Relationships Between Obsessive-Compulsive Symptomatology and Severity of Psychosis in Schizophrenia: A Systematic Review and Meta-Analysis

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Objective: The presence of obsessive-compulsive symptoms (OCS) or obsessive-compulsive disorder (OCD) is common in patients with schizophrenia. The impact of OCS and OCD on severity of psychotic symptoms has been assessed in several past studies yielding inconclusive results. In this report, we aim to integrate the findings of prior studies by means of a systematic review followed by a meta-analysis.

Data Sources: A search of studies in PubMed (from 1950 to September 2006) and PsycINFO (from 1966 to September 2006) databases was performed to assess the influence of OCS and OCD on severity of psychotic symptoms in patients with schizophrenia using as syntax ("schizophrenia" OR "psychosis" OR "psychotic") AND ("obsessive-compulsive disorder" OR "OCD" OR "obsession*" OR "compulsion*" OR "obsessiv*" OR "compulsiv*"). Reference lists of all retrieved articles were also hand-searched.

Study Selection: Twenty-three studies were included in the systematic review, and 18 articles provided usable data for the meta-analysis.

Data Extraction: All relevant data were extracted using a standardized report form by 2 investigators. Effect sizes and pooled estimates were calculated. Data were analyzed separately for studies using an OCS or OCD definition.

Data Synthesis: The presence of OCS was significantly associated with greater severity of global psychotic symptoms (standardized mean difference [95% CI], 0.39 [0.14 to 0.64]), positive psychotic symptoms (0.28 [0.00 to 0.56]), and negative psychotic symptoms (0.36 [0.11 to 0.62]). In contrast, no differences in the severity of global psychotic symptoms (0.19 [–0.14 to 0.51]), positive psychotic symptoms (–0.01 [–0.20 to 0.19]), or negative psychotic symptoms (–0.11 [–0.30 to 0.08]) were found for the OCD versus non-OCD subgroups.

Conclusion: This first meta-analysis revealed that the presence of obsessive-compulsive symptoms in schizophrenia is associated with higher global, positive, and negative psychotic symptoms. This association was not found when a categorical definition of obsessive-compulsive disorder was used.

J Clin Psychiatry 2009;70(1):70–82

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This study was partially supported by a grant from the Instituto de Salud Carlos III, Madrid, Spain (a national public research and scientific support organization dependent on the Spanish Ministry of Health) (Dr. Castells).

The authors report no other affiliations or financial relationships relevant to the subject of this article.

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Schizophrenia is a chronic and disabling disorder. The lifetime prevalence of schizophrenia ranges from 0.9% to 1.3%,[1] and it has been ranked as the fourth leading cause of disability in the western world in the 15- to 44-year-old age group.[2] Both obsessive-compulsive symptoms (OCS) and obsessive-compulsive disorder (OCD) are common among patients with schizophrenia. Since the 19th century, there have been reports of patients with both psychotic and obsessive-compulsive symptoms,[3] but the magnitude of their co-occurrence varies depending on the definitions of OCS and OCD and the samples studied. Fenton and McGlashan[4] first reported clinically significant OCS in 12.9% of a sample of hospitalized schizophrenia patients. More recent studies have continued to reveal high rates of OCS and OCD in schizophrenia: OCS has been found in up to 45% of the schizophrenia population,[5] while 7.8% to 25.0% of schizophrenia patients have been reported to have comorbid OCD.[6–12] The latter finding suggests that OCD co-occurs with schizophrenia more often than would be expected from its lifetime prevalence of 1.6% in the general population.[13]

The reasons for the high incidence of OCS and OCD in schizophrenia patients are not well understood. Case reports and uncontrolled retrospective studies have reported that atypical antipsychotics may induce or exacerbate OCS.[14] This finding is unlikely to account for a major portion of the comorbidity, since OCS and OCD were reported prior to the advent of antipsychotics as well as in

drug-naive schizophrenia patients.[9] An alternative explanation could be that patients with schizophrenia develop OCS in an attempt to reduce psychotic symptoms, and, thus, the presence of OCS is an indicator of a good prognosis. This hypothesis was proposed midway through the 20th century[15,16]; however, subsequent research failed to confirm it, yielding contradictory results.[14]

Meta-analysis, when done in the context of a systematic review, allows the identification, appraisal, synthesis, and, where appropriate, combination of quantitative data from identified studies in order to arrive at overarching conclusions about a common subject of research. This methodology is very popular for synthesizing results from randomized clinical trials, but it is also valid for observational studies.[17] In this report, we conducted a systematic review followed by a meta-analysis in order to determine whether the presence of OCS and OCD in schizophrenia is associated with greater severity of psychotic symptoms. The meta-analysis was carried out separately for those studies using a dimensional definition (OCS) versus a categorical definition (OCD).

METHOD

Data Sources

A search of PubMed (from 1950 to September 2006) and PsycINFO (from 1966 to September 2006) databases was performed twice (last search: 10/30/2006) by 2 investigators (R.C. and X.C.) using as syntax ("schizophrenia" OR "psychosis" OR "psychotic") AND ("obsessive-compulsive disorder" OR "OCD" OR "obsession*" OR "compulsion*" OR "obsessiv*" OR "compulsiv*"). The reference lists of all retrieved studies and reviews[14,18–21] were hand-searched in order to locate any additional studies that may not have been contained in the database search.

Study Selection

Our search was limited to studies written in English, French, Spanish, or Catalan. Studies were included in the systematic review if (1) schizophrenia patients with obsessive-compulsive features were compared with schizophrenia patients without obsessive-compulsive features and (2) the severity of psychotic symptoms was assessed in both groups. Studies that included patients under the age of 15 years were excluded. All abstracts were screened by 2 investigators (R.C. and X.C.), and all relevant articles were retrieved. The articles were reviewed independently by 2 investigators (R.C. and X.C.).

Subsequent to the systematic review, a meta-analysis was carried out for those studies included in the systematic review if (1) only 2 groups of schizophrenia patients, 1 with obsessive-compulsive features and the other without obsessive-compulsive features were studied; (2) means and SDs of psychotic symptom severity were reported or made available upon request for both the OCS/OCD and the non-OCS/OCD groups; and (3) the presence of OCS or OCD and the severity of psychotic symptoms were assessed at the same time point.

Data Extraction

All relevant data were extracted using a standardized report form by 2 investigators (R.C. and X.C.). Discrepancies were resolved by consensus. The following data were extracted: authorship, study design, sample size, participant characteristics, diagnostic criteria, definition of OCS or OCD, assessment methods, severity of psychotic symptoms, type and severity of OCS or OCD, and pharmacologic treatment. If information was missing from the original article, the first author of each study was contacted, and the missing data were requested. Quantitative measures of the global, positive, and negative psychotic symptom severity were used as the primary outcome. In longitudinal studies for which data were collected at several time points, for instance at acute, subacute, and stable phases, only data collected during the stable phase were used for the meta-analysis.

Data Synthesis and Statistical Analysis

The effect sizes of the association between the severity of global, positive, and negative psychotic symptoms and the presence of OCS and OCD were computed from the reported means and SDs. Pooled effect size was calculated separately for studies comparing OCS versus non-OCS patients and OCD versus non-OCD patients by means of the Review Manager 4.2.8 software package (The Cochrane Collaboration, Copenhagen, Denmark) using analysis-of-variance models for standardized mean differences (SMD). The random- and fixed-effects models were used depending on the presence or absence of heterogeneity, respectively. Statistical heterogeneity between studies was calculated by means of the χ^2 test.

