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Chronic obsessive–compulsive disorder: prognostic factors

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Original Article

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Abstract

Background. The course of illness in obsessive–compulsive disorder (OCD) varies significantly between patients. Little is known about factors predicting a chronic course of illness. The aim of this study is to identify factors involved in inducing and in maintaining chronicity in OCD.

Methods. The present study is embedded within the Netherlands Obsessive Compulsive Disorder Association (NOCDA) study, an ongoing multicenter naturalistic cohort study designed to identify predictors of long-term course and outcome in OCD. For this study, 270 subjects with a current diagnosis of OCD were included. Chronicity status at 2-year follow-up was regressed on a selection of baseline predictors related to OCD, to comorbidity and to stress and support.

Results. Psychotrauma [odds ratio (OR) 1.98, confidence interval (CI) 1.22–3.22, $p = 0.006$], recent negative life events (OR 1.42, CI 1.01–2.01, $p = 0.043$), and presence of a partner (OR 0.28, CI 0.09–0.85, $p = 0.025$) influenced the risk of becoming chronic. Longer illness duration (OR 1.46, CI 1.08–1.96, $p = 0.013$) and higher illness severity (OR 1.09, CI 1.03–1.16, $p = 0.003$) increased the risk of remaining chronic.

Conclusions. External influences increase the risk of becoming chronic, whereas the factors involved in maintaining chronicity are illness-related. As the latter are potentially difficult to modify, treatment should be devoted to prevent chronicity from occurring in the first place. Therapeutic strategies aimed at alleviating stress and at boosting social support might aid in achieving this goal.

Introduction

The course of illness of obsessive–compulsive disorder (OCD) varies significantly between patients. Some patients with OCD achieve full remission of symptoms after a single illness episode. Other patients go through two or more illness episodes that are separated by symptom-free intervals, following a course that is characterized by remission and relapse. Finally, there are patients whose symptoms do not remit over a prolonged period of time. These patients chronically suffer from debilitating obsessions and compulsions. A chronic course of illness in OCD has been associated with poorer quality of life in patients and affected families and caregivers and with substantial direct and indirect costs for society (Hollander *et al.* 2016). Despite the clinical relevance of course variations in OCD, determinants of chronicity in OCD have been scarcely studied. The Netherlands Obsessive Compulsive Disorder Association (NOCDA) study, in which the present study is embedded, is an ongoing naturalistic cohort study that was specifically designed to identify clinical predictors of course variations in OCD.

The aims of the present study are: (a) to quantify course variations with respect to chronicity in OCD over a period of 2 years; (b) to assess the clinical impact of a chronic course of illness in patients with OCD; and (c) to identify factors involved in inducing and in maintaining a chronic course of illness in OCD. Identifying those patients at risk of becoming or remaining chronically ill is an important first step towards more personalized preventative and treatment strategies for OCD.

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Methods

Design and setting

The NOCDA study is a multicenter naturalistic cohort study on the course and outcome of OCD (Schuurmans *et al.* 2012). Participants of NOCDA were recruited from seven Dutch mental health care centers with a longstanding history of collaborative efforts in studying OCD and anxiety disorders. The study included persons aged 18 years and over with a lifetime diagnosis of OCD, as determined by the administration of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First *et al.* 1999). As the NOCDA study is a naturalistic study, exclusion criteria were limited to an inadequate understanding of the Dutch language for the purposes of the completion of interviews and self-report questionnaires. All participants that were included at baseline were contacted at 2-year follow-up, irrespectively of their treatment status. For the present study, data from baseline (collected between 2005 and 2009) and 2-year follow-up were used. The study was approved by the Medical Ethical Committee of the VU-University Medical Centre. The design and performance of the NOCDA study and the preparation of this manuscript followed the guidelines of the STROBE statement (von Elm *et al.* 2008).

Participants

After intake at one of the contributing mental health care centers, 687 patients with a lifetime diagnosis of OCD were asked to participate in the NOCDA study. Of these, 419 patients (60.9%) gave written informed consent and enrolled in the study. A comparison on basic demographic characteristics between patients that did ($n = 419$) and did not ($n = 268$) agree to participate yielded no significant differences. For the present analyses, we excluded 37 of the 419 subjects because they did not meet the criteria for a current (1-month) diagnosis of OCD at baseline. Of the remaining 382 participants at baseline, 278 were willing to participate in the 2-year follow-up assessment. Compared with the subjects that refused participation at follow-up ($n = 104$), the subjects that did participate at follow-up ($n = 278$) were somewhat older, and had a slightly higher educational status and employment status. No other significant differences were found, indicating that attrition was not critically influenced by baseline chronicity status or baseline severity of OCD. Finally, eight subjects were excluded because data with regard to course of illness at follow-up were lacking, leaving a final study sample for the present analyses of 270 subjects. During the follow-up period, participants received treatment as usual that was based on Dutch multidisciplinary guidelines.

