OBSESSIVE-COMPULSIVE DISORDER (OCD) IN PATIENTS WITH FIRST- EPISODE PSYCHOSIS (FEP): A PROSPECTIVE STUDY

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Abstract

Objective: Obsessive Compulsive Disorder (OCD) is a severe condition tending to be chronic if untreated. Despite research indicating that OCD is a common co-morbidity in patients with psychotic disorders, there is sparse systematic knowledge about the clinical course in patients with psychosis and comorbid OCD. To compare, one year after the first psychotic episode (FEP), changes in a) psychotic symptoms and b) global functioning and global symptoms (GAFs) in patients with and without comorbid OCD.

Method: Two hundred and forty six FEP-patients who were consecutively referred to a special unit for psychosis, were screened for psychosis as well as comorbid diagnoses at admission. To ensure the quality of the OCD-diagnostics, there was a post-hoc reassessment of all the patients based on information from SCID-I, PANSS and full medical records. The Positive and Negative Syndrome Scale (PANSS) and Global Assessment of Functioning (GAF-F and GAF-S), were employed to evaluate symptom severity at admission and one- year follow-up.

Results: Despite no differences between the groups in psychotic symptoms or general functioning at admission, patients with comorbid OCD showed significantly less improvement in global function and symptom level from inclusion to one-year follow-up, even when depression was controlled for.

Conclusions: The findings suggest that comorbid OCD in FEP may be associated with a more negative course of GAF-F and GAF-S, even though the OCD-group responded adequately to the antipsychotic treatment. Whether interventions specifically targeting the OCD would have changed the level of symptoms and functioning one year after the FEP, is unknown. More studies focusing on diagnostic challenges combined with evidence based treatment is warranted.

Key words: obsessive-compulsive disorder, first-episode psychosis, comorbidity, follow-up

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Introduction

Obsessive compulsive disorder (OCD) is considered to be a severe condition which significantly influence everyday functioning (Huppert et al. 2009, Steketee 1997), and which tends to be chronic if untreated (Skoog and Skoog 1999). A number of studies indicate that OCD is a common comorbid disorder in patients with psychotic disorders, with prevalence rates varying between 8-26 % (Cunill et al. 2009). Despite seemingly high comorbidity between psychosis and OCD, little is known about the course of the psychotic symptoms and general functioning in patients with a comorbid OCD (Aydin et al. 2008, Cunill et al. 2009).

Early theories considered OCD to be a protective factor for individuals with schizophrenia (Rosen 1957, Stengel 1945). More recent research, however, indicate that comorbid OCD is associated with a more severe overall clinical presentation (de Haan et al. 2013, Fenton and McGlashan 1986, Hagen et al. 2013). Specifically, comorbid OCD in psychotic disorders has been reported to be associated with more depressive symptoms (de Haan et al. 2013, Gülec et al. 2008, Hagen et al. 2013, Ongur and Fava 2005, Rajkumar et

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al. 2008), worse premorbid functioning (de Haan et al. 2013), higher rates of suicidality (Hagen et al. 2013, Sevincok et al. 2007) and lower quality of life (Tiryaki and Ozkorumak 2010). However, comorbid OCD does not seem to be related to positive or negative psychotic symptoms (Craig et al. 2002, Cunill et al. 2009, de Haan et al. 2013, Hagen et al. 2013, Üçok et al. 2011).

We have been able to identify only two longitudinal studies focusing on psychotic patients with comorbid OCD (Craig et al. 2002, de Haan et al. 2013), and main findings are presented in the following. Craig and colleagues (2002) reported a prevalence rate of comorbid OCD of 3.8% (17 of 450) in a sample of patients with first admission psychosis. The study was a post-hoc analysis, which focused on patients who were diagnosed with schizophrenia, schizoaffective disorder, bipolar disorder with psychosis, or major depression with psychosis at 2-year follow-up after inclusion at the Suffolk County Mental Health Project. The study found no significant associations between the presence of OCD symptoms and clinical functioning at two-year follow-up. The low prevalence may be related to the fact that the diagnostics of OCD were solely based on SCID-I interview, unlike the diagnostics of the psychosis, which was based on best estimate procedures (Craig et al. 2002).