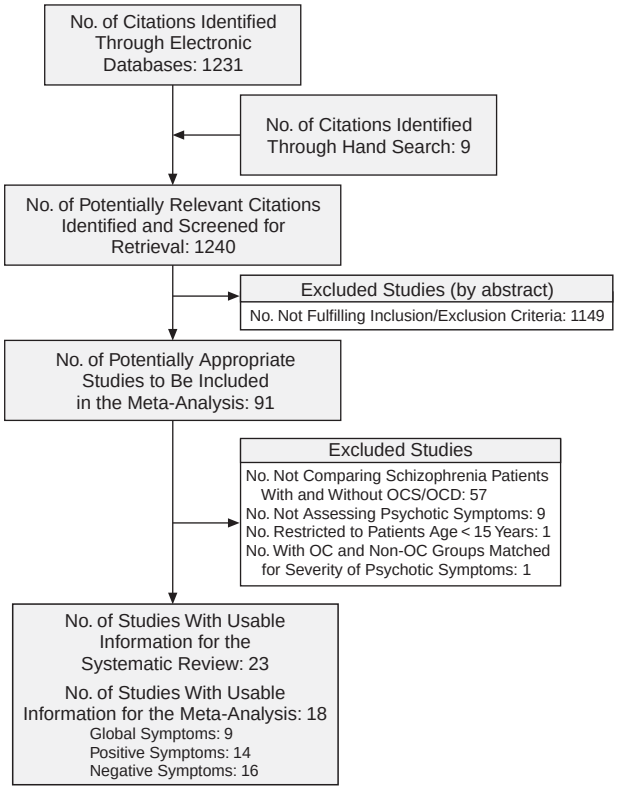
In order to determine whether results were unduly influenced by a single comparison, a sensitivity analysis was performed by recomputing the pooled effect size after withdrawing each study once and comparing whether the sense, direction, and confidence intervals were significantly altered with respect to the main analysis.[22] Publication bias was assessed graphically by plotting the SMD against its standard error (SE)[23] for comparisons including at least 10 studies.

RESULTS

Article Search

The initial database search yielded a total of 1231 references (Figure 1), and hand-searched references added 9 more potentially relevant articles, resulting in 1240 articles. Of these, 1149 publications were excluded by abstract because they did not meet the inclusion criteria,

Figure 1. Flow Diagram of Identified Citations and Inclusion and Exclusion Process



Abbreviations: OC = obsessive-compulsive, OCS = obsessive-compulsive symptoms, OCD = obsessive-compulsive disorder.

yielding 91 studies that were retrieved and examined more closely. After a more detailed evaluation, a total of 23 studies fulfilled all inclusion and exclusion criteria and were therefore included in the systematic review.[5–12,24–38] All of these studies were published in English.

Of these, 5 articles were not usable for the meta-analysis: 3 because they assessed 3 rather than 2 groups,[26,27,35] 1 because results were reported for subgroups based on psychosocial functioning rather than for the entire sample,[32] and 1 because psychotic symptom severity was not available.[30] Thus, a total of 18 articles were finally extracted with usable data for the meta-analysis, 8 employing a dimensional measure of OCS[5,25,28,29,31,32,34,38] and 10 employing a categorical definition of OCD.[6–12,24,36,37]

Study Characteristics

Fifteen of the 23 systematic review studies* were primarily aimed at comparing severity of psychotic symptoms between the OCS/OCD and non-OCS/OCD groups. In the remaining 8 studies, the severity of psychotic symptoms was a secondary variable, whereas the main aim was to compare schizophrenia patients with and without OCS and OCD regarding neuropsychological profiles,[5,8,24,38] motor symptoms,[6,8] neurologic soft signs,[37] coping preferences and hope,[34] and incidence of OCS during acute exacerbations of schizophrenia and between subtypes of schizophrenia.[28]

The characteristics of the studies included in the systematic review are detailed in Table 1. All studies were cross-sectional with the exception of 3 that were prospective, with fixed follow-up periods of 6 weeks,[27] 24 months,[26] and the duration of hospitalization for acute exacerbations.[28] The latter study,[28] although longitudinal, measured both the severity of psychotic symptoms and the presence of OCS at 3 time points (after remission of the acute phase, after clear improvement, and before discharge) and therefore could be used for the meta-analysis, whereas the remaining 2[26,27] were excluded from the meta-analysis because, as mentioned before, they assessed 3 rather than 2 groups of schizophrenia patients based on the severity of OCS and OCD.

Sample sizes ranged from 20[29] to 225.[26] Sampling was mostly consecutive or not described. Three studies[24,29,36] used a stratified or matched sampling method aimed at obtaining a comparable number of patients with and without OCS or OCD. With respect to psychotic disorder, several studies included not only schizophrenia but also schizoaffective patients[7,9,11,25–28,31–35,38] and patients with schizophreniform disorder.[9,27] The DSM-IV was the most widely used diagnostic system for both schizophrenia and OCD. Approximately half of the studies used inpatient samples,[5–7,9–11,26–29,36] almost half used outpatient samples,[12,25,31–35,38] and 3 studies included both inpatients and outpatients.[8,24,30] Schizophrenia patients were mostly stable, but acutely ill patients were also studied.[7,9,11,26–28]

Participant Characteristics

Participant characteristics for the studies included in the meta-analysis are presented in Table 2. The total sample consisted of 1096 patients, mostly male (77.6%). The mean (range of means) age was 37.7 years (range, 16.7–69.5 years). Most participants (88.0%) had a diagnosis of schizophrenia (47.3% paranoid, 30.2% undifferentiated, 10.1% disorganized, 8.8% residual, and 3.7% catatonic), while 11.2% were diagnosed with schizoaffective disorder and 0.9% with schizophreniform disorder. Mean age at onset of psychotic disorder was 23.9 years (range, 14.8–38.2 years), and mean duration of illness was 12.3 years (range, 1.8–31.4 years). It was not possible to systematically compare baseline characteristics for schizophrenia patients with and without OCS or OCD, as this information was typically available for the whole sample only.

Mean obsessive-compulsive symptom severity as measured by the Yale-Brown Obsessive Compulsive Scale (YBOCS) for the OCS versus non-OCS subgroups and

*References 7, 9–12, 25–27, 29–33, 35, 36.

Table 1. Characteristics of the 23 Studies Included in the Systematic Review of Schizophrenia Patients With and Without OCS or OCD and Severity of Psychotic Symptoms[a]

Study	Study Characteristics	Sample Characteristics	SCZ, OCD, and OCS Diagnostic Criteria and Psychotic Symptom Assessment	Results for Psychotic Symptoms
OCD				
Borkowska et al, 2003[24,b]	Cross-sectional Sample was stratified into 4 groups, OCD SCZ, non-OCD SCZ, OCD, and healthy controls, and matched for age and level of education	N = 60 OCD SCZ (N = 13), non-OCD SCZ (N = 15), OCD (N = 17), and healthy controls (N = 15) Inpatients and outpatients	SCZ: DSM-IV and ICD-10 OCD: DSM-IV and ICD-10 Psychotic symptoms: PANSS	No difference in global and negative symptoms in OCD SCZ and non-OCD SCZ groups Positive symptoms were not assessed
Krüger et al, 2000[6,b]	Cross-sectional Sampling: consecutive	N = 76 SCZ Inpatients Interviewed after resolution of acute phase	SCZ: DSM-III-R OCD: DSM-III-R (assessed by means of SCID) Psychotic symptoms: SAPS, SANS, and BPRS	No differences in overall negative and positive symptoms Greater general psychopathology in OCD SCZ group Less hallucinations, delusions, and poverty of speech in OCD SCZ group Greater bizarre behavior and lack of vocal inflection, circumstantiality, and pressure of speech in OCD SCZ group
Nechman et al, 2003[7,b]	Cross-sectional Sampling: consecutive	N = 50 SCZ (N = 39) and schizoaffective disorder (N = 11) Inpatients Acute phase Adolescents (mean age = 17 y, SD = 2.1 y)	SCZ: DSM-IV (assessed by means of SCID) OCD: DSM-IV, a minimum YBOCS total score of 7, and 6-mo duration Psychotic symptoms: SAPS and SANS	No difference in overall positive and negative symptoms Greater affective flattening in OCD SCZ group Positive correlation between OCS and negative symptoms
Ohta et al, 2003[8,b]	Cross-sectional Sampling: nonreferred	N = 71 SCZ Inpatients (N = 60) and outpatients (N = 11)	SCZ: DSM-IV OCD: DSM-IV (assessed by means of SCID) and YBOCS rating Psychotic symptoms: PANSS	No difference in psychotic symptoms between OCD SCZ and non-OCD SCZ groups
Poyurovsky et al, 1999[9,b,c]	Cross-sectional Sampling: consecutive	N = 50 SCZ (N = 37), schizoaffective disorder (N = 4), and schizophreniform disorder (N = 9) Inpatients Acute phase First episode	SCZ: DSM-IV (assessed by means of SCID-P) OCD: DSM-IV (assessed by means of SCID-P) Psychotic symptoms: SAPS and SANS	No correlation between obsessive-compulsive symptoms and positive or negative symptoms Less formal thought disorder and affective flattening in OCD SCZ group
Poyurovsky et al, 2001[10,b,c]	Cross-sectional Sampling: nonreferred	N = 68 SCZ Inpatients in long-term rehabilitation unit	SCZ: DSM-IV (assessed by means of SCID-P) OCD: DSM-IV (assessed by means of SCID-P), a minimum YBOCS total score of 7, and 6-mo duration Psychotic symptoms: SAPS and SANS	No difference in positive or negative symptoms between OCD SCZ and non-OCD SCZ groups No correlation between OCS and positive or negative symptoms

