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The Netherlands Obsessive Compulsive Disorder Association (NOCDA) study: design and rationale of a longitudinal naturalistic study of the course of OCD and clinical characteristics of the sample at baseline

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Abstract

In half of Obsessive Compulsive Disorder (OCD) patients the disorder runs a chronic course despite treatment. The factors determining this unfavourable outcome remain unknown.

The Netherlands Obsessive Compulsive Disorder Association (NOCDA) study is a multicentre naturalistic cohort study of the biological, psychological and social determinants of chronicity in a clinical sample. Recruitment of OCD patients took place in mental health organizations. Its design is a six-year longitudinal cohort study among a representative clinical sample of 419 OCD patients. All five measurements within this six-year period involved validated semi-structured interviews and self-report questionnaires which gathered

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information on the severity of OCD and its co-morbidity as well as information on general wellbeing, quality of life, daily activities, medical consumption and key psychological and social factors. The baseline measurements also include DNA and blood sampling and data on demographic and personality variables. The current paper presents the design and rationale of the study, as well as data on baseline sample characteristics. Demographic characteristics and co-morbidity ratings in the NOCDA sample closely resemble other OCD study samples. Lifetime co-morbid Axis I disorders are present in the majority of OCD patients, with high current and lifetime co-morbidity ratings for affective disorders (23.4% and 63.7%, respectively) and anxiety disorders other than OCD (36% current and 46.5% lifetime).

Introduction

Obsessive compulsive disorder (OCD) is a debilitating and prevalent anxiety disorder which was listed as the tenth most disabling medical disorder in the World Health Organization (WHO) burden of disease study (Murray *et al.*, 2004). It causes significant impairment in the sense that the disorder tends to interfere with the ability to work and the ability to form healthy relationships with others.

Although once considered rare, recent estimates indicate that OCD has a lifetime prevalence rate of approximately 1.5–2.5% worldwide (Kessler *et al.*, 2005; Weissman *et al.*, 1994). Despite the widespread dissemination of evidence-based treatments, OCD tends to run a chronic course. The Netherlands Obsessive Compulsive Disorder Association (NOCDA) study is an ongoing multicentre research effort investigating the naturalistic long-term course of OCD in patients referred to mental health care centres. The current paper presents the design and objectives of our study and provides data on demographic characteristics and co-morbidity ratings. The paper also addresses the representativeness of our sample and comparability to other clinical OCD samples. The study was designed to address three main objectives, discussed later.

Objectives

Objective 1. To describe the long-term prognosis of adult OCD in terms of its course, the development of co-morbidity, the development of chronicity and public health consequences.

Data on the long-term prognosis of OCD are scarce and studies to date suffer from a variety of methodological shortcomings (Pinto *et al.*, 2006). The available data suggest that OCD tends to run a chronic course or a course characterized by a waxing and waning of symptoms, but essentially no spontaneous recovery (Eisen *et al.*, 2010; Skoog and Skoog, 1999). However, most studies tend to focus on the presence or absence of OCD according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria at certain time intervals, rather than employing a dimensional model to examine the course of OCD symptoms over time. Although effective treatments are available and several options for treatment-refractory patients have been developed, long-term follow-up of adequately treated patients has shown that only 50% can be considered "cured" at five-year follow-up, in the sense that they no longer fulfil DSM criteria for OCD (Van Oppen *et al.*, 2005). Furthermore, recuperation from OCD in the strictest sense, where patients are truly asymptomatic, as defined by a score of seven or lower on the Yale–Brown Obsessive Compulsive Scale (Y-BOCS), is only achieved in 25% of treated patients (Fisher and Wells, 2005). The factors that are responsible for this unfavourable outcome are largely unknown (Kempe *et al.*, 2007). Because OCD is associated with a high use of health care services (Bijl and Ravelli 2000) and persistent impairment in social and work functioning (Hollander *et al.*, 2010; Steketee, 1997), the economic implications of OCD are presumed to be extensive. However, the exact nature of these ramifications remains unclear. The NOCDA study is designed to establish the course of both OCD episodes and symptoms, the presence and course of co-morbid disorders and symptoms, as well as the societal impact of OCD.

Objective 2. To examine biological and psychosocial determinants and their mutual interaction in predicting the course of OCD.