In a 5-year prospective study of schizophrenia and related disorders, de Haan and colleagues (2013) reported an 11.8% (22 of 186) prevalence rate of comorbid OCD. All patients were admitted to a centralized, specialized "Early Psychosis Department". Patients aged 15–28 years of age were eligible for the study. Exclusion criteria were not reported. The DSM-IV diagnostics were based on SCID-I interviews combined with available clinical information. de Haan and colleagues (2013) reported that comorbid OCD was related to more severe depressive symptoms, but not to severity of psychotic symptoms or to relapse of the psychotic disorder. OCD-symptoms were defined in accordance with SCID-I, and the symptoms of OCD had to be unrelated to psychotic content.

The present study is derived from a large catchment area based longitudinal study of patients with first episode psychosis. Specifically, we wanted to examine whether the co-occurrence of OCD at inclusion was associated with more severe global functioning (GAF-F) and -symptoms (GAF-S) as well as psychotic symptoms (PANSS) at one-year follow-up, compared to FEP-patients without OCD-comorbidity. Based on the knowledge that OCD is associated with severe impairment, we hypothesize that comorbid OCD would be related to worse general functioning and more severe symptoms measured by GAF symptoms (GAF-S) and function (GAF-F) at one-year follow-up compared to patients without comorbid OCD.

Methods

Participants and procedure

The study included patients in the South sector of Rogaland County, Norway, with a population of about 400 000, mainly in urban and suburban areas. Recruitment for the study continued consecutively from January 1st, 2002 to November 30th, 2010 (the TIPS-2 study). The criteria for inclusion in the study were a) Living in the catchment area; b) age 15–65 years; c) meeting the DSM-IV (APA 1994) criteria for schizophrenia, schizophreniform psychosis, schizoaffective psychosis, delusional disorder, brief psychosis, affective disorder with mood incongruent delusions, or psychosis not otherwise specified; d) being actively psychotic[1]; e) not previously receiving adequate treatment for psychosis[2]; f) no neurological or endocrine disorders with relationship to the psychosis; g) no contraindications to antipsychotic medication; h) understands and speaks Norwegian; i) IQ over 70[3]; j) willing and able to give informed consent.

The study has been approved by the Regional Committee for Medical Research Ethics Health Region West (015.03). Written informed consent was obtained from all study participants. For patients younger than 18 years of age, parents or legal guardians gave informed consent.

The patients could enter the study either through the TIPS-2 team or through the hospitals acute inpatient ward. After an initial screening interview, a senior psychiatrist or psychologist examined the patients. Demographics and supplementary information were collected, a diagnostic interview was conducted, and an independent rater later reassessed the diagnostic interview.

Altogether 481 consecutive patients were identified. Seventy patients were excluded (21 were not registered in the catchment area, 12 because of poor language skills, 11 because they were younger than 15 years of age, and 6 because of low IQ; 20 patients were lost for further study contact and were not asked). Of the 411 remaining patients, 166 refused participation. The rate of consent to participate was therefore 60% (246 patients). This report comprises data from the time of inclusion and one-year follow-up.

Trained personnel assessed all patients within a week of first contact. They were then assigned to the standard treatment program, which consisted of an antipsychotic medication algorithm, multifamily work, and active outreach-supportive psychotherapy (Joa et al. 2009).

Assessments

Assessment teams consisting of clinically experienced and trained research personnel carried out all assessments. The structured clinical interview for the DSM-IV (SCID-I; First et al. 1995) was used for diagnostics.