(continued)

Table 1 (continued). Characteristics of the 23 Studies Included in the Systematic Review of Schizophrenia Patients With and Without OCS or OCD and Severity of Psychotic Symptoms[a]

Study	Study Characteristics	Sample Characteristics	Diagnostic Criteria and Instrument Used for Psychotic Symptom Assessment	Results for Psychotic Symptoms
OCD (continued)				
Poyurovsky et al, 2003[36,b,c]	Cross-sectional Sample was stratified for the presence or absence of OCD; there were 2 groups, OCD SCZ and non-OCD SCZ, matched for age and number of hospitalizations	N = 110 OCD SCZ (N = 55) and non-OCD SCZ (N = 55) Inpatients Interviewed after resolution of acute phase	SCZ: DSM-IV (assessed by means of SCID-P) OCD: DSM-IV (assessed by means of SCID-P) Psychotic symptoms: SAPS and SANS	No differences in overall positive and negative symptoms Positive correlation between compulsions and bizarre behavior Greater bizarre behavior and lower delusions and formal thought disorder in OCD SCZ group
Poyurovsky et al, 2006[11,b,c]	Cross-sectional Sampling: consecutive	N = 50 SCZ (N = 41) and schizoaffective disorder (N = 9) Inpatients Acute phase Aged 63–83 y	SCZ: DSM-IV (assessed by means of SCID) OCD: DSM-IV (assessed by means of SCID), a minimum YBOCS total score of 15, and a 12-mo duration Psychotic symptoms: SAPS and SANS	No differences in positive or negative symptoms in OCD SCZ and non-OCD SCZ groups No correlation between OCS and positive or negative symptoms
Sevincok et al, 2004[37,b,c]	Cross-sectional Sampling: nonreferred	N = 77 SCZ (N = 53) and healthy subjects (N = 25)	SCZ: DSM-IV OCD: DSM-IV and a minimum YBOCS total score of 7 Psychotic symptoms: SAPS and SANS	No differences in positive or negative symptoms between OCD SCZ and non-OCD SCZ groups No correlation between OCS and positive or negative symptoms
Tibbo et al, 2000[12,b]	Cross-sectional Sampling: by advertisement	N = 52 SCZ Outpatients Stable on antipsychotic dose for the prior mo	SCZ: DSM-IV (assessed by means of SCID) OCD: DSM-IV (assessed by means of SCID) Psychotic symptoms: PANSS	Less negative symptoms in OCD SCZ group than in non-OCD SCZ group No difference in general psychopathology and positive and global symptoms between OCD SCZ and non-OCD SCZ groups
OCS				
Berman et al, 1998[5,b]	Cross-sectional Sampling: consecutive	N = 30 SCZ Chronically hospitalized inpatients	SCZ: DSM-III-R OCS: YBOCS checklist and YBOCS rating Psychotic symptoms: PANSS	No difference in positive, negative, and global symptoms between OCS SCZ and non-OCS SCZ groups No correlation between OCS and positive or negative symptoms
Byerly et al, 2005[25,b]	Cross-sectional Consecutive sampling in first 82 patients and nonconsecutive sampling in the following 18 patients	N = 100 SCZ (N = 78) and schizoaffective disorder (N = 22) Outpatients	SCZ: DSM-IV OCS: 2 or more OCS identified by FOCI and present for at least 6 mo Psychotic symptoms: PANSS	No differences in positive, negative, and global symptoms between OCS SCZ and non-OCS SCZ groups
Fabisch et al, 2001[28,b,c]	Prospective study (patients were followed during acute psychotic exacerbation) Sampling: nonreferred	N = 150 SCZ (N = 128) and schizoaffective disorder (N = 22) Inpatients Acute exacerbation	SCZ: DSM-IV OCS: YBOCS checklist Psychotic symptoms: PANSS	No association between OCS and severity of psychotic symptoms

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Table 1 (continued). Characteristics of the 23 Studies Included in the Systematic Review of Schizophrenia Patients With and Without OCS or OCD and Severity of Psychotic Symptoms[a]

Study	Study Characteristics	Sample Characteristics	Diagnostic Criteria and Instrument Used for Psychotic Symptom Assessment	Results for Psychotic Symptoms
OCS (continued)				
Hwang et al, 2000[29,b]	Cross-sectional Sample was stratified for the presence or absence of OCS; there were 2 groups, OCS SCZ and non-OCS SCZ, matched for age and gender	N = 20 OCS SCZ (N = 10) and non-OCS SCZ (N = 10) Inpatients After 4 wk of symptom stabilization with optimal antipsychotic dose	SCZ: DSM-III-R OCS: At least 3 of the operationalized symptom criteria described by Fenton and McGlashan[4] present for at least 6 mo Psychotic symptoms: PANSS	No difference in positive symptoms between OCS SCZ and non-OCS SCZ groups Greater negative symptoms and general psychopathology in OCS SCZ group
Lysaker et al, 2000[31,b]	Cross-sectional Sampling: consecutive	N = 46 SCZ (N = 35) and schizoaffective disorder (N = 11) Outpatients Stable or postacute phase	SCZ: DSM-IV OCS: Minimum YBOCS obsessions or YBOCS compulsions scores of 8 Psychotic symptoms: factor analytical–derived PANSS scales	Greater positive and emotional discomfort symptoms in OCS SCZ group No differences in negative symptoms in OCS SCZ and non-OCS SCZ groups
Lysaker et al, 2002[32,b]	Cross-sectional Sampling: consecutive	N = 63 SCZ and schizoaffective disorder Outpatients Postacute phase	SCZ: DSM-IV OCS: minimum YBOCS total score of 17 Psychotic symptoms: factor analytical–derived PANSS scales	No differences in positive symptoms between OCS SCZ and non-OCS SCZ groups Greater negative and emotional discomfort symptoms in OCS SCZ group
Lysaker et al, 2004[33]	Cross-sectional Sampling: nonreferred	N = 66 SCZ (N = 41) and schizoaffective disorder (N = 25) Outpatients Stable or postacute phase	SCZ: DSM-IV (assessed by means of SCID) OCS: cluster analysis based on YBOCS total scores Psychotic symptoms: factor analytical–derived PANSS scales	Lower levels of negative symptoms in OCS SCZ/good function and non-OCS SCZ/moderate function groups than in OCS SCZ/poor function and non-OCS SCZ/poor function groups No differences in positive symptoms between the 4 groups
Lysaker et al, 2006[34,b]	Cross-sectional Sampling: nonreferred	N = 67 SCZ (N = 43) and schizoaffective disorder (N = 25) Outpatients Stable or postacute phase	SCZ: DSM-IV (assessed by means of SCID) OCS: ≥ 2 items in YBOCS obsessions or YBOCS compulsion subscales rated as moderate Psychotic symptoms: factor analytical–derived PANSS scales	No differences in global symptoms between OCS SCZ and non-OCS SCZ groups
Ongur and Goff, 2005[35,c]	Cross-sectional Sampling: consecutive	N = 118 SCZ and schizoaffective disorder Outpatients Stable phase	SCZ: DSM-IV (assessed by means of SCID) OCS: YBOCS total score between 1 and 11 and YBOCS total score ≥ 12 Psychotic symptoms: PANSS	Greater positive symptoms in group with higher OCS No difference in negative and global symptoms between the 3 groups