Definition and assessment of chronicity and course trajectories

Previous studies on the course of illness in OCD have used different definitions of chronicity (Ravizza *et al.* 1997; Tükel *et al.* 2007; Visser *et al.* 2014). In this study, we adopted the relatively strict definition by Visser *et al.* (Visser *et al.* 2014), namely the continuous presence of at least moderately severe obsessive–compulsive (OC) symptoms during a period of at least 2 years. The presence of chronicity at baseline was retrospectively determined with a life-chart interview (LCI) (Lyketsos *et al.* 1994). The methodology of LCI has shown high validity and reliability (Warshaw *et al.* 1994). This instrument uses a calendar method (with help of age and calendar-linked personal memory cues) to determine the course of life history and OCD during the past 2 years. The respondents were provided with a clear definition of OCD. Duration could vary from (0) no OCD symptoms during the examined year, to (1) a small part of the year, (2) half of the year, (3) the majority of the year, or (4) the whole year. Severity of the OC symptoms was rated on a five-point scale [not to be confused with the Yale-Brown Obsessive Compulsive Severity Scale (Y-BOCS)], with (1) no OC symptoms, (2) minimally severe, (3) moderately severe, (4) severe, or (5) very severe OCD. The LCI thus yielded four variables: two ordinal variables that represent the duration of symptoms, one for the first year and one for the second (range 0–4), and two ordinal variables that represent the severity of symptoms, one for the first and one for the second year (range 1–5). The definition of chronic OCD was operationalized as the combination of a rating of 4 on the duration subscale and a rating of 3 or higher on the severity subscale, for two consecutive years. Assessment of chronicity at follow-up proceeded in a similar vein: the patients that met the criteria for OCD according to the SCID-I and met the criteria for chronicity on the LCI were labelled 'chronic', and all other patients were labelled 'non-chronic'. Based on their chronicity status at baseline and at follow-up, patients were assigned to one of four course trajectories (see Fig. 1):

(a) Patients with a chronic course of illness at baseline and a chronic course at follow-up were labelled 'C_B–C_{FU}';
(b) patients with a chronic course of illness at baseline and a non-chronic course at follow-up were labelled 'C_B–nC_{FU}';
(c) patients with a non-chronic course of illness at baseline and a chronic course at follow-up were labelled 'nC_B–C_{FU}';
(d) patients with a non-chronic course of illness at baseline and a non-chronic course at follow-up were labelled 'nC_B–nC_{FU}'.

Impact of chronicity: assessments at follow-up

Four parameters at follow-up served as indicators of the clinical impact of the different course trajectories. The severity of OC symptoms was measured with the Y-BOCS (range 0–40) (Goodman *et al.* 1989). The severity of comorbid depressive symptoms was measured with the self-rated 21-item Beck Depression Inventory (BDI; range 0–63) (Beck *et al.* 1961). The severity of comorbid anxiety symptoms was measured with the Beck Anxiety Inventory (BAI; range 0–63) (Beck *et al.* 1988). Quality of life was assessed with the EuroQol, yielding a utility score ranging from −0.59 to 1.00 (EuroQol Group, 1990).

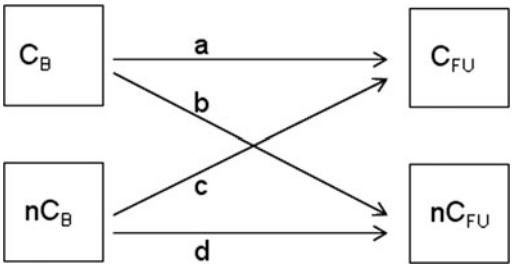

Fig. 1. Course trajectories based on chronicity status at baseline and at follow-up. C_B, chronic at baseline; nC_B, non-chronic at baseline; C_{FU}, chronic at 2-year follow-up; nC_{FU}, non-chronic at 2-year follow-up; a = C_B–C_{FU}; b = C_B–nC_{FU}; c = nC_B–C_{FU}; d = nC_B–nC_{FU}.

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Determinants of chronicity: assessments at baseline

In addition to *demographic characteristics* (sex, age, education, employment status, partner status), we assessed a number of predictors related to OCD, to comorbidity and to stress and support.

OCD-related

A diagnosis of OCD in first-degree relatives indicated a positive family history of OCD (yes/no) and was established with a family tree, based on information provided by the participants. The age at which participants first fulfilled DSM-IV criteria for OCD was established with the SCID-I and marked as the age at onset. Illness duration was defined as the difference between the age at baseline and the age at onset of OCD. Current severity of OC symptoms was assessed as described above. A self-report version of the Yale-Brown Obsessive-Compulsive Scale symptom checklist (Y-BOCS-SC) was used to establish the lifetime presence of four OCD symptom dimensions (yes/no): aggression/checking (20 items), symmetry/ordering (10 items), contamination/washing (nine items), and hoarding (two items) (Anholt *et al.* 2009). OCD-related cognitions were assessed using the Interpretation of Intrusions Inventory (Triple-III) (range 0–3100) (Obsessive Compulsive Cognitions Working Group, 2003).

