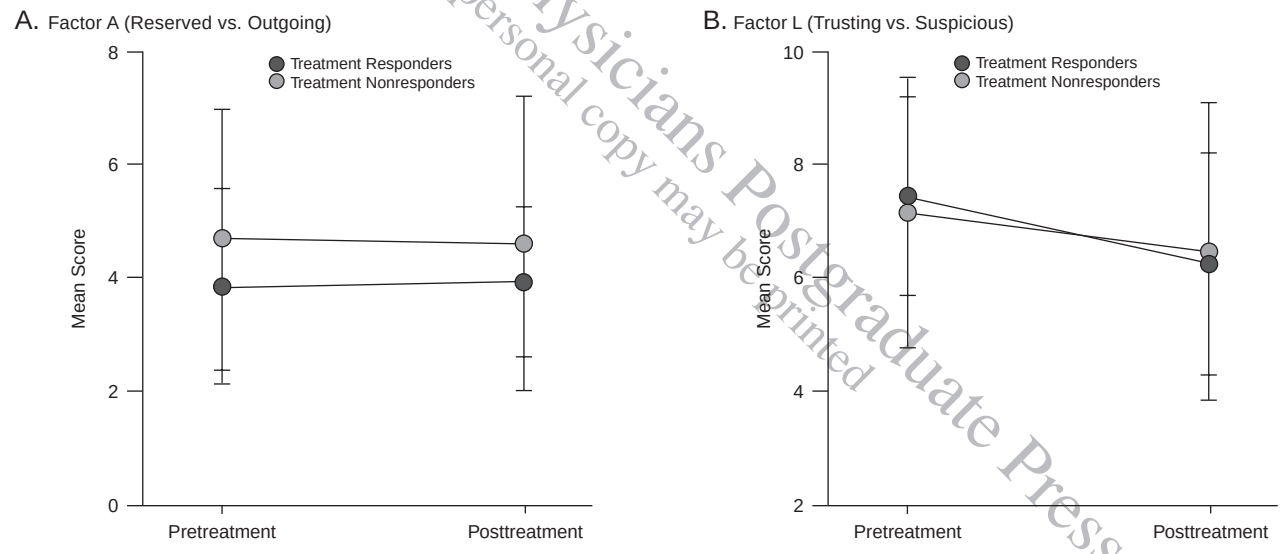


Figure 3. Mean Changes for Treatment Responders and Nonresponders in 16-PF Factors Relating to Hostility in Social Situations



with OCD. Despite this fact, we continued to use disease state as a between-subject factor because of concerns that personality factors might change differentially in subjects with MDD versus those with OCD.

Results of the ANOVAs for the 7 16-PF factors of interest are summarized according to their related personality dimensions in Table 2. No differences between subjects with OCD and MDD approached significance for any of the factors of interest (pretreatment to posttreatment by diagnosis interaction), other than a trend for subjects with OCD to have a greater decrease in factor L (more trust) ($F = 3.90$, $p = .06$).

For 2 of the 3 16-PF factors relating to harm avoidance (C and O), there were significant interactions between time (pretreatment to posttreatment) and treatment response, with responders showing a greater increase in emotional stability ($F = 16.97$, $p < .0005$) and a greater decrease in apprehension ($F = 9.57$, $p = .004$; Figures 1A and 1B) than nonresponders. Factor O also had a significant main effect with time ($F = 6.84$, $p = .01$), indicating that the group as a whole became less apprehensive with treatment. Analysis of factor Q4 (relaxed vs. tense) (Figure 1C) revealed no significant main effect with time or interactions with diagnosis or treatment response.

Table 2. Repeated-Measures Analyses of Variance for the Cattell 16 Personality Factor Inventory (16-PF) Factors of Interest (df = 1,33)

16-PF Factors	Time (p value)	Time × Response (p value)
Harm avoidance		
Factor C	NS	< .0005
Factor O	.01	.004
Factor Q4	NS	NS
Social dominance		
Factor E	.03	NS
Factor H	.01	.053
Social affiliation/hostility		
Factor A	NS	NS
Factor L	< .0005	NS

For 16-PF factors relating to social dominance (E and H), there were significant main effects of time (pretreatment to posttreatment) for both factors ($F = 5.51$, $p = .03$ for factor E; $F = 7.16$, $p = .01$ for factor H), and the interaction between time and treatment response approached significance in factor H ($F = 4.08$, $p = .053$). These findings indicate that subjects became more assertive (factor E) regardless of whether or not their depressive or OCD symptoms improved with treatment, but that treatment responders appeared to become considerably more bold (factor H) than nonresponders (Figures 2A and 2B).

As for hostility and social affiliative behavior, analysis of factors A and L revealed different patterns of change. Factor A (reserved vs. outgoing) had a significant time by diagnosis by response interaction ($F = 5.58$, $p = .02$), but examination of mean changes for the patient groups (Figure 3A) did not reveal a meaningful pattern of change. Factor L (trusting vs. suspicious), on the other hand, had a significant main effect with time ($F = 18.05$, $p < .0005$). This change was not associated with treatment response, indicating that subjects became more trusting and less hostile, regardless of response to paroxetine (Figure 3B). No significant differences between personality change in men and women were found when gender was used as a covariate.