(continued)

Table 1 (continued). Characteristics of the 23 Studies Included in the Systematic Review of Schizophrenia Patients With and Without OCS or OCD and Severity of Psychotic Symptoms[a]

Study	Study Characteristics	Sample Characteristics	Diagnostic Criteria and Instrument Used for Psychotic Symptom Assessment	Results for Psychotic Symptoms
OCS (continued)				
Whitney et al, 2004[38,b,c]	Cross-sectional Sampling: nonreferred	N = 65 SCZ (N = 40), schizoaffective disorder (N = 14), and OCD (N = 11) Outpatients Stable phase	SCZ: DSM-IV (assessed by means of SCID) OCS: minimum YBOCS obsessions or YBOCS compulsions scores of 8 Psychotic symptoms: PANSS	No differences in global, positive, or negative symptoms between OCS SCZ and non-OCS SCZ groups
OCS and OCD				
Craig et al, 2002[26,c]	Prospective (24-mo follow-up) Sampling: nonreferred	N = 450 SCZ and schizoaffective disorder (N = 225), bipolar disorder with psychosis (N = 138), and major depression with psychosis (N = 87) Inpatients Acute phase First episode or current admission within 6 mo of first	SCZ: DSM-III-R (assessed by means of SCID) OCS: symptomatic criteria in SCID for OCS OCD: full diagnostic criteria in SCID for OCD Psychotic symptoms: SAPS and SANS	No association between the presence of OCS or OCD at baseline and the severity of positive and negative symptoms at 24-mo follow-up
De Haan et al, 2005[27]	Prospective (6 wk) Sampling: consecutive	N = 113 SCZ (N = 97), schizoaffective disorder (N = 9), and schizophreniform disorder (N = 7) Inpatients Acute phase Recent onset of psychotic disorder	SCZ: DSM-IV OCS: DSM-IV symptomatic criteria (assessed by means of SCID-P) OCD: DSM-IV full criteria (assessed by means of SCID-P) Psychotic symptoms: PANSS	Less severe negative symptoms in OCS group compared with OCD and non-OCS/OCD SCZ groups at baseline No difference in positive and negative symptoms after 6 wk of treatment in OCS, OCD, and non-OCS/OCD SCZ groups
Kayahan et al, 2005[30]	Cross-sectional Sampling: nonreferred	N = 100 SCZ Inpatients and outpatients	SCZ: DSM-IV (assessed by means of SCID-P) OCS: symptomatic criteria in SCID-P OCD: DSM-IV (assessed by means of SCID-P), a minimum YBOCS total score of 7, and 6-mo duration Psychotic symptoms: PANSS	Positive correlation between OCS and general psychopathology and positive and global symptoms No correlation between OCS and negative symptoms

[a]Studies assessing the presence of OCD are listed first, studies assessing the presence of OCS are listed second, and studies assessing both OCD and OCS are listed at the end.
[b]Studies for which results could be used in the meta-analysis.
[c]Studies for which additional information was provided by authors.
Abbreviations: BPRS = Brief Psychiatric Rating Scale, FOCI = Florida Obsessive Compulsive Inventory, non-OCD SCZ = schizophrenia without OCD, non-OCD/OCS SCZ = schizophrenia without OCD or OCS, non-OCS SCZ = schizophrenia without OCS, OCD = obsessive-compulsive disorder, OCD SCZ = schizophrenia with OCD, OCS = obsessive-compulsive symptoms, OCS SCZ = schizophrenia with OCS, PANSS = Positive and Negative Syndrome Scale, SANS = Scale for the Assessment of Negative Symptoms, SAPS = Scale for the Assessment of Positive Symptoms, SCID = Structured Clinical Interview for DSM-III-R/DSM-IV Axis I Disorders, SCID-P = Structured Clinical Interview for DSM-IV Axis I Disorders, Patient Edition, YBOCS = Yale-Brown Obsessive Compulsive Scale.

Table 2. Participant Characteristics for the Studies Included in the Meta-Analysis When Data Were Available for at Least 50% of Patients

Characteristic	Value	Patients, N[a] (no. of studies)[b]
Sample size, N	1096	1096 (18)
Male, %	77.6	1096 (18)
Age, y		
Mean	37.7	1096 (18)
Range	16.7–69.5	
Type of schizophrenia population, %		986 (15)
Acute	30.4	
Stable	59.6	
Chronically hospitalized	9.9	
Type of psychotic disorder, %		1038 (17)
Schizophrenia	88.0	
Schizoaffective disorder	11.2	
Schizophreniform disorder	0.9	
Subtype of schizophrenia, %		567 (9)
Paranoid	47.3	
Undifferentiated	30.2	
Disorganized	10.1	
Residual	8.8	
Catatonic	3.7	
Age at onset of psychotic disorder, y		763 (12)
Mean	23.9	
Range	14.8–38.2	
Duration of psychotic disorder, y		756 (12)
Mean	12.3	
Range	1.8–31.4	

[a]Represents the number of subjects from which the rate of the baseline feature has been assessed.
[b]Represents the number of studies from which the specific characteristic has been assessed.

the OCD versus non-OCD subgroups was 19.5 (range, 16.1–27.9) versus 1.2 (range, 0–2.9) and 20.9 (range, 15.7–22.8) versus 5.3 (range, 0.1–10.3), respectively.

Nine studies reported information regarding the influence of the type and dose of administered antipsychotic medications. Results were markedly heterogeneous, with 2 studies[6,36] suggesting that schizophrenia patients with OCD or OCS were more likely to be treated with higher doses of antipsychotics or with a higher proportion of atypical antipsychotics than non-OCS/OCD patients, other studies favoring the opposite notion,[10] and most finding no differences in the exposure to antipsychotics.[5,8,11,12,29,38]

Severity of Psychotic Symptoms

Most studies included in the systematic review found no differences in psychotic symptom severity between the OCS/OCD and non-OCS/OCD groups (Table 1) or, at most, found differences in 1 psychotic symptom, such as hallucinations, formal thought disorder, or bizarre behavior, but not in overall positive or negative symptoms. Among the studies that did find differences, 6[7,29,30–32,35] supported the hypothesis that the presence of OCS or OCD was associated with greater overall positive or negative psychotic symptom severity, whereas only 1 study[12] reported lower severity of positive symptoms among patients with OCS or OCD. One study[33] reported that the relationship between the presence of OCS and the severity of negative psychotic symptoms was dependent on psychosocial functioning; OCS and non-OCS patients with better psychosocial functioning demonstrated less severe negative symptoms than OCS and non-OCS patients with poorer psychosocial functioning. Another study[27] found that the lesser negative symptoms in the OCS group were only present during the acute phase and faded away after a few weeks of treatment.

As mentioned, 18 studies could be included in the meta-analysis. Effect sizes and confidence intervals for global, positive, and negative psychotic symptoms for studies assessing the presence of OCD are presented in Figure 2 and for studies assessing OCS in Figure 3.

No differences in the severity of global psychotic symptoms (SMD [95% CI]) (0.19 [–0.14 to 0.51]), positive psychotic symptoms (–0.01 [–0.20 to 0.19]), or negative psychotic symptoms (–0.11 [–0.30 to 0.08]) were found for the OCD versus non-OCD subgroups. In contrast, the presence of OCS was significantly associated with greater severity of global psychotic symptoms (0.39 [0.14 to 0.64]), positive psychotic symptoms (0.28 [0.00 to 0.56]), and negative psychotic symptoms (0.36 [0.11 to 0.62]). No statistically significant heterogeneity was found for any comparison. For negative symptoms, a trend ($p = .07$) toward heterogeneity was found for the meta-analysis of the OCS versus non-OCS subgroups, and a random-effects model used to calculate the pooled effect size for this comparison yielded a similar result (0.41 [0.04 to 0.79]).