Comorbidity

The current number of comorbid DSM-IV diagnoses (psychotic disorder, bipolar and unipolar depressive disorder, anxiety disorders, substance-related disorders, somatoform disorders, and eating disorders) was assessed with the SCID-I (Spitzer *et al.* 1992). Since tic disorders, attention-deficit hyperactivity disorder (ADHD) and autism are not diagnosed with the SCID-I, a proxy diagnosis was derived from the following three assessor-ratings: the Yale Global Tic Severity Scale (YGTSS) (Leckman *et al.* 1989), the ADHD rating scale-IV (Kooij *et al.* 2005) and the Autism-Spectrum Quotient (ASQ) (Baron-Cohen *et al.* 2001). The severity of comorbid depressive and anxiety symptoms was measured as described above. The severity of psychotic symptoms was measured using the psychosis subscale of the assessor-rated Comprehensive Psychopathological Rating Scale (CPRS; range 0–72) (Goekoop *et al.* 1991).

Stress and support

The degree of social support was measured with the Social Support Inventory (SSI) (Brown *et al.* 1987). The level of expressed emotion was measured with the Level of Expressed Emotion scale (LEE) (Cole & Kazarian, 1988). The number of different categories of childhood physical and/or sexual abuse was inventoried with the Structured Trauma Interview (STI) (Draijer & Langeland, 1999). The number of negative life events in the past year was assessed with a list of 12 negative life events, based on previous epidemiological research (De Graaf *et al.* 2002).

Treatment status

To be able to investigate the relation between treatment status and course variations, patients were asked at follow-up about their current use of medication and their contact with health care professionals in the period between baseline and follow-up.

Statistical analyses

To assess the clinical impact of the different course trajectories, we compared the means of the four outcome variables at follow-up for the corresponding subgroups, using one-way analysis of variance with *post hoc* group comparisons, correcting for multiple comparisons. The predictive value of baseline chronicity with regard to chronicity at follow-up was determined with a bivariate logistic regression analysis. We then assessed the predictive value of the baseline variables described above with regard to OCD chronicity at follow-up. To investigate factors involved in *inducing* chronicity, we considered the subgroup of patients with a non-chronic course at baseline and we regressed chronicity status at follow-up on the predictors using bivariate and multivariate logistic regression with a backward stepwise entry method. To investigate factors involved in *maintaining* chronicity, we performed similar analyses for the subgroup of patients with a chronic course at baseline. The threshold for inclusion of predictor variables in the multivariate analyses was set at 0.10. As chronicity could be the result of a lack of treatment, we investigated whether the patients that became or remained chronic had a lower chance of having contact with mental health professionals and/or using medication than the patients that remained or became non-chronic, using χ^2-tests.

Results

Baseline characteristics

The characteristics of the 270 participants included in this study are presented in Table 1. The sample included 144 females (53.3%), subjects had a mean age of 37.08 years (S.D. = 11.15) and a mean educational level of 13.04 years (S.D. = 3.12 years). About half of the participants (55.2%) was employed and 62.3% had a partner. The mean score on the Y-BOCS was 20.86 (S.D. = 7.06) reflecting a moderate mean severity of OCD. The mean age at onset of OCD was 17.81 years (S.D. = 9.35). The mean number of current comorbid Axis I mental disorders was 0.89 (S.D. = 1.09).

Course trajectories

Of the 270 subjects, 100 (37.0%) had a non-chronic course at baseline. Of these 100 subjects, 21 met the criteria for chronicity at follow-up and thus became chronic (nC_B–C_{FU}), whereas 79 subjects retained their non-chronic course (nC_B–nC_{FU}). Of the 170 subjects with a chronic course at baseline, 78 met the criteria for chronicity at follow-up and thus remained chronic (C_B–C_{FU}), whereas 92 subjects entered a non-chronic course (C_B–nC_{FU}). Baseline chronicity status was a significant predictor of chronicity status at follow-up (Wald-statistic $z = 4.00$, $p < 0.001$). The odds of having a chronic course at follow-up were 3.19 times higher for the subjects with a chronic course at baseline compared with the subjects with a non-chronic course at baseline [95% confidence interval (CI) 1.81–5.63, $p < 0.001$, McFadden pseudo-$R^2 = 0.050$]. These results show that baseline chronicity is an important predictor of chronicity at follow-up.

Impact of chronicity

Findings regarding the clinical impact of chronicity are presented in Table 2. As follows from this table, there is a clear gradient in all four outcome variables (Y-BOCS, BAI, BDI, EuroQol), with the most favorable outcome for the nC_B–nC_{FU} subgroup, followed by the C_B–nC_{FU} subgroup, the nC_B–C_{FU} subgroup and finally the C_B–C_{FU} subgroup.

