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Directionality of change in obsessive compulsive disorder and depression over six years of prospective follow-up

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ABSTRACT

Major Depressive Disorder (MDD) is often comorbid with obsessive-compulsive disorder (OCD) yet little is known about the directionality of the association between OCD and depression symptoms. We aim to investigate the effect OCD symptoms has on depression symptoms and vice versa over an extended period of time. This is one of the first longitudinal studies to evaluate the relationship between OCD and depression in a large clinical sample. Participants (n = 324) were treatment-seeking adults with a primary diagnosis of OCD. OCD and depression symptoms were assessed annually over the six-year follow-up period. Random intercepts cross-lagged panel models (RI-CLPM) were conducted to compare unidirectional and bidirectional models over time. The best-fitting and most parsimonious model included paths with OCD symptoms predicting depression symptoms, but not vice versa. OCD symptom severity in a given year predicted next year depression severity. However, depression severity did not predict next-year OCD symptom severity in this sample. Our results suggest that depression severity may be secondary to OCD symptoms and treating OCD should be prioritized over treating depression.

1. Introduction

Obsessive-compulsive disorder (OCD) is characterized by (a) repetitive intrusive thoughts or images that cause distress (obsessions) and/or (b) mental or physical acts performed to neutralize or remove the distress (compulsions; American Psychiatric Association, 2013). Although OCD and unipolar major depressive disorder (MDD) present as distinct disorders, individuals with OCD often report co-occurring depressive symptoms. One of the most common comorbidities in patients with OCD is MDD (Pallanti et al., 2011; Pinto et al., 2006), with a lifetime prevalence of 40.7% (Ruscio et al., 2010). A substantive proportion of individuals experience recurrent chronic course of illness (60% chronic OCD, Angst et al., 2004; 67% recurrent MDD, Hardeveld et al., 2010; 20% chronic MDD, Rush, 2007) with intermittent remission and relapse (Eisen et al., 2013; Marcks et al., 2011). The presence of MDD in individuals with OCD has been associated with higher rates of OCD severity and chronicity, comorbidity with other anxiety disorders, and disability experience (Besiroglu et al., 2007; Millet et al., 2004; Tükel et al., 2006; Viswanath et al., 2012). Notably, those with OCD and comorbid depression face a 3 to 4 times higher risk of suicide and attempts than patients with OCD without comorbid depression (Torres et al., 2006; Viswanath et al., 2012).

Despite extant research highlighting the negative implications of comorbid MDD and OCD, the temporal relationship between OCD symptoms and depression symptoms remains unclear. Although some treatment studies suggest that depression resolves following OCD treatment (Anholt et al., 2011; Zandberg et al., 2015), other studies have found that a reduction in depression precedes improvements in OCD (Olatunji et al., 2013). In a randomized control trial of 121 patients with OCD, Anholt et al. (2011) found that across all five years of their study, reductions in depression symptoms were largely driven by reductions in OCD symptoms. Additionally, changes in depressive symptoms only explained a small percentage of changes in OCD symptoms. Similarly, Zandberg et al. (2015) found that reductions in co-morbid depressive symptoms during combined behavioral and pharmacological OCD treatment were largely driven by reductions in OCD symptoms. Indeed,

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reduced OCD severity accounted for 65% of the reduction in depression symptoms, while the reduction in depression symptoms only accounted for 20% of the reduction in OCD symptoms. In contrast, in a treatment study comparing behavioral and cognitive therapy in 62 patients with OCD, Olatunji et al. (2013) found that a reduction in depressed mood mediated improvements in OCD symptoms. This study suggests that reducing depression symptoms is crucial to obtain significant improvement in OCD symptoms. Recently, a study in a residential treatment setting of 137 adult patients with OCD, Simkin et al. (2022) found that OCD and depressive symptoms had a reciprocal and equal relationship over the course of 12–16 weeks of cognitive behavioral therapy. These results contrast previous treatment studies and suggest a bidirectional relationship between OCD and depression and advocate for depression as a specific treatment target during treatment for OCD.