A graph analysis for detecting publication bias could not be performed because no comparison reached the cutoff of 10 studies.[39] On the other hand, the sensitivity analysis revealed that the impact of OCS on global psychotic severity did not change after removing each study once, whereas on positive symptoms, it lost its statistical significance after 2 studies[5,31] were removed, and on negative symptoms, it turned into a statistical trend (0.24 [–0.03 to 0.52], $p = .09$) when 1 study[32] was removed. No changes with respect to the main analysis were found when the same procedure was applied to the studies using an OCD definition.

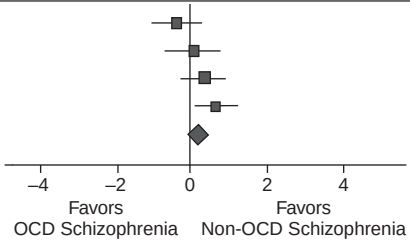
A post hoc exploratory analysis was attempted by type of schizophrenia population (acute, stable, first episode, and chronically hospitalized), but it was only possible in the stable schizophrenia group as too few studies were available for the remaining groups (Table 1). A total of 9 studies included stable samples.[6,12,25,29,31,32,34,36,38] Results for this group were similar to the overall results of the main analysis. No association was found between the presence of OCD and the severity of psychotic symptoms, whereas the presence of OCS in stable schizophrenia patients was associated with higher scores in global psychotic symptoms (0.33 [0.06 to 0.60]), positive symptoms

Figure 2. Comparison of the Severity of Global, Positive, and Negative Psychotic Symptoms Between Schizophrenia Patients With and Without Obsessive-Compulsive Disorder (OCD)

A. Global Symptoms

Study or Subcategory	N	OCD, Mean (SD)	N	Non-OCD, Mean (SD)	Weight, %	SMD (fixed) (95% CI)
Tibbo et al, 2000[12]	13	67.90 (15.20)	39	73.40 (13.70)	26.04	–0.38 (–1.02 to 0.25)
Borkowska et al, 2003[24]	13	109.00 (32.00)	15	108.00 (15.00)	18.88	0.04 (–0.70 to 0.78)
Ohta et al, 2003[8]	13	88.54 (21.11)	58	81.25 (20.27)	28.51	0.35 (–0.25 to 0.96)
Krüger et al, 2000[6]	12	57.40 (9.20)	64	49.30 (12.40)	26.56	0.67 (0.04 to 1.30)
Total	51		176		100.00	0.19 (–0.14 to 0.51)

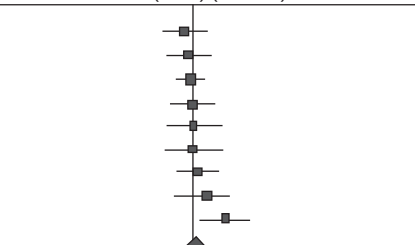
Test for Heterogeneity: $\chi^2 = 5.86$, df = 3 (p = .12), $I^2 = 48.8\%$
Test for Overall Effect: z = 1.13 (p = .26)



B. Positive Symptoms

Study or Subcategory	N	OCD, Mean (SD)	N	Non-OCD, Mean (SD)	Weight, %	SMD (fixed) (95% CI)
Sevincok et al, 2004[37]	15	21.00 (17.50)	38	27.42 (22.40)	10.39	–0.30 (–0.90 to 0.30)
Krüger et al, 2000[6]	12	30.00 (23.00)	64	35.00 (25.00)	9.83	–0.20 (–0.82 to 0.42)
Poyurovsky et al, 2003[36]	55	1.70 (1.10)	55	1.85 (1.13)	26.77	–0.13 (–0.51 to 0.24)
Tibbo et al, 2000[12]	13	19.50 (4.00)	39	20.10 (6.10)	9.50	–0.10 (–0.73 to 0.52)
Poyurovsky et al, 2006[11]	8	2.60 (1.80)	42	2.70 (1.40)	6.55	–0.07 (–0.82 to 0.69)
Poyurovsky et al, 1999[9]	7	1.95 (1.10)	43	2.04 (1.26)	5.87	–0.07 (–0.87 to 0.73)
Poyurovsky et al, 2001[10]	16	7.20 (2.80)	52	7.10 (3.10)	11.94	0.03 (–0.53 to 0.59)
Ohta et al, 2003[8]	13	20.85 (7.82)	58	19.22 (5.52)	10.30	0.27 (–0.33 to 0.87)
Nechman et al, 2003[7]	13	10.90 (3.10)	37	8.60 (2.90)	8.84	0.77 (0.12 to 1.42)
Total	152		428		100.00	–0.01 (–0.20 to 0.19)

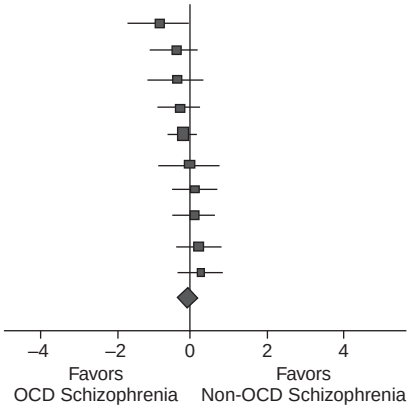
Test for Heterogeneity: $\chi^2 = 8.12$, df = 8 (p = .42), $I^2 = 1.5\%$
Test for Overall Effect: z = 0.06 (p = .96)



C. Negative Symptoms

Study or Subcategory	N	OCD, Mean (SD)	N	Non-OCD, Mean (SD)	Weight, %	SMD (fixed) (95% CI)
Poyurovsky et al, 2006[11]	8	14.60 (1.10)	42	15.60 (1.20)	5.85	–0.83 (–1.60 to –0.06)
Tibbo et al, 2000[12]	13	14.40 (5.60)	39	17.10 (6.90)	8.77	–0.40 (–1.04 to 0.23)
Borkowska et al, 2003[24]	13	28.00 (10.00)	15	31.00 (8.00)	6.27	–0.32 (–1.07 to 0.42)
Sevincok et al, 2004[37]	15	32.60 (17.20)	38	38.60 (24.70)	9.76	–0.26 (–0.86 to 0.34)
Poyurovsky et al, 2003[36]	55	2.00 (1.04)	55	2.20 (1.10)	25.03	–0.19 (–0.56 to 0.19)
Poyurovsky et al, 1999[9]	7	2.02 (1.20)	43	2.03 (1.38)	5.50	–0.01 (–0.81 to 0.79)
Ohta et al, 2003[8]	13	22.46 (7.10)	58	21.74 (7.81)	9.70	0.09 (–0.51 to 0.69)
Poyurovsky et al, 2001[10]	16	16.10 (3.60)	52	15.70 (3.80)	11.18	0.11 (–0.46 to 0.67)
Krüger et al, 2000[6]	12	65.00 (21.00)	64	60.00 (22.00)	9.21	0.23 (–0.39 to 0.84)
Nechman et al, 2003[7]	13	12.50 (4.60)	37	11.10 (4.80)	8.72	0.29 (–0.34 to 0.92)
Total	165		443		100.00	–0.11 (–0.30 to 0.08)

Test for Heterogeneity: $\chi^2 = 8.57$, df = 9 (p = .48), $I^2 = 0\%$
Test for Overall Effect: z = 1.14 (p = .25)



Abbreviation: SMD = standardized mean difference.

(0.26 [–0.04 to 0.57]), and negative symptoms (0.36 [0.08 to 0.63]).

