Schizophrenia and Obsessive-Compulsive Disorder: Are They Related Disorders?

BY THOMAS H. MCGLASHAN, MD

INTRODUCTION

Older nosologic schemes in the field of neuropsychiatry regarded schizophrenia (SCZ) and obsessive-compulsive disorder (OCD) as mutually exclusive disorders, completely separate and unrelated, with no coexistence between them. Such categorical dogmatism is curious considering that this “rule” was totally unfounded by empirical observation. However, the rule was gradually ignored, and data emerged that contradicted mutual exclusivity and introduced much uncertainty and confusion to the heretofore neat and orderly picture of SCZ and OCD as separate entities.

This article reviews the papers presented in the March and April issues of CNS Spectrums that represent an initial look at the cooccurrence and interaction between SCZ and OCD at the levels of description and treatment response. All of them prove, by the examples described herein, that these two disorders are not mutually exclusive. In fact, the data they present suggest that SCZ and OCD may be related, and they offer clues as to the nature of that linkage. The data presented in this collection of papers are very preliminary and almost entirely descriptive in nature. Yet they are compelling and provocative, suggesting that the study and treatment of comorbid SCZ and OCD will yield much in the future about the nature of these disorders, their interaction, and their treatment.

HYPOTHESIZING THE RELATIONSHIP OF SCHIZOPHRENIA AND OBSESSIVE-COMPULSIVE DISORDER

In their profile of obsessive-compulsive (OC) symptoms in schizophrenia, Porto and colleagues present a comprehensive assessment of OC symptoms in a sample of 50 chronic schizophrenic outpatients. OC symptoms were present in 46% of the sample, and OCD was present in 26%, which shows considerable overlap indeed, especially if the sample was not preselected for OC features. Where overlap occurred, there appeared to be three patterns. In the first pattern, the OCD symptoms appeared unrelated to the psychotic symptoms. In the second, the OC signs and symptoms appeared related, but not restricted, to the psychotic signs and symptoms. In the third, the OC symptoms appeared to be on a continuum with psychosis in so far as obsessions would become delusions during more active phases and return to obsessions (with insight) during remissions. While the work of this group is descriptive at the symptomatic level, their phenomenologic groupings may be extrapolated into the following alternate hypotheses about the relationship between SCZ and OCD as disorders: (1) SCZ and OCD are separate entities that can cooccur; (2) SCZ and OCD are one disorder and represent different aspects of a continuum; and (3) SCZ and OCD are different disorders with shared elements of psychopathology and symptom pathophysiology.

WHAT EVIDENCE DO THE PAPERS IN THESE ISSUES PRESENT FOR OR AGAINST EACH HYPOTHESIS?

If, in their published literature, Sasson et al are correct in asserting that 15% of chronic schizophrenic patients also suffer from OCD, then our first hypothesis that SCZ and OCD are separate disorders must be invalid. Schizophrenia occurs at a prevalence of 1% in the general population and OCD at a prevalence of roughly 2%. If they were independent categories, their rate of overlap would range between 1% and 2%. Fifteen percent certainly suggests some kind of linkage. These data are provocative and clearly call for more clinical epidemiologic studies to test the frequency and comorbidity with rigor and reliability. Most reports to date have counted the frequency of OC symptoms and OCD in chronic schizophrenic samples. At least two types of clinical epidemiologic studies are needed: the rate of SCZ in OCD and the rate of OCD in SCZ. Furthermore, the latter studies should involve SCZ samples that are acutely, as well as chronically, disabled.
Could SCZ and OCD be one entity? Yaryura-Tobias and colleagues address this question most directly by comparing patients with OCD and with SCZ on a variety of symptom profiles. They conclude that SCZ and OCD share symptoms and behaviors without losing nosological individuality. This suggests that the assumption of syndromal unity is incorrect. Failure to support this hypothesis probably would generate little criticism among workers in the field, especially clinicians who regard and usually treat these disorders as different. While overlap between the disorders is frequent, it is also clear that both SCZ without OCD and OCD without SCZ are common. If they were but different manifestations of the same entity, we could probably expect to see far greater comorbidity, as well as more confluence of one disorder into the other on the basis of acuteness and/or severity.

At the same time, the hypothesis of unity should not be dismissed. Many of the non-symptomatic clinical parameters are similar between the disorders. Both tend to begin in adolescence and early adulthood, and the age of onset in both is earlier in males. The timing of onset in both can be variable, i.e., gradual or acute, and the longitudinal course can fluctuate in severity depending upon ambient levels of stress. Episodic exacerbations and longitudinal deterioration can occur in both disorders. Finally, familial patterns are present in both disorders, i.e., higher frequencies of disorder in first-degree relatives versus the general population, and higher frequencies in monozygotic twins versus dizygotic twins. None of these observations suggest identity, but they do imply that we should be cautious in rejecting such a possibility.