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Table 1. Baseline characteristics of the total study sample ($n = 270$)

	Mean/percentage	S.D.
Demographics		
Age	37.08	(11.15)
Female sex, yes	53.3%	
Education, years	13.04	(3.12)
Employed, yes	55.2%	
Partner, yes	62.3%	
OCD-related		
Familial, yes	44.1%	
Age at onset	17.81	(9.35)
Illness duration, years	19.09	(12.26)
Y-BOCS, total	20.86	(7.06)
Symptom dimensions		
Aggression/checking, yes	92.4%	
Symmetry/ordering, yes	73.8%	
Contamination/washing, yes	63.9%	
Hoarding, yes	19.0%	
Triple-I, total (/1000)	1.46	(0.71)
Comorbidity		
Nr. of current comorbid Axis-1 disorders	0.89	(1.09)
Tic disorder, yes	24.9%	
Autism, yes	7.7%	
ADHD, yes	3.7%	
BAI, total	17.25	(11.17)
BDI, total	15.22	(9.42)
CPRS, psychosis subscale	0.84	(1.83)
Stress and support		
SSI	50.49	(7.74)
LEE	63.87	(18.12)
STI	1.43	(1.19)
Nr. of recent negative life events	1.69	(1.51)

Y-BOCS, Yale-Brown Obsessive Compulsive Scale; Triple-I, Interpretation of Intrusions Inventory; ADHD, attention-deficit/hyperactivity disorder; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CPRS, Comprehensive Psychiatric Rating Scale; SSI, Social Support Inventory; LEE, Level of Expressed Emotion; STI, Structured Trauma Interview.

Predictors of chronicity

Factors involved in inducing chronicity

Based on the results of the bivariate analyses on the subgroup of patients with a non-chronic course at baseline, the following variables were entered into the multivariate model (see Table 3): presence/absence of a partner, severity of comorbid anxiety, the level of expressed emotion, the number of negative life events in the past year and the number of different categories of adverse childhood experiences. A higher number of negative life events in the past year and a higher number of different categories of adverse childhood experiences were independently associated with a higher risk of meeting the criteria for chronicity at follow-up (and thus of entering a chronic course of illness) [life events: odds ratio (OR) 1.42, CI 1.01–2.01, $p = 0.043$; trauma: OR 1.98, CI 1.22–3.22, $p = 0.006$], whereas having a partner was associated with a lower risk of becoming chronic (OR 0.28, CI 0.09–0.85, $p = 0.025$). The predictive value of the total model, expressed as the McFadden pseudo-R^2, amounted to 0.147.

Factors involved in maintaining chronicity

For the subgroup of patients with a chronic course at baseline, the following variables were entered into the multivariate model (see Table 4): age at onset of OCD, illness duration, severity of OCD symptoms, the presence of symmetry/ordering symptoms, the presence of contamination/washing symptoms, the intensity of OCD-related cognitions, the presence of comorbid autism, the severity of comorbid depressive symptoms, and the number of different categories of adverse childhood experiences. A longer duration of illness and a higher severity of OCD symptoms were independently associated with a higher risk of meeting the criteria for chronicity at follow-up, and thus of remaining in a chronic course of illness (illness duration: OR 1.46, CI 1.08–1.96, $p = 0.013$; severity: OR 1.09, CI 1.03–1.16, $p = 0.003$). The predictive value of the total model, expressed as the McFadden pseudo-R^2, was 0.092.

Effect of treatment status

The patients that became chronic did not have a lower chance of having contact with mental health professionals and using medication than the patients that remained non-chronic [contact: 95.2% *v.* 86.1%, $\chi^2(1) = 1.32$, $p = 0.251$; medication: 50% *v.* 39.1%, $\chi^2(1) = 0.75$, $p = 0.385$]. The patients that remained chronic had a (significantly) higher, not a lower chance of having contact with mental health professionals and using medication than the patients that became non-chronic [contact: 96.2% *v.* 88.0%, $\chi^2(1) = 3.67$, $p = 0.055$; medication: 63.2% *v.* 45.8%, $\chi^2(1) = 4.58$, $p = 0.032$]. Therefore, it seems unlikely that lack of treatment played a role in inducing or maintaining chronicity.

Discussion

In this study, we set out to describe course variations in OCD with respect to chronicity, to assess the clinical impact of chronicity in OCD and to identify predictors of a chronic course of illness in OCD. Baseline chronicity appeared to be an important predictor of future chronicity. Subjects with a chronic course of illness had a significantly worse outcome with respect to severity of OC symptoms, severity of comorbid anxiety and depressive symptoms and quality of life compared with those with a non-chronic course. A higher number of negative life events in the past year and a higher number of different categories of adverse childhood experiences were independently associated with a higher risk of entering a chronic course of illness, whereas having a partner appeared to be protective of developing chronic symptoms. For those patients that already had a chronic course of illness, a longer duration of illness and a higher severity of OCD symptoms were independently associated with a higher risk of remaining in that chronic course.