DISCUSSION

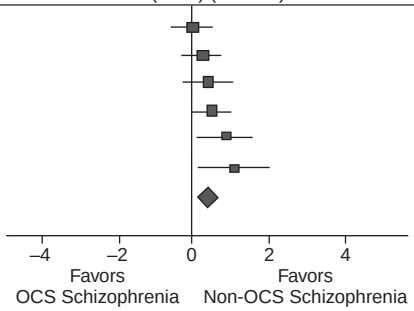
A fairly large number of studies have assessed, as a primary or a secondary aim, the impact of the presence of OCS or OCD on the severity of psychotic symptoms in schizophrenia patients. Taken individually, these studies have yielded heterogeneous results. This was the first meta-analysis combining the data from all studies to date and showed that the impact of OCS and OCD on the severity of psychotic symptoms was dependent on the definition of OCS. When a categorical definition was used,

Figure 3. Comparison of the Severity of Global, Positive, and Negative Psychotic Symptoms Between Schizophrenia Patients With and Without Obsessive-Compulsive Symptoms (OCS)

A. Global Symptoms

Study or Subcategory	N	OCS, Mean (SD)	N	Non-OCS, Mean (SD)	Weight, %	SMD (fixed) (95% CI)
Byerly et al, 2005[25]	21	68.60 (15.60)	37	68.90 (16.00)	22.54	–0.02 (–0.55 to 0.52)
Whitney et al, 2004[38]	26	72.32 (12.35)	28	69.04 (12.66)	22.49	0.26 (–0.28 to 0.79)
Lysaker et al, 2006[34]	11	85.70 (7.50)	56	80.20 (14.40)	15.29	0.40 (–0.25 to 1.05)
Fabisch et al, 2001[28]	14	68.07 (11.55)	136	62.47 (11.56)	21.15	0.48 (–0.07 to 1.03)
Berman et al,1998[5]	14	90.00 (10.40)	16	78.10 (15.70)	11.37	0.86 (0.10 to 1.61)
Hwang et al, 2000[29]	10	108.50 (15.50)	10	90.10 (17.60)	7.16	1.06 (0.11 to 2.01)
Total	96		283		100.00	0.39 (0.14 to 0.64)

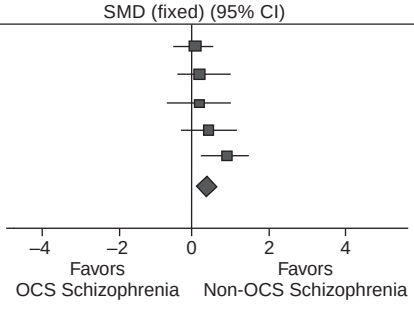
Test for Heterogeneity: $\chi^2 = 5.98$, df = 5 (p = .31), $I^2 = 16.4\%$
Test for Overall Effect: z = 3.01 (p = .003)



B. Positive Symptoms

Study or Subcategory	N	OCS, Mean (SD)	N	Non-OCS, Mean (SD)	Weight, %	SMD (fixed) (95% CI)
Whitney et al, 2004[38]	26	20.08 (5.57)	38	20.04 (5.83)	27.19	0.01 (–0.53 to 0.54)
Byerly et al, 2005[25]	21	16.00 (5.40)	37	15.30 (5.70)	26.97	0.12 (–0.41 to 0.66)
Hwang et al, 2000[29]	10	24.20 (4.80)	10	23.30 (7.10)	10.05	0.14 (–0.74 to 1.02)
Berman et al, 1998[5]	14	22.10 (5.60)	16	19.80 (6.30)	14.77	0.37 (–0.35 to 1.10)
Lysaker et al, 2000[31]	21	20.40 (6.30)	25	15.30 (5.70)	21.02	0.84 (0.23 to 1.45)
Total	92		116		100.00	0.28 (0.00 to 0.56)

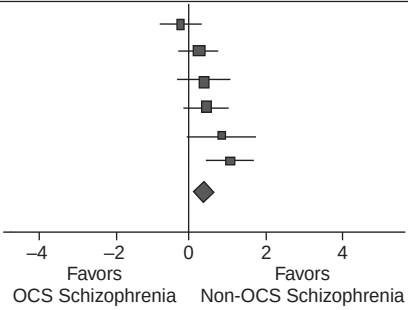
Test for Heterogeneity: $\chi^2 = 4.74$, df = 4 (p = .32), $I^2 = 15.6\%$
Test for Overall Effect: z = 1.98 (p = .05)



C. Negative Symptoms

Study or Subcategory	N	OCS, Mean (SD)	N	Non-OCS, Mean (SD)	Weight, %	SMD (fixed) (95% CI)
Byerly et al, 2005[25]	21	17.30 (5.90)	37	18.80 (6.50)	22.98	–0.24 (–0.77 to 0.30)
Whitney et al, 2004[38]	26	17.28 (6.26)	28	15.75 (5.10)	23.06	0.27 (–0.27 to 0.80)
Berman et al, 1998[5]	14	22.80 (3.80)	16	20.90 (5.20)	12.60	0.40 (–0.32 to 1.13)
Lysaker et al, 2000[31]	21	17.00 (6.40)	25	14.10 (6.40)	19.19	0.45 (–0.14 to 1.03)
Hwang et al, 2000[29]	10	28.90 (5.10)	10	24.00 (6.00)	7.78	0.84 (–0.08 to 1.77)
Lysaker et al, 2002[32]	11	25.00 (5.60)	52	19.40 (5.00)	14.38	1.08 (0.40 to 1.76)
Total	103		168		100.00	0.36 (0.11 to 0.62)

Test for Heterogeneity: $\chi^2 = 10.34$, df = 5 (p = .07), $I^2 = 51.6\%$
Test for Overall Effect: z = 2.77 (p = .006)



Abbreviation: SMD = standardized mean difference.

no differences were found between OCD schizophrenia and non-OCD schizophrenia, whereas when a dimensional definition was used, OCS schizophrenia showed a greater severity of psychotic symptoms than non-OCS schizophrenia.

To the degree that global symptoms refer to overall psychopathology, including anxiety, tension, preoccupation, and depression, in addition to positive and negative psychotic symptoms, it may not be surprising that patients with OCS schizophrenia scored higher on global symptoms than those with non-OCS schizophrenia. However, OCS schizophrenia also scored higher in positive and negative symptoms, indicating that the presence of OCS was also associated with more severe psychotic symptoms. This finding contradicts earlier studies that postulated that the presence of OCS had a protective role and was an indicator of good prognosis in schizophrenia.[15,16] It has been suggested that the presence of OCD in the first stages of schizophrenia may be associated with less formal thought disorder and affective flattening,[9] rendering a protective effect against some, but not all, positive or negative psychotic symptoms. Nevertheless, this meta-analysis was not aimed at assessing specific types of psychotic symptoms, and, therefore, such a possibility cannot be ruled out.

It is striking that, unlike OCS, the presence of OCD was not associated with more severe psychotic symptoms. This

seemingly contradictory finding may not be so, and may have both methodological and statistical explanations. Depending on the definition of schizophrenia with obsessive-compulsive features (OC schizophrenia), dimensional or categorical, a notably different composition for the schizophrenia without obsessive-compulsive features (non-OC schizophrenia) control group appears to have resulted in the various studies.

Since an OCS definition is less restrictive than one of OCD, patients with obsessive-compulsive symptoms who may not fulfill diagnostic criteria for OCD would be classified in the OC schizophrenia group if a dimensional definition was used but would be placed in the non-OC schizophrenia group if a categorical definition was used instead. Thus, the control group will differ in terms of obsessive-compulsive severity depending on the definition of OC schizophrenia, with a greater severity of obsessive-compulsive features in the control group when a categorical definition was used. In accordance with that, a markedly higher weighted mean of total YBOCS scores was found in the non-OCD group compared with the non-OCS group: 5.3 (range, 0.1–10.3) versus 1.2 (range, 0–2.9). In other words, when the OCD definition was used, the control groups most likely included some subjects with varying degrees of OCS resulting in a dilution of the effect of obsessions and compulsions on the severity of psychotic symptoms.

It could be that the relationship between OCS and severity of psychotic symptoms was nonlineal, and it took place from a certain level of OCS severity. In this line, 1 study[35] that divided schizophrenia patients into 3 subgroups depending on YBOCS scores found greater severity of positive and global psychotic symptoms in the group with greater OCS severity, but this was not found in the group without OCS or in the group with milder OCS severity. Further research is warranted to address this issue.