The last hypothesis is a hybrid of the first two: OCD and SCZ are different disorders that share elements of symptomatology, psychopathology, and pathophysiology. The data of Berman and colleagues support this view. They assessed 30 schizophrenic patients and found 25% to have significant OC symptoms. The OC and non-OC schizophrenic patients were not different on the positive and negative psychotic symptoms, suggesting independence of OC and psychosis phenomenology. On the other hand, the schizophrenic patients with OC symptoms scored deviantly on several neuropsychological subtests that are typically abnormal in nonschizophrenic OC patients. These tests involve visual-spatial skills, delayed nonverbal memory, and cognitive shifting abilities. Berman and colleagues say nothing about how schizophrenic patients without OCD score on these subtests; however, given the well-known pervasive deficits across neuropsychological profiles among schizophrenic patients, especially on tests of executive functioning such as the Wisconsin Card Sorting Test, it is unlikely the deficits recorded here are unique to OCD psychopathology. A study comparing neuropsychological profiles among three groups, i.e., SCZ without OCD, OCD without SCZ, and SCZ with OCD, should be the next step. In the meantime, the study by Berman et al suggests that while there is independence between OCD and SCZ at the symptom level (OC symptoms vs positive and negative psychotic symptoms), there may be less independence at the level of cognitive functioning.

The treatment response data are mixed and confusing. Sasson and colleagues found that open-label clomipramine reduced OC symptoms and psychosis in a significant subset of 18 patients with comorbid OCD and SCZ. Bermanzohn et al reported cross reactivity of anti-obessional agents on psychosis in refractory delusional states, arguing that...
Cross-reactivity of neuroleptics for OC symptoms has recently been reported in the form of risperidone augmentation of SSRI treatment of refractory OCD. Overall, data suggest both specificity and cross-reactivity, but the evidence is very preliminary. The field is in need of well-designed augmentation trials that are randomized, placebo-controlled, and blinded. Also, the study of comorbid samples demands the presence of three comparison groups: the comorbid group and two control groups consisting of each disorder alone.

Perhaps the least contested finding in this burgeoning field is that comorbidity confers a poor prognosis for both SCZ on OCD course and OCD on SCZ course. This finding does not support any of our three hypotheses differentially since all three might predict this finding. It does raise questions as to the degree of homogeneity versus heterogeneity of the combined pathology. From a purely descriptive, phenomenologic point of view, there may be reason to favor homogeneity. This rests upon the assumption that a cardinal feature of mental illness is repetitive mental content, in the sense of there being less variance of content, less freedom and richness of association, truncated complexity of language, more rigid coupling of thought with affective hue, and less play of will in the "choice" of mentation. These are, almost by definition, the core features of OCD.

A closer look at schizophrenia, especially the hallucinations and delusions of psychosis, finds many of the same elements. Delusions are often preemptory and repetitive in theme, appear linked predictively with certain (usually primitive) affective states, and seem to empty the mind of any interest in other ideas or experiences. Hallucinations, especially auditory hallucinations, are often experienced as repeated phrases with simple sentence structure and little variation in content. Unlike OCD symptoms, they are regarded as externally generated, but like OCD symptoms, they are unwillingly experienced.

Given that both SCZ and OCD bind mentation and empty it of richness and associative depth, it is no wonder that their co-occurrence can be so devastating. Whether or not this represents a confluence of similar psychopathology and pathophysiology is a highly relevant but currently unanswered question that awaits pursuit.

REFERENCES
There's a new reason to smile...

Now available for the treatment of Obsessive-Compulsive Disorder.

Zoloft®
(sertraline HCl)

Please see Zoloft® (sertraline HCl) prescribing information on adjacent page.
ZOLOFT® (sertraline HCl, 50 mg and 100 mg scored tablets) is indicated for the treatment of obsessions and compulsions in patients with obsessive-compulsive disorder (OCD). The most common side effects are nausea, insomnia, diarrhea, decreased libido, anorexia, dyspepsia, ejaculation failure (primarily ejaculatory delay), tremor, and increased sweating.

**BRIEF SUMMARY**

**ZOLOFT (sertraline)**

**INDICATIONS**

ZOLOFT is indicated for the treatment of obsessive-compulsive disorder (OCD). It is also indicated for the treatment of major depressive disorder (MDD), anxiety disorders, including panic disorder and social anxiety disorder, and obsessive-compulsive disorder (OCD).

**CONTRAINDICATIONS**

Contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping ZOLOFT before starting an MAOI. ZOLOFT is contraindicated in patients with a history of suicide attempt or in those with a history of drug abuse and follow such patients closely, observing them for signs of ZOLOFT misuse or abuse (e.g., development of tolerance, incrementation of dose, drug-seeking behavior).