Course trajectories

Our finding that baseline chronicity is an important predictor of future chronicity is consistent with the classical study on the long-term course of OCD by Skoog and Skoog (Skoog & Skoog, 1999), in which baseline chronicity emerged as one of the important

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Table 2. Clinical impact of course variations – mean scores of Y-BOCS, BAI, BDI, and EuroQol at follow-up

	Y-BOCS		BAI		BDI		EuroQol	
Group	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. nC_B–nC_{FU}	10.3	7.4	11.8	9.9	9.2	9.8	0.82	0.22
2. C_B–nC_{FU}	13.5	8.1	10.6	9.1	10.2	9.4	0.80	0.21
3. nC_B–C_{FU}	20.0	6.2	15.8	11.8	14.7	9.1	0.70	0.24
4. C_B–C_{FU}	22.9	6.7	20.0	12.9	16.4	10.8	0.64	0.26
Omnibus test	$F(3266) = 44.0$, $p < 0.001$		$F(3237) = 7.64$, $p < 0.001$		$F(3235) = 10.9$, $p < 0.001$		$F(3237) = 8.47$, $p < 0.001$	
Multiple-comparison test	1 < 2 < 3 < 4		1,2 < 4		1,2 < 4		1,2 > 4	

C_B, chronic at baseline; nC_B, non-chronic at baseline; C_{FU}, chronic at 2-year follow-up; nC_{FU}, non-chronic at 2-year follow-up; Y-BOCS, Yale-Brown Obsessive Compulsive Scale; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory.
'1 < 2' indicates that the mean of group 1 is significantly smaller than the mean of group 2 using a two-sided test with $\alpha = 0.05$ and using Bonferroni correction.

predictors of long-term outcome. Still, more than half of the patients in our study that met the criteria for chronicity at baseline managed to enter a non-chronic course in the two subsequent years, which is consistent with the results of a recent study by Garnaat *et al.* (2015). Other long-term studies on the natural course of OCD, however, show lower rates of improvement during this timeframe (Steketee *et al.* 1999; Marcks *et al.* 2011), but these differences can at least in part be explained by the fact that these studies used the stricter requirement of partial or full remission as the main outcome parameter. The relatively high rate of improvement after 2 years of chronic symptoms in our study does raise the question of whether our timeframe of 2 years [based on the study by Visser *et al.* (2014)] is adequate in delineating a chronic course of illness, or whether a longer timeframe would be more appropriate. In their 5-year follow-up study, Garnaat *et al.* (2015) showed that marked improvement was rare after 3 years of severe illness. Marcks *et al.* (2011), however, showed that the recovery rate for OCD keeps increasing (albeit slowly and modestly) over a 15-year period of time. The appropriate timeframe for delineating chronicity in OCD, therefore, remains open to debate.

Clinical impact of chronicity

A chronic course of illness in OCD appears to have a significant impact on clinical outcome and quality of life. These results, however, have to be interpreted with some caution. The presence of a chronic course of illness between baseline and follow-up was retrospectively assessed at follow-up, at the same time as the assessment of the outcome variables. Retrospective assessments open up the possibility of state-dependent recall bias. In the case of our study, for example, a current state of depression at follow-up could lead to an overestimation of severity of OC symptoms between baseline and follow-up. Notwithstanding these concerns, these findings, combined with the fact that chronicity itself is an important predictor of future chronicity, underline the importance of identifying factors that increase the risk of chronicity in OCD.

Factors involved in inducing and maintaining chronicity

The results presented in Tables 3 and 4 show that different factors are involved in inducing and in maintaining chronicity. The factors involved in inducing chronicity can be categorized as predisposing (number of categories of childhood trauma), precipitating (number of recent negative life events), and protective (presence of a partner). With every category of childhood trauma endorsed, the odds of entering a chronic course of illness almost doubled. Previous research has shown that rates of childhood trauma are higher in subjects with OCD than in normal controls (Grisham *et al.* 2011; Lafleur *et al.* 2011), that the presence of childhood trauma is associated with a higher severity of OC symptoms (Cromer *et al.* 2007), and that the association between trauma and OCD might be partly mediated by comorbid depressive and anxiety disorders and by personality factors (Mathews *et al.* 2008; Vidal-Ribas *et al.* 2015). As there was no bivariate association in our study between baseline severity of comorbid depressive symptoms and the risk of becoming chronic, we did not include this predictor in the multivariate analysis. Severity of comorbid anxiety symptoms, however, did predict chronicity when considered on its own and was therefore included in the multivariate analysis, but then failed to account for the association between trauma and OCD chronicity. As we did not include predictors related to personality in our study, we cannot rule out their potential role as mediating factor. Having a partner reduced the odds of developing chronic symptoms more than threefold. The protective role of having a partner against developing chronic OC symptoms is consistent with a number of previous studies (Steketee *et al.* 1999; Boschen *et al.* 2010; Marcks *et al.* 2011). As the association was corrected for the severity of OC symptoms, this association does not appear to be spurious but likely points to a genuine effect of social support provided by the partner in addressing symptoms and bringing about change. However, it is also possible that partners accommodate to the illness behavior of the patient, thereby leading to a perceived reduction of illness burden that translates into a lower (but not a genuinely lower) score on the chronicity scale (Steketee *et al.* 1999; Marcks *et al.* 2011). With each recent negative life event, the odds of entering a chronic course increased with 42%. It is possible that the general stress that usually accompanies these types of events deprives the patient of energy resources that are necessary to resist obsessions and compulsive behavior, thereby contributing to the downward spiral of negative reinforcement that characterizes OCD.