The OCD-diagnostics were based on a three-step procedure. The first step is the original SCID-I interview, which was done by the TIPS team (for details see earlier publications, Joa et al. 2008, Larsen et al. 2010). The second step was a post-hoc reassessment, were all the patients' SCID-I and PANSS reports, as well as the patients' full medical records were independently re-assessed by the first author and a psychologist with extensive training in OCD diagnostics. The medical records are electronically stored, which made it possible to search each one for OCD-relevant information. Search words were; «obsessive», «compulsive», «ritual», «exposure», and «SSRI». The third step was a reassessment of all cases with indications of

[1] Defined by a score at the Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987) on four (moderate) or more on at least one of the following PANSS items; P1, (delusions), P3 (hallucinations), P5 (grandiose thinking), P6 (suspiciousness) and A9 (unusual thought content)

[2] Defined as antipsychotic medication of 3.5 haloperidol equivalents for 12 weeks or until remission of the psychotic symptoms

[3] Measured by the Wechsler intelligence scales for adults (WAIS; Wechsler 1981)

possible OCD obtained in step two. These cases were re-examined jointly by a senior psychiatrist (T.K.L) and a senior psychologist (B.H), both with extensive experience in the diagnostics of OCD and psychosis. The diagnostics were based on a strict definition of OCD based on the criteria for differentiating OCD from psychosis from Bottas and colleagues (2005); the patient had to meet the full DSM-IV criteria for OCD, and the obsessive-compulsive symptoms had to be unrelated to the psychotic content. Of the 246 participants, 16 patients were originally diagnosed with OCD, and 10 more cases were diagnosed with OCD after the post-hoc reassessment. All patients initially diagnosed with OCD were also diagnosed with OCD at the post-hoc reassessment.

The patients' level of psychotic symptoms was measured by the Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987). Symptom domains are represented by the corresponding PANSS components (positive, negative, excitative, depressive and cognitive) (Bentsen et al. 1996). Remission of psychotic symptoms was defined in accordance with the standardized criteria defined by Andreasen and colleagues (2005); no score of 4 or higher for the past 6 months on any of the following PANSS items: P1 (delusions), P2 (disorganized thought), P3 (hallucinatory behavior), N1 (affective flattening), N4 (passive social withdrawal), N6 (lack of spontaneity), G5 (bizarre posture), or G9 (unusual thought content).

Global functioning was measured by the Global Assessment of Functioning Scale (GAF; APA 1994). The scores were split into symptom [GAF-S] and function [GAF-F] scores (Pedersen et al. 2007).

The assessors were specially trained in using the instruments. Reliability of measurements were calculated and ranged from fair to very good (GAF-S score, 0.63; GAF-F score, 0.88; PANSS positive sum score, 0.88; PANSS negative sum score, 0.76; and PANSS general sum score, 0.56 [all intra-class correlations, 1.1]; for diagnostic categories, K = 0.76) (Joa et al. 2009).

Statistics

Continuous data are presented as means with standard deviations (SD).

In order explore possible changes- and interaction effects in symptoms from inclusion to one-year follow up, 2x2 ANOVAs with time as a repeated factor and group (Psychosis with- or without OCD) as between factor were performed (Kirk 1977).

Intention to treat analyses. In order to allow participants with missing data to be included in the ANOVAs, Full Information Maximum Likelihood procedure (FIML) was applied to impute missing data. This procedure provides unbiased estimates of the missing data and their standard errors based on the assumption that data are missing at random (MAR), and has been shown to perform better than alternative methods to estimate missing data (Enders 2001a, 2001b).

Categorical variables were analyzed using Chi-square. Significance level was set at $p< .05$. Analyses were performed using SPSS 22.0.

Table 1. *Baseline demographics and clinical characteristics*

Demographic variable	OCD (220)	Non-OCD (226)
Males (%)	43.2	58.6 %
Single (%)	88.5	81.9
Age at entrance*	23.0 (8.0)	27.1 (10.3)
Years of education	11.4 (1.7)	11.8 (2.6)
* = Significant at $p< .05$		

Results

Demographic variables

Demographic variables are presented in **table 1**.Twenty-six out of 246 patients had comorbid OCD, which gives a prevalence rate of 10.7 %. The patients with comorbid OCD were younger compared to the non-OCD patients (t=1.986, p=.053, mean age in patients with OCD was 23.0 (SD=8.0) and mean age in patients without OCD was 27.1 (SD=10.3). There were no significant differences on other demographic variables.