In naturalistic longitudinal studies, the findings have been similarly inconsistent. Bolhuis et al. (2014) investigated the longitudinal relationship between OCD and depression symptoms in an adolescent twin sample of 2651 participants. Their results showed that OCD symptoms predicted future depression symptoms to the same extent that depression symptoms predicted future OCD symptoms which suggests a bidirectional relationship between OCD and depression symptoms. In a large naturalistic follow up study, Rickelt et al. (2016) reported a causal relationship between the severity of depressive symptoms and the severity of OCD symptoms in a sample of 276 patients with OCD. Of note, this study could not draw conclusions about the effect of OCD symptoms on the course of depression symptoms. Instead, they highlighted the lack of support for the idea that depressive symptoms always improve with reduction in OCD symptoms and suggested that depression symptoms could be maintaining OCD symptoms. In an extension to Rickelt et al. (2016), Tibi et al. (2017) investigated the directionality of OCD and depression symptoms in 382 patients with OCD. They found that OCD symptom severity at baseline predicted depressive symptoms at two year follow up, but not vice versa, demonstrating a unidirectional relationship between OCD and depression. Interestingly, when extended to four year follow up, the relationship between OCD and depression was no longer significant. In summary, a clear directional relationship has yet to be established between OCD and depression symptoms.

Given the chronic and debilitating nature of these disorders, there is a need to elucidate the directionality of OCD and depression by closely monitoring their progression across a longer period of time with more frequent assessments. Because of the inconsistent findings in prior literature on the relationship between OCD and depression symptoms, we sought to replicate and extend current research in the field by using a large clinical sample of patients with OCD to examine directionality of change between OCD and depression over six years. We hypothesized that over time, reductions in OCD would be associated with reductions in depressive symptoms. If we understand the relationship between OCD and depression, we can better determine the most effective course of treatment for patients with OCD.

2. Material and methods

2.1. Participants

Participants (n = 324) were part of the Brown Longitudinal Obsessive-Compulsive Study, a large naturalistic prospective study of OCD course. Detailed methods and primary outcomes of this study have been published (Pinto et al., 2006). Inclusion criteria were age 19 or older, a primary Diagnostic and Statistical Manual for Mental Disorders 4th Edition (*DSM-IV*; American Psychiatric Association, 2013) diagnosis of OCD (defined as the disorder participants considered their biggest problem overall across their lifetime), and having sought treatment for OCD within five years prior to the study. The only exclusion criterion was evidence of an organic mental disorder or other condition that would prevent participants from providing informed consent.

2.2. Assessments

Intake diagnoses were established at baseline using the Structured Clinical Interview for *DSM-IV* Axis I Disorders-Patient Edition (SCID-IV; First et al., 2002) Demographic and clinical information was conducted using a semi-structured rater administered questionnaire from the Butler Hospital OCD Database (Rasmussen et al., 1994). Depression symptoms were measured using the well-validated, rater-administered 25-item Modified Hamilton Rating Scale for Depression (MHRSD; Miller et al., 1985). The MHRSD has specific probes and anchors and has been shown to have good validity in comparison to the original HRSD and the Beck Depression Inventory (Miller et al., 1985). Higher scores indicate greater depression severity. Cronbach's alpha scores for MHRSD ranged from 0.69 to 0.89 throughout the study. OCD severity was measured using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; Goodman et al., 1989), a 10-item rater-administered interview with good reliability and validity (Goodman et al., 1989). The scale contains five items that assess the severity of compulsions and five that assess the severity of obsessions in the past week. Total scores range from 0 to 40 with higher scores indicating greater symptom severity. Cronbach's alpha scores for Y-BOCS ranged from 0.93 to 0.96 throughout the study. Prior to the Y-BOCS, interviewers administered the Y-BOCS Symptom Checklist (Y-BOCS-SC) to gather information on specific current symptoms. The Y-BOCS-SC comprises 15 separate categories of obsessions and compulsions.