For those patients that already had a chronic course of illness, the nature of the relevant predictors for future chronicity shifted from external influences to illness-related factors. The odds of remaining chronic increased by 46% with every 10-year increase in illness duration and by 9% for every point increase on the

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Table 3. Factors associated with inducing chronicity – results of bivariate and multivariate regression analyses

	nC_B		nC_B–C_{FU}		nC_B–nC_{FU}		Bivariate model			Multivariate model		
	n = 100		*n* = 21		*n* = 79							
	Mean	S.D.	Mean	S.D.	Mean	S.D.	OR	95% CI	p	OR	95% CI	p
Demographics												
Age/10	3.58	(1.15)	3.64	(0.95)	3.56	(1.21)	1.06	(0.70–1.60)	0.791			
Female sex, yes	47.0%		47.6%		46.8%		1.03	(0.39–2.71)	0.949			
Education, years	13.15	(3.06)	12.52	(3.16)	13.32	(3.04)	0.92	(0.78–1.08)	0.292			
Employed, yes	64.0%		57.1%		65.8%		0.69	(0.26–1.85)	0.463			
Partner, yes	**64.3%**		**47.6%**		**68.8%**		**0.41**	**(0.15–1.10)**	**0.077**[a]	**0.28**	**(0.09–0.85)**	**0.025**
OCD-related												
Familial, yes	43.0%		57.1%		39.2%		2.06	(0.78–5.47)	0.145			
Age at onset/10	1.86	(0.94)	1.75	(0.98)	1.89	(0.93)	0.84	(0.46–1.56)	0.588			
Illness duration/10, years	1.71	(1.22)	1.89	(1.00)	1.67	(1.27)	1.16	(0.75–1.78)	0.503			
Y-BOCS, total	18.48	(7.02)	20.35	(7.15)	18.00	(6.95)	1.05	(0.98–1.13)	0.184			
Symptom dimensions												
Aggression/checking, yes	91.7%		100.0%		89.5%		1.00	(1.00–1.00)				
Symmetry/ordering, yes	64.6%		80.0%		60.5%		2.61	(0.79–8.56)	0.114			
Contamination/washing, yes	49.0%		55.0%		47.4%		1.36	(0.50–3.65)	0.544			
Hoarding, yes	14.6%		20.0%		13.2%		1.65	(0.46–5.94)	0.444			
Triple-I, total (/1000)	1.39	(0.64)	1.39	(0.64)	1.40	(0.65)	0.97	(0.46–2.08)	0.947			
Comorbidity												
Nr. of current comorbid Axis-1 disorders	0.66	(0.81)	0.76	(0.89)	0.63	(0.79)	1.21	(0.68–2.15)	0.514			
Tic disorder, yes	26.8%		20.0%		28.6%		0.62	(0.19–2.08)	0.443			
Autism, yes	6.2%		4.8%		6.6%		0.71	(0.08–6.43)	0.761			
ADHD, yes	4.0%		9.5%		2.5%		4.05	(0.54–30.6)	0.175			
BAI, total	**16.54**	**(10.24)**	**21.14**	**(13.98)**	**15.26**	**(8.62)**	**1.05**	**(1.01–1.10)**	**0.025**[a]			
BDI, total	12.84	(7.53)	15.00	(8.36)	12.24	(7.23)	1.05	(0.98–1.12)	0.141			
CPRS, psychosis subscale	0.71	(1.68)	0.76	(1.73)	0.70	(1.68)	1.02	(0.77–1.35)	0.873			
Stress and support												
SSI	50.84	(7.49)	49.05	(7.98)	51.33	(7.33)	0.96	(0.91–1.02)	0.222			
LEE	**64.30**	**(18.42)**	**70.62**	**(21.00)**	**62.55**	**(17.39)**	**1.02**	**(1.00–1.05)**	**0.081**[a]			
STI	**1.32**	**(1.09)**	**1.86**	**(1.20)**	**1.18**	**(1.02)**	**1.75**	**(1.11–2.75)**	**0.015**[a]	**1.98**	**(1.22–3.22)**	**0.006**
Nr. of recent negative life events	**1.71**	**(1.45)**	**2.29**	**(1.90)**	**1.56**	**(1.28)**	**1.37**	**(1.00–1.89)**	**0.051**[a]	**1.42**	**(1.01–2.01)**	**0.043**
Fit multivariate model										*Pseudo-*R^2 = 0.147		

C_B, chronic at baseline; nC_B, non-chronic at baseline; C_{FU}, chronic at 2-year follow-up; nC_{FU}, non-chronic at 2-year follow-up; Y-BOCS, Yale-Brown Obsessive Compulsive Scale; Triple-I, Interpretation of Intrusions Inventory; ADHD, attention-deficit/hyperactivity disorder; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CPRS, Comprehensive Psychiatric Rating Scale; SSI, Social Support Inventory; LEE, Level of Expressed Emotion; STI, Structured Trauma Interview. Bold indicates a significance of $p < 0.1$.
[a]Variable was considered to construct a predictive (multivariate) model.