Changes in global functioning (GAF-F)

The ANOVAs revealed a significant main effect of time $F(1,26)= 23.26$, p=.000, indicating that the patients significantly improved on GAF-F from inclusion to one year follow up. The ANOVAs also showed a significant interaction effect between time and group (with or without comorbid OCD) $F(1,26)=5.74$, p=.017. There were no significant differences in GAF-F scores between the groups at inclusion (t=.64, p=.138), indicating that the significant interaction effect was due to less improvement in GAF-F scores in OCD-patients at one year-follow up (t=2.32, p=.027). When an analogous analysis was conducted with the depression-component on PANSS as covariate, the difference between the groups remained significant $F(1,26)=6.05$, p=.015 which indicate that patients with comorbid OCD had less improvement when controlling for depressive symptoms, measured by the depression component of the PANSS, at inclusion.

Changes in global symptoms (GAF-S)

The ANOVAs revealed a significant main effect of time $F(1,26)= 43.85$, p=.000, indicating that the patients significantly improved on GAF-S from inclusion to one year follow up. The ANOVAs also showed a significant interaction effect between time and group (with or without comorbid OCD) $F(1,26)=4.18$, p=.042. There were no differences between in GAF-S scores between

the groups at inclusion (t=.1.54, p=.134), indicating that the significant interaction effect was due to less improvement in GAF-F scores in OCD-patients at one year-follow up (t=2.66, p=.011). When an analogous analysis was conducted with the depression-component on PANSS as covariate, the difference between the groups remained significant $F(1,26)$=4.72, p=.031, which indicate that patients with comorbid OCD had less improvement even when controlling for depressive symptoms, measured by the depression component of the PANSS, at inclusion.

Changes in negative psychotic symptoms (PANSS-N)

The ANOVAs revealed a significant main effect of time $F(1,26)$=7.59, p=.006, indicating that the patients significantly improved on PANSS-N from inclusion to one-year follow-up. The ANOVAs showed no interaction effect between time and group (with or without comorbid OCD). When an analogous analysis was made with the depression-component on PANSS as covariate, the difference remained insignificant.

Changes in positive psychotic symptoms (PANSS-P)

The ANOVAs revealed a significant main effect of time $F(1,26)$= 70.99, p=.000, indicating that the patients significantly improved on PANSS-P from inclusion to one year follow up. The ANOVAs showed no interaction effect between time and group (with or without comorbid OCD). When an analogous analysis was made with the depression-component on PANSS as covariate, the difference remained insignificant.

Changes in cognitive symptoms, (PANSS-C)

The ANOVAs revealed a significant main effect of time $F(1,26)$=21.76, p=.000, indicating that the patients significantly improved on PANSS-C from inclusion to one year follow up. The ANOVAs showed no interaction effect between time and group (with or without comorbid OCD. When an analogous analysis was made with the depression-component on PANSS as covariate, the difference remained insignificant.

Changes in excitative symptoms (PANSS-E)

The ANOVAs revealed a significant main effect of time $F(1,26)$=36.30, p=.000, indicating that the patients significantly improved on PANSS-E from inclusion to one year follow up. The ANOVAs showed no interaction effect between time and group (with or without comorbid OCD. When an analogous analysis was made with the depression-component on PANSS as covariate, the difference remained insignificant.

Changes in depression (PANSS-D)

The ANOVAs revealed a significant main effect of time $F(1,26)$=66.71, p=.000, indicating that the patients significantly improved on PANSS-D from inclusion to one year follow up. The ANOVAs showed no interaction effect between time and group (with or without comorbid OCD).

Remission Status at one-year follow-up

There were no differences between the groups at rate of remission at follow-up (χ^2=.724, p. =.395).

Table 2. *Means, standard deviations for GAF and PANSS, Intention to treat at one year follow-up*

	Non-OCD (N=220)		OCD (N=26)	
Measure	Inclusion	Follow-up	Inclusion	Follow-up
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
GAF-Function	39.50 (9.51)	50.30 (14.89)	40.77 (10.38)	44.40 (11.95)*
GAF-Symptoms	31.19 (7.35)	46.80 (15.85)	33.08 (5.73)	41.32 (8.90)*
PANSS- Depressive	12.31 (3.60)	9.34 (3.36)	14.51 (3.10)	10.62 (2.46)
PANSS- Excitative	7.93 (3.31)	5.96 (2.11)	8.82 (2.63)	6.41 (2.16)
PANSS- Cognitive	5.81 (2.91)	4.12 (1.95)	5.52 (2.80)	4.48 (2.09)
PANSS- Negative	18.73 (7.29)	16.04 (5.75)	19.69 (8.11)	17.81 (5.14)
PANSS- Positive	14.57 (3.95)	9.58 (4.03)	14.46 (3.92)	10.90 (4.41)