The link between OCS and greater severity of psychotic symptoms found in this meta-analysis can be conceptualized in different ways. One possible explanation could be that it is an artifact of the phenomenologic overlap of OCD and schizophrenia. Obsessions and compulsions can resemble symptoms of psychosis,[40] and in patients with both obsessions and delusions, these symptoms can be intertwined in ways that are difficult or almost impossible to disentangle.[41] For example, it can be difficult to distinguish obsessions with poor insight from delusions, compulsions from mannerisms, and obsessional slowness from thought blocking. Thus, it could be that subjects with OC schizophrenia showed higher psychotic symptom severity because those obsessive-compulsive symptoms that resembled psychotic symptoms were contributing to the quantification of psychosis.

In order to facilitate the identification of OCS in the presence of psychosis, it has been suggested that a recurrent, intrusive, ego-dystonic thought should not be considered an obsession if it revolves exclusively around delusional themes and that a repetitious act should only be considered a compulsion if it occurs in response to an obsession, not if it occurs in response to a delusion.[18] However, since most studies did attempt to exclude from the OCS/OCD subgroup those patients with obsessions and compulsions that were related to schizophrenia symptoms, and evidence indicates that obsessions and compulsions can be reliably identified by instruments valid for OCD,[20] this explanation of symptom overlap seems unlikely to account for the current meta-analysis finding.

Since atypical antipsychotics have been cited for inducing or exacerbating OCS, it could be that those subjects with more severe psychotic symptoms were being treated with different types and doses of antipsychotics and, consequently, were at a higher risk of developing drug-induced OCS. Although this possibility exists, it is unlikely to explain our findings.

First, evidence for an impact of atypical antipsychotics on the development or exacerbation of OCS comes mainly from case reports, chart reviews,[14] and retrospective studies,[42] being that clozapine is the antipsychotic with more evidence in exacerbation or de novo emergence of OCS and OCD in schizophrenia.[14] Only 1 placebo-controlled study has been carried out addressing this issue, and it failed to confirm such a relationship[43] with olanzapine.

Second, antipsychotics have actually been shown to be efficacious for the treatment of refractory OCD.[44] Third, and most importantly, most of the studies included in this meta-analysis reporting data on antipsychotic administration found no differences in the exposure to antipsychotics between the OC schizophrenia and non-OC schizophrenia subgroups. Only 2 studies[6,36] found that the OC schizophrenia subgroup was more frequently treated with antipsychotics (including clozapine), and 1 of them[36] found that all clozapine-treated patients were diagnosed with OCD prior to clozapine initiation. Nevertheless, to more definitively conclude on the influence of drugs on our findings, a multivariate analysis including type and dose of antipsychotic as a covariate would have been helpful. However, such an analysis could not be performed because treatments were reported in a very heterogeneous fashion across studies.

The finding of a greater severity of psychosis in schizophrenia patients with OCS is in line with several studies suggesting a graver clinical picture for these patients. OC schizophrenia compared with non-OC schizophrenia has been associated with poorer social and vocational functioning,[4,45] increased risk of suicide ideation or attempt,[46] longer hospitalizations,[4,45] and more motor symptoms including catatonia.[6] Similarly, schizophrenia patients with OCS or OCD have been shown to perform poorly on neuropsychological testing, including measures of executive functioning, nonverbal memory, visual-spatial skills, and vigilance.[5,29,31,32,38]

The graver picture of schizophrenia patients with OCS features revealed by the current meta-analysis suggests that the presence of OCS augments the severity of psychosis. OCS in schizophrenia may be the reflection of 2 comorbid diseases that functionally exacerbate one another.[31] However, it is also possible that the presence of OCS in schizophrenia represents a unique entity with its own pathophysiology, course, and prognosis. Although this study was not aimed at examining whether schizo-obsessive disorder represents a distinct nosology, our results provide useful data for enriching this debate.[18,20]

The current study favors a dimensional definition of schizo-obsessive disorder with prognostic value in terms of severity of psychotic symptoms. Nevertheless, this debate is complex, and phenomenologic findings would need to be analyzed together with genetic, familial aggregation, neuropsychological, neuroimaging, and psychopharmacologic features that are beyond the scope of this systematic review meta-analysis.

The limitations of this study must be stressed starting with heterogeneity. Heterogeneity arises from both different study designs and different sample features. Two types of study design were included in this meta-analysis: cross-sectional and longitudinal. In order to remove any heterogeneity from this source, data from only 1 time point were analyzed from longitudinal studies. The most important source of heterogeneity came from the use of 2 notably different definitions of OC schizophrenia: categorical versus dimensional. This type of heterogeneity resulted in notably different baseline characteristics that invalidated a pooled analysis of all studies, resulting in separate meta-analyses for OCD and OCS schizophrenia. These precautions in the statistical analysis resulted in no statistically significant heterogeneity for any analyzed comparison. Nevertheless, for negative symptoms in OCS versus non-OCS schizophrenia, a trend toward a significant heterogeneity was found. For this reason, a random-effects model was also used for this comparison, and almost identical results were obtained, suggesting that heterogeneity is very unlikely.

Another source of clinical heterogeneity came from the inclusion of inpatients and outpatients, subjects in acute exacerbation and in stable phase, subjects with a first psychotic episode, and chronically ill patients. To control for this source of heterogeneity, a subanalysis for these features was attempted but could not be performed because splitting up the meta-analysis for all these clinical categories resulted in very small numbers hindering a statistical synthesis. Nevertheless, since no heterogeneity was found, one must conclude that the impact of OCS or OCD on the severity of psychotic symptoms is homogeneous across the different phases of schizophrenia.

The results of the sensitivity analysis showed that the magnitude of the association between OCS and severity of positive and negative psychotic symptoms was mild, and withdrawing from the analysis the studies with the largest effects resulted in a loss of this association. This loss of association did not occur for global psychotic symptoms since the magnitude of the difference was larger.

Reporting bias can also limit our findings. Publication bias occurs when positive results are more likely to be published and included in meta-analyses than negative results. A great effort was made to minimize the effect of this source of bias. Publication bias is unlikely to occur in this meta-analysis for several reasons.

This meta-analysis was performed in the context of a systematic review, and a comprehensive search strategy was followed. This search was not limited to English-language articles but also included studies published in 3 additional languages: French, Spanish, and Catalan. Two databases were used to search for studies of interest, and references of included studies and reviews of the topic were checked. Furthermore, because statistically significant results may have been more likely to be reported than nonsignificant results, first authors of all included studies were contacted if needed information was missing from the original article. This process resulted in a notable increase of the available and analyzed data (Table 1). In addition, the fact that most studies showed no differences in psychotic symptom severity between OC and non-OC schizophrenia suggests that negative findings are less likely to be underreported in this area compared to clinical trials, for example. Finally, to limit meta-analysis flaws, recommendations from the Meta-Analysis of Observational Studies in Epidemiology statement[17] were used to carry out and write this study.

In conclusion, this is the first meta-analytic study assessing the relationship between obsessive-compulsive symptomatology and the severity of psychosis. The presence of OCS in schizophrenia was associated with higher global, positive, and negative psychotic symptoms. This association was not found when a categorical definition of OCD was used, supporting a dimensional conceptualization of the obsessive-compulsive schizophrenia spectrum. Further research is warranted to investigate this finding beyond the phenomenologic level, as well as to examine its possible treatment implications.

Drug names: clozapine (FazaClo, Clozaril, and others), olanzapine (Zyprexa).