2.3. Procedure

Participants were recruited between July 2001 and February 2006 from multiple psychiatric treatment settings in Rhode Island and Massachusetts including a hospital-based OCD specialty clinic, a private psychiatric hospital inpatient unit, community mental health centers, general outpatient psychiatric practices, and private psychotherapy practices. All participants signed statements of informed consent prior to enrollment. Participants completed a series of baseline interviews and follow-up interviews annually thereafter for up to 12 years. All interviewers had at least a bachelor's degree and completed a series of didactic, observational, and participatory training activities culminating in conducting assessments with feedback from expert interviewers and audiotaping for interrater reliability calculations. All new interviewers were required to achieve excellent inter-rater reliability with trainers and senior raters (intraclass correlation coefficient>0.85) prior to the independent administration of SCID, Y-BOCS and MHRSD. Fidelity to training was monitored throughout the study via weekly meetings to review ratings and periodic, random calculation of inter-rater reliability statistics. The Butler Hospital and Brown University Institutional Review Boards approved the study.

2.4. Data analysis

Data analysis was performed using R version 4.0.5 (R Core Team, 2021). Random intercepts cross-lagged panel models (RI-CLPM; Hamaker et al., 2015) were conducted to compare the association between OCD (Y-BOCS total score) and depression (MHRSD total score) symptoms. This approach was chosen to explore the reciprocal and longitudinal relations between OCD and depression symptom severity while controlling for contemporaneous associations between the severity scores. The RI-CLPM improves upon traditional cross-lagged panel models by separating the variance of observed variables into two parts: (1) trait-like, time invariant or "between-person level" variance and (2) state-like, time-variant or "within-person level" variance (Hamaker et al., 2015; Keijsers, 2016; Lucas, 2022; Mulder and Hamaker, 2021). Because of increasingly missing data beyond 72 months (31.1% of data available at 72 months versus 28.1% of data available at 84 months and 19.1% available at 96 months) only observations until 72 months were included.

Our analyses involved four iterations of model-testing to determine directionality. To measure the within-person level variance, the autoregressive model (Model 1) only accounted for the change over time within each measure. Specifically, MHRSD at baseline was entered as a predictor of MHRSD at month 12, and MHRSD at month 12 was entered as a predictor of MHRSD at month 24 with that pattern repeating for each time point. The model fit was improved by adding predictive paths from the baseline observation of each variable to each subsequent observation of the variable. Similarly, Model 1 included the same Y-BOCS paths, with baseline Y-BOCS entered as a predictor of Y-BOCS at month 12 with that pattern repeating for each time point. We also correlated the baseline MHRSD and Y-BOCS scores, as well as the errors of each subsequent observation across the MHRSD and Y-BOCS. Model 2 included all paths from Model 1 plus paths from each MHRSD observation to the subsequent Y-BOCS observation (i.e. MHRSD at month 12 to Y-BOCS at month 24). Model 3 included all paths from Model 1 plus paths from each Y-BOCS observation to the subsequent MHRSD observation (i.e. Y-BOCS at month 12 to MHRSD at month 24). The full saturated model (Model 4) included all of the paths specified in the first 3 models. Using a RI-CLPM design allowed us to examine the cross-lagged paths between Y-BOCS scores and MHRSD scores, while accounting for between-person level variance and within-person level variance that can influence the stability of variables over time.

Comparison between Models 1 and 2 allows for a determination of improvement in autoregressive model fit after accounting for prediction of OCD severity from depression severity. Comparison between Models 1 and 3 allows for a determination of improvement in autoregressive model fit after adding paths predicting depression severity from OCD severity. Comparison between Models 2 and Model 4 allows for a determination of the importance of paths that are excluded from Model 2 to determine the relative importance of these paths compared to the full model. Comparison between Models 3 and 4 allows for a determination of the importance of paths that are excluded from Model 3 to determine the relative importance of these paths compared to the full model. To determine the optimal model (the model that balances parsimony with fit), and determine the directionality of change in OCD and depression symptoms over the course of six years, we compared each of the four models using the likelihood ratio test.

To determine acceptable fit of the models, the root mean square error of approximation (RMSEA), the comparative fit index (CFI), the Tucker-Lewis index (TLI), and the standardized root mean square residual (SRMR) were used. RMSEA values between 0.05 and 0.08 reflect reasonable fit and values < 0.05 suggest a good fit. CFI and TLI values $>$ 0.90 suggest acceptable fit and values > 0.95 are considered a good fit. SRMR values < 0.08 are considered an adequate fit (Hu and Bentler, 2009).