Table 4. Factors associated with maintaining chronicity – results of bivariate and multivariate regression analyses

	C_B		C_B–C_{FU}		C_B–nC_{FU}		Bivariate model			Multivariate model		
	n = 170		*n* = 78		*n* = 92							
	Mean	S.D.	Mean	S.D.	Mean	S.D.	OR	95% CI	*p*	OR	95% CI	*p*
Demographics												
Age/10	3.78	(1.09)	3.89	(1.15)	3.70	(1.03)	1.17	(0.89–1.55)	0.261			
Female sex, yes	57.1%		52.6%		60.9%		0.71	(0.39–1.31)	0.276			
Education, years	12.97	(3.17)	12.85	(2.98)	13.08	(3.33)	0.98	(0.89–1.08)	0.636			
Employed, yes	50.0%		47.4%		52.2%		0.83	(0.45–1.51)	0.538			
Partner, yes	61.1%		56.6%		64.8%		0.71	(0.38–1.32)	0.277			
OCD-related												
Familial, yes	44.7%		42.3%		46.7%		0.84	(0.46–1.53)	0.563			
Age at onset/10	**1.73**	**(0.93)**	**1.58**	**(0.86)**	**1.87**	**(0.98)**	**0.71**	**(0.49–1.01)**	**0.060**[a]			
Illness duration/10, years	**2.02**	**(1.22)**	**2.30**	**(1.25)**	**1.78**	**(1.15)**	**1.45**	**(1.10–1.90)**	**0.008**[a]	**1.46**	**(1.08–1.96)**	**0.013**
Y-BOCS, total	**22.24**	**(6.73)**	**23.60**	**(6.36)**	**21.07**	**(6.85)**	**1.06**	**(1.01–1.11)**	**0.016**[a]	**1.09**	**(1.03–1.16)**	**0.003**
Symptom dimensions												
Aggression/checking, yes	92.8%		96.1%		90.1%		2.67	(0.70–10.2)	0.152			
Symmetry/ordering, yes	**79.0%**		**86.8%**		**72.5%**		**2.50**	**(1.11–5.61)**	**0.026**[a]			
Contamination/washing, yes	**72.5%**		**82.9%**		**63.7%**		**2.76**	**(1.32–5.75)**	**0.007**[a]			
Hoarding, yes	21.6%		26.3%		17.6%		1.67	(0.80–3.52)	0.174			
Triple-I, total (/1000)	**1.50**	**(0.74)**	**1.67**	**(0.73)**	**1.37**	**(0.72)**	**1.74**	**(1.11–2.74)**	**0.016**[a]			
Comorbidity												
Nr. of current comorbid Axis-1 disorders	1.03	(1.21)	1.19	(1.41)	0.89	(1.00)	1.23	(0.95–1.60)	0.109			
Tic disorder, yes	23.8%		28.2%		20.0%		1.57	(0.77–3.21)	0.215			
Autism, yes	**8.5%**		**13.7%**		**4.4%**		**3.45**	**(1.04–11.5)**	**0.044**[a]			
ADHD, yes	3.6%		3.9%		3.3%		1.22	(0.24–6.22)	0.812			
BAI, total	17.67	(11.70)	19.16	(11.90)	16.47	(11.45)	1.02	(0.99–1.05)	0.144			
BDI, total	**16.65**	**(10.14)**	**18.14**	**(10.40)**	**15.45**	**(9.81)**	**1.03**	**(1.00–1.06)**	**0.096**[a]			
CPRS, psychosis subscale	0.92	(1.91)	1.10	(1.99)	0.76	(1.83)	1.10	(0.93–1.29)	0.251			
Stress and support												
SSI	50.28	(7.90)	50.23	(7.53)	50.32	(8.25)	1.00	(0.96–1.04)	0.943			
LEE	63.61	(18.00)	65.46	(18.59)	62.08	(17.45)	1.01	(0.99–1.03)	0.233			
STI	**1.50**	**(1.25)**	**1.71**	**(1.39)**	**1.31**	**(1.09)**	**1.29**	**(1.00–1.66)**	**0.046**[a]			
Nr. of recent negative life events	1.68	(1.55)	1.78	(1.74)	1.59	(1.37)	1.09	(0.89–1.32)	0.413			
Fit multivariate model										*Pseudo-*R^2 = 0.092		

C_B, chronic at baseline; nC_B, non-chronic at baseline; C_{FU}, chronic at 2-year follow-up; nC_{FU}, non-chronic at 2-year follow-up; Y-BOCS, Yale-Brown Obsessive Compulsive Scale; Triple-I, Interpretation of Intrusions Inventory; ADHD, attention-deficit/hyperactivity disorder; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CPRS, Comprehensive Psychiatric Rating Scale; SSI, Social Support Inventory; LEE, Level of Expressed Emotion; STI, Structured Trauma Interview.
[a]Variable was considered to construct a predictive (multivariate) model.