In our exploratory analyses of the remaining 9 16-PF factors, only 1 factor, factor N (forthright vs. shrewd), had a significant main effect of change with time ($F = 10.20$, $p = .003$). There were no other interactions between change in this factor and disease or treatment response, indicating that the group as a whole became more forthright, regardless of disease or clinical response. No other significant main effects or interactions were found on the ANOVAs for the remaining 16-PF factors.

To further characterize the relationship between change in personality and change in symptom severity, we also performed exploratory Kendall correlations between change in HAM-D, HAM-A, and Y-BOCS scores and change in the 7 16-PF factors of interest, using a conservative value for significance ($p \leq .01$). Change in factors C and O (emotional stability and apprehensiveness) correlated strongly with change in HAM-D score ($\tau = -0.38$, $p = .002$ and $\tau = 0.35$, $p = .005$, respectively) and change in HAM-A score ($\tau = -0.36$, $p = .004$ and $\tau = 0.40$, $p = .001$, respectively). Neither the other correlations with the HAM-D or HAM-A scores nor the correlations with the Y-BOCS scores reached significance.

DISCUSSION

Our results indicate that dimensions of personality change during treatment with paroxetine and that these dimensions have varying relationships to changes in clinical symptoms of OCD and MDD.

Changes in 16-PF factor scores regarding harm avoidance (C [emotional stability] and O [apprehensiveness]) were significantly associated with treatment response and correlated strongly with changes in HAM-D and HAM-A scores. These findings suggest that the personality dimension of harm avoidance decreases during paroxetine treatment as symptoms of MDD and OCD improve. These findings are consistent with the prior report[6] of harm avoidance decreasing in subjects with MDD who responded to treatment with an SSRI, but extends that finding to subjects with OCD. The strong correlations between decreases in harm avoidance and improvement in depression and anxiety symptoms suggest that the personality trait of harm avoidance is tightly linked with Axis I mood and anxiety symptoms.

Social dominance 16-PF factor scores (E [assertiveness] and H [boldness]) increased significantly during the course of treatment, but appeared to change somewhat independently from clinical improvement in OCD or MDD symptoms. These findings extend prior animal research and human anecdotal reports of SSRI effects on social dominance to significant findings in a human clinical population.

For social affiliative and hostility factors, factor A (reserved vs. outgoing) had no meaningful pattern of change, but factor L (trusting vs. suspicious) and a related factor (N [forthright vs. shrewd]) changed over time, regardless of treatment response. These findings indicate that both treatment responders and nonresponders became more trusting and forthright and less hostile from pretreatment to posttreatment. The lack of correlation between change in factor L and change in symptom rating scales supports the conclusion that this dimension of personality is independent of clinical state.

The personality changes found in this study during standardized SSRI treatment are consistent with naturalistic studies examining the relationship between personality and Axis I mood and anxiety disorders.[41–48] Those studies have shown that some personality dimensions are state dependent (worsening as mood and anxiety symptoms worsen and improving as these symptoms improve), whereas others are independent of mood and anxiety

symptoms. Specifically, neuroticism (described as a temperamental sensitivity to negative stimuli) has repeatedly been reported to be state dependent in MDD.[41–46] This personality characteristic is similar to our harm avoidance dimension, which was also found to change with clinical state. The relationship between social dominance and mood and anxiety symptoms has not been widely reported. However, extraversion (similar to our social affiliative behavior/hostility dimension) has been found occasionally (but not consistently) to have a significant relationship with mood and anxiety symptoms.[41–45] Agreeableness (another trait similar to our social affiliative/hostility dimension) has been found to remain unchanged as mood changes.[44] Our finding that social affiliative behavior and hostility did not have a significant relationship with mood and anxiety changes is consistent with the relative lack of association between extraversion (and agreeableness) and mood and anxiety states in prior reports.

While we were able to address our central hypotheses with the data set, 2 important limitations of the present study point to the need to interpret our results with caution. First, there was no placebo-treated group of subjects. This limitation hampers our ability to firmly link personality changes with SSRI administration, because the changes we found may have been due to other factors. Because previous work does indicate that personality factors remain stable during the time frame of the study (without intervention), time alone is unlikely to account for the changes observed here. However, participating in the study, engaging in treatment, taking a pill, and contact with study clinicians may have contributed to changes on the personality questionnaire seen here. Second, several of our results in which significance was not reached were surprising, pointing to the need for a larger, more diverse sample to help clarify these areas. For example, while the means for all patient groups decreased toward becoming more relaxed on factor Q4 (relaxed vs. tense) with SSRI treatment (see Figure 1C), this change did not reach significance on any of our measures. Given the wealth of evidence that treatment with SSRIs reduces tension, a larger study (using additional personality measures) would likely confirm this relationship.

SSRIs have been found to affect a wide variety of psychiatric conditions.[49,50] Our findings, coupled with those of prior studies, indicate that SSRIs affect several dimensions of personality, including some that are independent of mood and anxiety symptomatology. This is not surprising, given the widespread distribution of serotonergic terminals in the brain. Our findings further delineate the complex relationship between personality and depressive and obsessive-compulsive symptoms. Research into the effects of psychotropic medications on personality variables may help to improve our understanding of the neurobiological underpinnings of human personality.

Drug names: fluoxetine (Prozac), paroxetine (Paxil).

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