**WARNINGS**

Cases of serious sometimes fatal reactions have been reported in patients receiving ZOLOFT in combination with an MAOI. Therefore, it is recommended that ZOLOFT not be used in combination with an MAOI. If ZOLOFT is used in such a patient, it should be discontinued at once and the MAOI should not be reinstated until at least 14 days have elapsed and the plasma levels of ZOLOFT are below 1 ng/mL. If an MAOI is needed, ZOLOFT can be reinstated only after at least 4 weeks have elapsed. If ZOLOFT is used in such a patient, it should be discontinued at once and the MAOI should not be reinstated until at least 14 days have elapsed and the plasma levels of ZOLOFT are below 1 ng/mL. If an MAOI is needed, ZOLOFT can be reinstated only after at least 4 weeks have elapsed.

**ADVERSE REACTIONS**

Common: pian fatigue, decreased appetite, nausea,weight loss, diarrhea, anxiety, sleep disturbances, palpitations, tremor, sexual dysfunction, and malaise. These may disappear as treatment continues.

Infrequent: headache, nervousness, sweating, dizziness, insomnia, tremor, muscle twitching, restlessness, confusion, agitation, irritability, and abnormal dreams.

Rare: mania, delirium, hallucinations, fever, and seizures.

**PREGNANCY**

ZOLOFT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. There is no information on the use of ZOLOFT in pregnant women. However, in rats and rabbits, sertraline was not teratogenic at doses up to 10 times the maximum recommended human dose (MRHD) on a body-weight basis, and no evidence of impaired fertility was observed at doses up to 15 times the MRHD on a body-weight basis. The results of animal studies in rodents do not necessarily predict the absence of risk to the fetus.

**NURSING MOTHERS**

ZOLOFT is excreted in human milk. Although clinically important effects have not been observed, it is not known whether ZOLOFT is excreted in human milk or if it has any appreciable excretory potential. Because many drugs are excreted in human milk, caution should be exercised when ZOLOFT is administered to a nursing woman.

**PEDIATRIC USE**

The safety and effectiveness of ZOLOFT in children and adolescents have not been established.

**GERIATRIC USE**

In patients over 65 years of age, there were no apparent differences between these patients and younger patients in terms of the effectiveness or tolerability of ZOLOFT.

**CONTRAINDICATIONS**

Contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping ZOLOFT before starting an MAOI. ZOLOFT is contraindicated in patients with a history of suicide attempt or in those with a history of drug abuse and follow such patients closely, observing them for signs of ZOLOFT misuse or abuse (e.g., development of tolerance, incrementation of dose, drug-seeking behavior). ZOLOFT is also contraindicated in patients who have shown a significant response to an antidepressant in the past but who have not been stable on that treatment for at least 4 weeks.

**WARNINGS**

Cases of serious sometimes fatal reactions have been reported in patients receiving ZOLOFT in combination with an MAOI. Therefore, it is recommended that ZOLOFT not be used in combination with an MAOI. If ZOLOFT is used in such a patient, it should be discontinued at once and the MAOI should not be reinstated until at least 14 days have elapsed and the plasma levels of ZOLOFT are below 1 ng/mL. If an MAOI is needed, ZOLOFT can be reinstated only after at least 4 weeks have elapsed. If ZOLOFT is used in such a patient, it should be discontinued at once and the MAOI should not be reinstated until at least 14 days have elapsed and the plasma levels of ZOLOFT are below 1 ng/mL. If an MAOI is needed, ZOLOFT can be reinstated only after at least 4 weeks have elapsed.

**ADVERSE REACTIONS**

Common: pian fatigue, decreased appetite, nausea,weight loss, diarrhea, anxiety, sleep disturbances, palpitations, tremor, sexual dysfunction, and malaise. These may disappear as treatment continues.

Infrequent: headache, nervousness, sweating, dizziness, insomnia, tremor, muscle twitching, restlessness, confusion, agitation, irritability, and abnormal dreams.

Rare: mania, delirium, hallucinations, fever, and seizures.

**PREGNANCY**

ZOLOFT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. There is no information on the use of ZOLOFT in pregnant women. However, in rats and rabbits, sertraline was not teratogenic at doses up to 10 times the maximum recommended human dose (MRHD) on a body-weight basis, and no evidence of impaired fertility was observed at doses up to 15 times the MRHD on a body-weight basis. The results of animal studies in rodents do not necessarily predict the absence of risk to the fetus.

**NURSING MOTHERS**

ZOLOFT is excreted in human milk. Although clinically important effects have not been observed, it is not known whether ZOLOFT is excreted in human milk or if it has any appreciable excretory potential. Because many drugs are excreted in human milk, caution should be exercised when ZOLOFT is administered to a nursing woman.

**PEDIATRIC USE**

The safety and effectiveness of ZOLOFT in children and adolescents have not been established.

**GERIATRIC USE**

In patients over 65 years of age, there were no apparent differences between these patients and younger patients in terms of the effectiveness or tolerability of ZOLOFT.