Y-BOCS. A substantial amount of studies have identified both illness duration (Ravizza *et al.* 1997; Catapano *et al.* 2006; Dell'Osso *et al.* 2013; Eisen *et al.* 2013; Mancebo *et al.* 2014) and baseline severity of OC symptoms (Catapano *et al.* 2006; Kempe *et al.* 2007; Tükel *et al.* 2007; Eisen *et al.* 2010, 2013) as important predictors of long-term outcome in OCD. The predictive value of illness duration in maintaining chronicity stresses the importance of early detection and treatment of OCD. The fact that baseline symptom severity (as assessed with the Y-BOCS) was associated with the chance of remaining chronic can partly be explained by the fact that our definition of chronicity also included a measure of symptom severity (severity subscale of the LCI). Still, the association could also point to the importance of rigorous treatment of those patients that are most ill. From our limited analysis of the relation between treatment status and course of illness, it follows that it is unlikely that chronicity in our sample was due to a lack of treatment. However, as NOCDA is a naturalistic cohort study, it is not designed to systematically investigate the impact of treatment on course of illness. Whether symptom severity and chronicity were related to treatment resistance could therefore not be assessed. The fact that the patients that remained chronic had a higher chance of having contact with professional mental health care and using medication than the patients that became non-chronic is probably a spurious finding due to a treatment bias effect, in which subjects with more severe and/or longstanding pathology tend to receive more treatment. It is an effect that is often observed in naturalistic cohort studies (Steketee *et al.* 1999; Eisen *et al.* 2010, 2013; Marcks *et al.* 2011). The fact that baseline chronicity in OCD predicts future chronicity, combined with the fact that factors involved in maintaining a chronic course of illness might be difficult to modify, points to the importance of preventing chronicity from occurring in the first place. Our results suggest that OCD patients with a traumatic history, patients without a partner, and patients that have recently experienced one or more negative life events have an increased risk of entering a chronic course of illness. Therapeutic strategies aimed at alleviating event-related stress and at boosting social support might aid in reducing the risk of chronicity for these patients.

Strengths and limitations

The main strengths of our study are the relatively large size of the cohort, its extensive clinical phenotyping and its representativeness, which follows from the fact that the demographic and clinical characteristics of our sample closely resemble those of OCD study samples from other countries (LaSalle *et al.* 2004; Pinto *et al.* 2006; Samuels *et al.* 2006). Several limitations of the study have to be addressed. The fact that all participants were treatment-seeking limits the generalizability of our findings, as patients with poor or absent insight who do not consider themselves to be ill are probably under-represented in our sample. Secondly, our array of clinical predictors did not include a validated measure of insight. Lack of insight has been related to a poorer outcome in OCD (Catapano *et al.* 2010). Several variables, such as chronicity status, the age at onset of OCD, and the presence of childhood adverse events were assessed retrospectively, which opens up the possibility of recall bias. Differences in the predictors involved in inducing and in maintaining chronicity could also be influenced by a lack of statistical power, as the nC_B–C_{FU} subgroup was relatively small ($n = 21$) compared with the C_B–C_{FU} subgroup ($n = 78$).

Future directions

This study is based on the largest sample thus far when compared with previous studies on the course of illness in OCD and incorporated most of the predictors that have been investigated before. Despite these facts, the total predictive values of our models with respect to chronicity are relatively low. This raises the interesting question of what it is that we have missed in our models. The large array of clinical predictors that we included essentially represents the information that is gathered during routine diagnostic work-up in everyday practice. If the inclusion of all these variables only amounts to a limited predictive value, it seems important to broaden the scope of predictors (Bernardini *et al.* 2016). Promising avenues for future research might be the inclusion of neurobiological variables (Ball *et al.* 2014; Göttlich *et al.* 2015) or within-person, overtime symptom dynamics as assessed with experience sampling methodology (Höhn *et al.* 2013).

Conclusion

The present study shows that the presence of a chronic course of illness in OCD predicts future chronicity, and that chronicity is associated with a poor clinical outcome. As factors involved in maintaining chronicity (illness duration and severity) are potentially difficult to modify, attention and care should be devoted to prevent chronicity from occurring in the first place. Therapeutic strategies aimed at alleviating event-related stress and at boosting social support might aid in achieving this goal.

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Contributions

- Conception and design/analysis and interpretation of data: LvO, ME, HvM, AH, PvO, AvB;
- Drafting/revising article: LvO, ME, HvM, HV, KS, GH, NvdW, AH, PvO, AvB;
- Final approval: LvO, ME, HvM, HV, KS, GH, NvdW, AH, PvO, AvB.

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