3. Results

The mean age of our participants was 40.1 years (SD = 12.8). The sample was primarily white (97.5%), female (54.6%), married (44.1%), college educated (56.5%), and employed (58.3%). Of the 324 participants, 65.7% ($n = 213$) had a lifetime diagnosis of MDD. Of those who met criteria for both lifetime OCD and MDD, 65.7% ($n = 140$) had an onset of OCD before their onset of MDD. Only 18.3% ($n = 39$) of participants with both diagnoses reported MDD onset earlier than OCD onset. On average, participants reported a moderate level of OCD symptoms (Y-BOCS, $M = 20.6$, $SD = 8.43$) and a mild level of depression symptoms (MHRSD, $M = 10.6$, $SD = 9.33$) at baseline. As shown in Table 1, all four Models demonstrated acceptable fit statistics (RMSEA = 0.048-0.056, CFI = 0.974-0.982, TLI = 0.963-0.973, SRMR = 0.053-0.092).

The autoregressive model (Model 1) was significantly improved with the addition of paths from Y-BOCS to MHRSD (Model 2; $\chi^2 = 110.20$). However, Model 1 did not significantly improve with the addition of paths from MHRSD to Y-BOCS (Model 3; $\chi^2 = 127.02$). The fully saturated model (Model 4) significantly improved model fit compared to Models 1 and 3 (Model 1, $\chi^{2\ \text{difference}} = 31.29$, $p < .001$; Model 3, $\chi^{2\ \text{difference}} = 26.16$, $p < .001$) but did not significantly improve model fit compared to Model 2 ($\chi^{2\ \text{difference}} = 9.35$, $p = .155$). Because Model 2 is not significantly different than Model 4, but is more parsimonious given that it excludes paths from MHRSD to Y-BOCS, it is determined to be the optimal final model. The best performing model (Model 2) is shown in Fig. 1.

In Model 2, Y-BOCS predicted MHRSD from 24 to 36 months, 36–48 months, and 60–72 months. In all three cases, higher OCD symptom severity in that year was associated with higher depression symptom severity in the following year. In Model 2, for Y-BOCS scores, there was stability in within-variable paths from one time point to the next. For MHRSD scores, there were four non-significant paths up until 48 months. Y-BOCS scores were more predictive of MHRSD than the inverse, which is reflected in the overall comparisons of relative model performance.

4. Discussion

The present study examined the relationship between OCD and depression symptoms in adults with OCD over the course of six years. Our hypothesis that over time, reductions in OCD would be associated with reductions in depressive symptoms was supported. We observed a unidirectional relationship between OCD and depression symptoms where more severe OCD symptoms predicted more severe depression symptoms in the following year. Additionally, more severe depression symptoms at a given observation did not predict more severe OCD symptoms at a subsequent time point. When observing the overall pattern across six years, Y-BOCS scores were more predictive of MHRSD scores than the other way around, and this is reflected in the overall comparisons of relative model performance. Though there is significant research establishing a relationship between OCD and depression (Marcks et al., 2011; Pallanti et al., 2011; Tükel et al., 2006; Viswanath et al., 2012), there is minimal consensus on the strength or direction of the relationship. The current study extends the findings of Tibi et al. (2017) by examining a longer time period and increasing the number of time points with repeated high-quality assessments. Our study strengthens their findings by producing comparable results while employing a more rigorous statistical approach that accounts for both the state and trait like variance of OCD versus depressive symptom change over a longer time period.

Our findings indicate that a reduction in OCD symptoms is responsible for the majority of subsequent decreases in depression symptoms.

Table 1
Model comparison and fit.

	χ2	df	Difference from Model 1	Difference from Model 4	AIC	BIC	CFI	TLI	RMSEA	SRMR
Model 1 (Autoregressive)	132.138	69	–	31.29	18,193.64	18,382.68	.975	0.967	.053	.089
Model 2 (Y-BOCS → MHRSD)	110.20	63	21.94	9.35	18,183.70	18,395.42	.981	0.973	.048	.066
Model 3 (MHRSD → Y-BOCS)	127.02	63	5.12	26.16	18,200.52	18,412.24	.974	0.963	.056	.092
Model 4 (Fully Saturated)	100.85	57	31.29	–	18,186.36	18,420.76	.982	0.972	.049	.053

Note. AIC, Akaike's Information Criterion, BIC, Bayesian Information Criterion, CFI, Comparative Fit Index, df, Degrees of Freedom, RMSEA, Root Mean Squared Error of Approximation, SRMR, Standardized Root Mean Square Residual, TLI, Tucker Lewis Index.