REFERENCES

1. Kendler KS, Gallagher TJ, Abelson JM, et al. Lifetime prevalence, demographic risk factors, and diagnostic validity of nonaffective psychosis as assessed in a US community sample. The National Comorbidity Survey. Arch Gen Psychiatry 1996 Nov;53(11):1022–1031
2. Murray CJL, Lopez AD, eds. The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability From Diseases, Injuries and Risk Factors in 1990 and Projected to 2020. Cambridge, Mass: Harvard School of Public Health on behalf of the World Health Organization and the World Bank; 1996 [Global Burden of Disease and Injury Series, Vol. I]

3. Berrios GE. Obsessive-compulsive disorder: its conceptual history during the 19th century. Compr Psychiatry 1989 Jul–Aug;30(4):283–295
4. Fenton WS, McGlashan TH. The prognostic significance of obsessive-compulsive symptoms in schizophrenia. Am J Psychiatry 1986;143: 437–441
5. Berman I, Merson A, Viegner B, et al. Obsessions and compulsions as a distinct cluster of symptoms in schizophrenia: a neuropsychological study. J Nerv Ment Dis 1998;186:150–156
6. Krüger S, Bräunig P, Höffler J, et al. Prevalence of obsessive-compulsive disorder in schizophrenia and significance of motor symptoms. J Neuropsychiatry Clin Neurosci 2000;12:16–24
7. Nechman A, Ratzoni G, Poyurovsky M, et al. Obsessive-compulsive disorder in adolescent schizophrenia patients. Am J Psychiatry 2003; 160:1002–1004
8. Ohta M, Kokai M, Morita Y. Features of obsessive-compulsive disorder in patients primarily diagnosed with schizophrenia. Psychiatry Clin Neurosci 2003;57:67–74
9. Poyurovsky M, Fuchs C, Weizman A. Obsessive-compulsive disorder in patients with first-episode schizophrenia. Am J Psychiatry 1999;156: 1998–2000
10. Poyurovsky M, Hramenkov S, Isakov V, et al. Obsessive-compulsive disorder in hospitalized patients with chronic schizophrenia. Psychiatry Res 2001;102:49–57
11. Poyurovsky M, Bergman J, Weizman R. Obsessive-compulsive disorder in elderly schizophrenia patients. J Psychiatr Res 2006;40:189–191
12. Tibbo P, Kroetsch M, Chue P et al. Obsessive-compulsive disorder in schizophrenia. J Psychiatr Res 2000;34:139–146
13. Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62:593–602
14. Poyurovsky M, Weizman A, Weizman R. Obsessive-compulsive disorder in schizophrenia: clinical characteristics and treatment. CNS Drugs 2004; 18:989–1010
15. Rosen I. The clinical significance of obsessions in schizophrenia. J Ment Sci 1957;103:773–785
16. Stengel E. A study of some clinical aspects of the relationship between obsessional neurosis and psychotic reaction types. J Ment Sci 1945;91: 166–187
17. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000 Apr;283(15):2008–2012
18. Bottas A, Cooke, RG, Richter MA. Comorbidity and pathophysiology of obsessive-compulsive disorder in schizophrenia: is there evidence for a schizo-obsessive subtype of schizophrenia? J Psychiatry Neurosci 2005;30:187–193
19. Hwang MY, Hollander E. Schizo-obsessive disorders. Psychiatr Ann 1993;23:396–401
20. Poyurovsky M, Koran LM. Obsessive-compulsive disorder (OCD) with schizotypy vs schizophrenia with OCD: diagnostic dilemmas and therapeutic implications. J Psychiatr Res 2005;39:399–408
21. Tibbo P, Warneke L. Obsessive-compulsive disorder in schizophrenia: epidemiologic and biologic overlap. J Psychiatry Neurosci 1999;24: 15–24
22. Egger M, Smith GD, Phillips AN. Meta-analysis: principles and procedures. BMJ 1997;315:1533–1537
23. Egger M, Davey Smith G, Schneider M et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–634
24. Borkowska A, Pilaczynska E, Rybakowski JK. The frontal lobe neuropsychological tests in patients with schizophrenia and/or obsessive-compulsive disorder. J Neuropsychiatry Clin Neurosci 2003; 15(3):359–362
25. Byerly M, Goodman W, Achlonu W, et al. Obsessive compulsive symptoms in schizophrenia: frequency and clinical features. Schizophr Res 2005;76:309–316
26. Craig T, Hwang MY, Bromet EJ. Obsessive-compulsive and panic symptoms in patients with first-admission psychosis. Am J Psychiatry 2002;159:592–598
27. De Haan L, Hoggenboom B, Beuk N, et al. Obsessive-compulsive symptoms and positive, negative, and depressive symptoms in patients with recent-onset schizophrenic disorders. Can J Psychiatry 2005;50:519–524
28. Fabisch K, Fabisch H, Langs G, et al. Incidence of obsessive-compulsive phenomena in the course of acute schizophrenia and schizoaffective disorder. Eur Psychiatry 2001;16:336–341
29. Hwang MY, Morgan JE, Losconzcy MF. Clinical and neuropsychological profiles of obsessive-compulsive schizophrenia: a pilot study. J Neuropsychiatry Clin Neurosci 2000;12:91–94
30. Kayahan B, Ozturk O, Veznedaroglu B, et al. Obsessive-compulsive symptoms in schizophrenia: prevalence and clinical correlates. Psychiatry Clin Neurosci 2005;59:291–295
31. Lysaker PH, Marks KA, Picone JB, et al. Obsessive and compulsive symptoms in schizophrenia: clinical and neurocognitive correlates. J Nerv Ment Dis 2000;188:78–83
32. Lysaker PH, Bryson GJ, Marks KA, et al. Association of obsessions and compulsions in schizophrenia with neurocognition and negative symptoms. J Neuropsychiatry Clin Neurosci 2002;14:449–453
33. Lysaker PH, Lancaster RS, Nees MA, et al. Patterns of obsessive-compulsive symptoms and social function in schizophrenia. Psychiatry Res 2004;125:139–146
34. Lysaker PH, Whitney KA, Davis LW. Obsessive-compulsive and negative symptoms in schizophrenia: associations with coping preference and hope. Psychiatry Res 2006;141:253–259
35. Ongur D, Goff DC. Obsessive-compulsive symptoms in schizophrenia: associated clinical features, cognitive function and medication status. Schizophr Res 2005;75:349–362
36. Poyurovsky M, Kriss V, Weisman G, et al. Comparison of clinical characteristics and comorbidity in schizophrenia patients with and without obsessive-compulsive disorder: schizophrenic and OC symptoms in schizophrenia. J Clin Psychiatry 2003 Nov;64(11):1300–1307
37. Sevincok L, Akoglu, A, Topaloglu B, et al. Neurological soft signs in schizophrenic patients with obsessive-compulsive disorder. Psychiatry Clin Neurosci 2004;58:274–279
38. Whitney KA, Fastenau PS, Evans JD, et al. Comparative neuropsychological function in obsessive-compulsive disorder and schizophrenia with and without obsessive-compulsive symptoms. Schizophr Res 2004;69:75–83
39. Lau J, Ioannidis JP, Terrin N, et al. The case of the misleading funnel plot. BMJ 2006;333:597–600
40. Insel TR, Akiskal HS. Obsessive-compulsive disorder with psychotic features: a phenomenologic analysis. Am J Psychiatry 1986;143: 1527–1533
41. Bermanzohn PC. Prevalence and prognosis of obsessive-compulsive phenomena in schizophrenia: a critical view. Psychiatr Ann 1999;29: 508–512
42. Mahendran R, Liew E, Subramaniam M. De novo emergence of obsessive-compulsive symptoms with atypical antipsychotics in Asian patients with schizophrenia or schizoaffective disorder: a retrospective, cross-sectional study. J Clin Psychiatry 2007 Apr;68(4):542–545
43. Baker RW, Ames D, Umbricht DS et al. Obsessive-compulsive symptoms in schizophrenia: a comparison of olanzapine and placebo. Psychopharmacol Bull 1996;32:89–93
44. Gao K, Muzina D, Gajwani P, et al. Efficacy of typical and atypical antipsychotics for primary and comorbid anxiety symptoms or disorders: a review. J Clin Psychiatry 2006 Sep;67(9):1327–1340
45. Berman I, Kalinowski A, Berman SM. Obsessive and compulsive symptoms in chronic schizophrenia. Comp Psychiatry 1995 Jan–Feb;36(1): 6–10
46. Sevincok L, Akoglu A, Kokcu F. Suicidality in schizophrenic patients with and without obsessive-compulsive disorder. Schizophr Res 2007; 90:198–202