Note. GAF = Global assessment of functioning, PANSS = Positive and Negative Syndrome, Scale, * = significantly interaction between groups and time. p< .05

Discussion

In the current study, patients with psychosis and comorbid OCD were compared to patients without such comorbidity, one year after the first psychotic episode. Firstly, it is noteworthy that the groups did not differ in general functioning or in psychotic symptoms at the time of inclusion. At one-year follow-up, the OCD-group did, however, show significantly more general symptoms and worse general functioning, even when

the level of depression was controlled for. OCD is found to be frequently accompanied by major social and occupational dysfunction (Huppert et al. 2009, Steketee 1997), and the finding may indicate that comorbid OCD adds a significant burden to patients with a psychotic condition.

The results give no support to the initial claims that OCD is a protective factor for patients with psychosis (Poyurovsky et al. 1999, Rosen 1957, Stengel 1945).

At one-year follow up, there were no differences between the groups in term of psychotic functioning, as measured by PANSS sub-scales. This is in line with findings from Craig and colleagues (2002), who reported no association between comorbid OCD and level of psychosis at 24 months follow-up in a sample of patients with first episode psychosis. de Haan and colleagues (2013) also reported no association between comorbid OCD and level of psychosis either at inclusion, 6 months, or three-years follow-up. This finding is interesting, since all patients in the current study were included in a standardized psychosis treatment program after admission (Joa et al. 2009), and based on the PANSS sub-scales at one-year follow-up, the OCD patients responded equally well to this program.

de Haan and colleagues (2013) found that OCD was related to more depressive symptoms and poorer social functioning. In our study, there was no significant difference between the groups with respect to depression and the significantly less degree of improvement in general functioning and general symptoms in the OCD-patients at one-year follow up, supports the notion that the negative course might specifically be related to the comorbid OCD.

Whether specific OCD-treatment could have influenced general functioning and general symptoms in the OCD-group at one year follow up, is not known. Exposure and response prevention (ERP) is considered to be the treatment of choice for OCD (Abramowitz 2006, Franklin and Foa 2011). The efficacy of ERP for OCD in patients with psychotic disorders is, however, not yet established (Rodriguez et al. 2010), although case studies have reported that the treatment might be effective for OCD patients with psychosis (e.g. Hagen et al. 2014, Kobori et al. 2008). Some patients might also benefit from medication (i.e. SRI) in order to reduce the severity of both obsessive-compulsive and depressive symptoms (Poyurovsky et al. 2004). Controlled trials are needed to establish the clinical utility, safety and tolerability of both ERP-treatment as well as SRIs in patients with psychosis and OCD (Poyurovsky et al. 2008).

The current study has some limitations. Firstly, nearly half of the patients with first-episode psychosis did not consent to participation, which challenges the estimates of prevalence. Furthermore, no inter-rater reliability tests on the initial diagnostics were performed, and ten of the patients received the OCD-diagnose post hoc. Issues related to diagnostics may both influence the estimates of prevalence and have consequences for evaluation of the clinical course, and are thus to be carefully considered.

Conclusion

The findings suggest that comorbid OCD in FEP is associated with a less positive course in global functioning and symptom level one year after the first psychotic episode. There were however no differences on any of the subscales of the PANSS. The results indicate that it might be of importance to screen FEP-patients for OCD symptoms, although more knowledge about differential diagnostics and evidence-based treatment of OCD in patients with FEP is needed.

Authors' contributions

KH, BH, IJ, SS,GK and TKL contributed to the study design. KH, BH, IJ, and TKL contributed to data collection. KH, GK, SS and IJ conducted the statistical analysis. KH, BH, IJ, GK, SS, IJ and TKL interpreted the data and drafted the manuscript. All authors participated in critical revision of manuscript drafts and approved the final version.

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