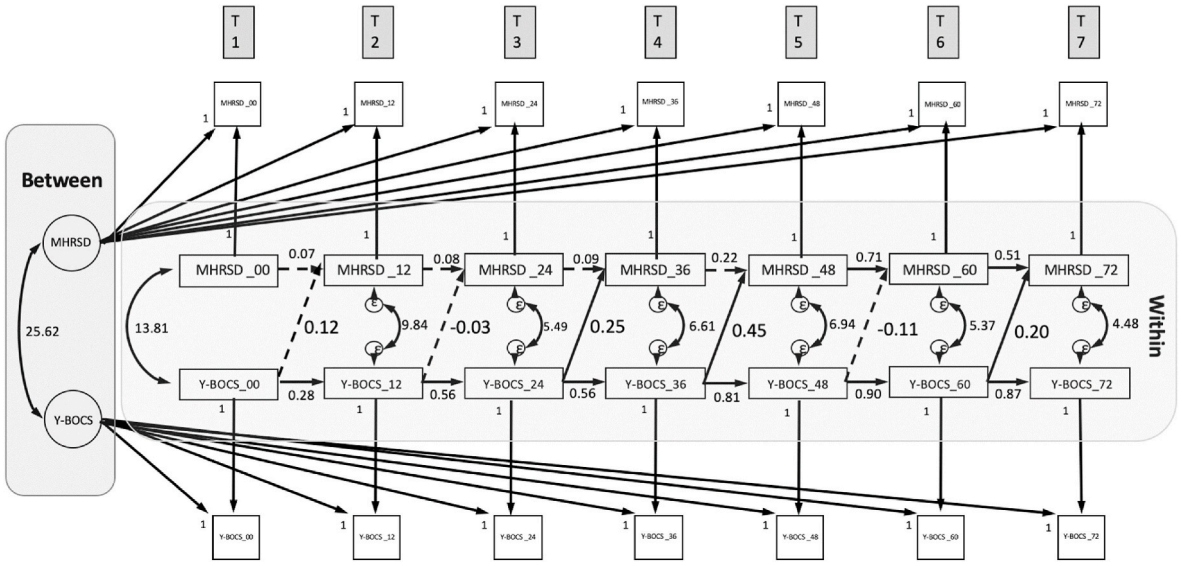

Fig. 1. Model of change over time in MHRSD scores and Y-BOCS scores (Model 2).

OCD may drive depression due to its adverse effects on cognitive and social functioning. Negative self-evaluation and hopelessness – core intrapersonal features of depression – stem from distressing obsession content and difficulty controlling compulsive behaviors (Storch et al., 2010, 2012; Yap et al., 2012). Although indirectly, OCD treatment may reduce symptoms of depression by improving social and occupational functioning and enhancing feelings of self-efficacy (Pittenger and Bloch, 2014). Additionally, consistent with the results of our sample, OCD onset typically occurs earlier than the onset of comorbid depression (Abramowitz, 2004; Rickelt et al., 2016; Zitterl et al., 2000). This suggests that when depression onset is secondary to OCD, depression symptoms are likely a functional consequence of distressing and debilitating OCD symptoms. In cases where OCD is primary, as OCD severity decreases during OCD treatment, depression symptoms are expected to diminish. However, in rarer instances where patients present with primary depression and secondary OCD, depression may be unrelated to the distress associated with OCD and require prioritization of depression treatment.

Some limitations for the present study should be noted. First, the participants in our sample are predominantly White and all were treatment seeking which limits the generalizability of our findings. Thus, future research should aim to replicate this study across a broader range of individuals with OCD. Additionally, because a primary diagnosis of OCD was required for inclusion in our study, our results may not generalize to individuals with primary MDD. Due to the length of the study, we had a substantial amount of missing data beginning at year 6 (31.1% of data available at 72 months). Because the study spanned many years, increasingly missing data is to be expected and was considered in the original design of the study. Even with missing data in the last year, the analyses are still based on a large sample size of participants. Finally, there are other variables of potential interest such as personality traits and OCD symptom subtypes that we were not able to include due to limited statistical power; these are meaningful areas for future research to explore. Future research might also explore factors associated with both OCD and depression symptoms such as distress tolerance, rumination, and experiential avoidance which was observed in Browning et al. (2022). Despite these limitations, our study is the first to utilize RI-CLPM with the specific aim of examining the relationship between OCD and depressive symptoms over time.

This study has a number of methodological strengths. Most notable is the use of a longitudinal design to examine changes in OCD and depression symptoms rather than a cross-sectional design. The longitudinal design allows for prospective associations and to determine the direction of the relationship across six years. Additionally, the study has a large sample size with recruitment spanning many settings and levels of care. Study participants had varying levels of OCD symptom severity and less stringent exclusion criteria than traditional randomized control trials, which allowed for a more representative understanding of how depression symptoms change in response to variation in OCD symptom severity. Additionally, depression was measured as a continuous variable and captured a wide range of symptom severity beyond a categorical measurement of OCD with or without comorbid depression. Due to the fluctuating course of depressive symptoms, our measurement aims to accurately capture how OCD and depression symptoms interact naturalistically in a clinical sample.

The findings of our current study have several important clinical implications. First, our results suggest OCD symptoms are the main driver of change in depression symptoms for individuals with OCD. Due to the high rate of comorbid MDD in individuals with OCD, it is important to understand the relationship between the two disorders. Because comorbid MDD in OCD has been associated with greater OCD severity and chronicity, greater comorbidity with other anxiety disorders, and higher rates of disability, there is a need for individuals with this presentation to seek treatment promptly and find treatment that will most effectively treat their symptoms. Our findings suggest that treating OCD first is the most appropriate treatment approach that will likely also reduce depression symptoms. This is largely consistent with prior treatment research (Anholt et al., 2011; Zandberg et al., 2015).

Because of the debilitating nature of OCD and the increased suicide risk due to depression (Torres et al., 2006; Viswanath et al., 2012), it is important to continue monitoring depression symptoms and suicidal ideation alongside OCD symptoms. Additionally, there is still a possibility that for patients with severe depression and low motivation, especially in activities of daily living, their ability to engage in OCD treatment may be impacted. In those instances, it might be appropriate to first treat their depressive symptoms to a degree that allows engagement in OCD treatment. There have been some studies, although limited in sample size, that demonstrate success in explicitly targeting depression as part of OCD treatment (Arco, 2015; Rector et al., 2009). However, we did not find support for the suggestion that depression symptoms may be the more important variable driving change in OCD symptoms and did not observe the relationship to be bidirectional. Changes in depressive symptoms explain only a minor percentage of change in OCD symptoms, whereas changes in OCD symptoms explain most change in depressive symptom. Thus, OCD symptoms should be prioritized as treatment targets.

In summary, this study establishes that OCD symptom severity is predictive of future depression symptoms across several years in a large clinical sample. Additionally, depression symptoms were not meaningfully predictive of future OCD symptom severity. The current findings support a unidirectional relationship between OCD and depression symptoms with change in OCD symptoms largely responsible for subsequent change in depression symptoms suggesting that it is essential to prioritize OCD treatment in individuals with comorbid MDD.

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Author statement

Gina M. Belli - Writing - Original draft, Conceptualization, Methodology, Formal analysis, Clara Law - Writing - Original draft, Maria Mancebo - Supervision, Writing - Review and Editing, Investigation, Jane Eisen - Supervision, Writing - Review and Editing, Investigation, Steven Rasmussen - Funding acquisition, Supervision, Writing - Review and Editing, Investigation, Christina L. Boisseau - Writing - Review and Editing, Conceptualization, Investigation.

Data statement

The data that support the findings of this study are available on request from the corresponding author.

Declaration of competing interest

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

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