The primary aim of the NOCDA study is to investigate the biological, psychological and social factors associated with OCD outcomes. In addition to the paucity of data

on the long-term course of OCD in patients, predictive studies have predominantly aimed at determining the psychosocial factors involved in outcomes (Skoog and Skoog, 1999). In recent years, researchers studying the underlying pathways that determine the onset and course of psychiatric disorders have come to acknowledge that it is highly unlikely that any single environmental or psychosocial factor or subset of psychosocial factors is responsible (Merikangas *et al.*, 2002; Penninx *et al.*, 2008). A vulnerability-stress model incorporating both a genetic predisposition to develop OCD as well as environmental factors that trigger and sustain this disposition may be more appropriate (Grisham *et al.*, 2008).

Several studies have reported on heritability and genetic factors that increase the likelihood of onset of OCD. In a recent comprehensive review of adult and child twin studies, Van Grootheest and colleagues (Van Grootheest *et al.*, 2007a, 2007b) conclude that in adults, genetic factors are responsible for 27–47% of the variance in OCD symptoms, the remaining part of the variance (55–73%) being explained by unique environmental factors. Although it is important to take into account genetic factors, estimates of heritability vary widely between studies, as well as findings on the candidate genes that are likely to be involved in the onset of OCD. Furthermore, as studies on the psychosocial determinants tend to ignore genetic vulnerability issues, studies on the genetic influences tend to disregard the influence of environmental factors, while they may well explain some of the conflicting results in this area of research (Moffitt *et al.*, 2005). Therefore, studies that investigate the interaction of genetic factors with environmental influences such as life events are likely to be more fruitful in determining the dynamics of chronicity and change in OCD.

The conflicting results might also be explained by the heterogeneous nature of the disorder. For instance, since there is evidence that early-onset OCD has a stronger familial and hereditary component than late-onset OCD, early-onset OCD (commonly defined as an onset before the age of 18) might represent a more aetiologically and genetically homogeneous subset of patients (do Rosario-Campos *et al.*, 2005; Hanna *et al.*, 2005; Nestadt *et al.*, 2000; Pauls *et al.*, 1995).

As genetic factors and their interaction with environmental factors are likely to be important in the onset of OCD, the same dynamics are also likely to be important in determining the treatability and course of the disorder. Indeed, studies on genetic and environmental influences have shown that both are important in determining the stability of and change in OCD symptoms (Van Grootheest *et al.*, 2007a, 2007b). As the NOCDA study incorporates DNA sampling, data collection on symptom dimensions of OCD over time, as well as perinatal factors and environmental factors such as life events and early life trauma that are presumed to be of influence in OCD, our study may contribute to investigating the interaction between genetic and environmental factors in the treatability and course of OCD.

Objective 3. To study the reliability, validity and usefulness of a multidimensional approach to OCD in a six-year prospective longitudinal design.

The diagnosis of OCD according to DSM-IV criteria can be assessed in a reliable fashion using a structured psychiatric interview such as the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First *et al.*, 1999). A major limitation, however, is the fact that classification systems such as DSM-IV and the International Classification of Diseases, 10th Revision (ICD-10) consider OCD as a unitary diagnostic entity. Whilst the disorder is uniformly characterized by the presence of obsessions and/or compulsions, the content of these symptoms are heterogeneous and any two individuals with OCD may have highly different symptom patterns. Multiple factor and cluster-analytical studies conducted in a number of countries and involving over 4000 patients have consistently identified at least four symptom dimensions, but the exact content of these dimensions differs between studies (Mataix-Cols *et al.*, 2005; Leckman *et al.*, 2007; Katerberg *et al.*, 2010). Frequently identified dimensions include: contamination/washing, harm or somatic obsessions/checking, symmetry/order and hoarding. Some studies have also identified a fifth dimension consisting of sexual and religious obsessions (Pinto *et al.*, 2007), but further replication is needed in order to establish the validity of this concept (Mataix-Cols *et al.*, 2005; Leckman *et al.*, 2007).

These findings have recently led to the proposal of a multidimensional model of OCD, in which it is hypothesized to be a compendium of multiple, potentially overlapping syndromes, each with distinct aetiological factors (Mataix-Cols *et al.*, 2005). As a consequence, those biological and environmental factors that determine chronicity may be distinct between the different OCD symptom dimensions. Studies of treatability and the course of different symptom dimensions have yielded conflicting results (Keeley *et al.*, 2008). The ambiguity in results appears to be a consequence of an insufficient sample size across the various symptom dimensions. An important factor to take into account when evaluating the validity of the multidimensional approach is the fact that it is still unclear whether these dimensions remain stable over time

(Mataix-Cols *et al.*, 2002). In children, one recent epidemiological twin study has found that stability over time was only moderate in children between the ages of 7 and 12, with genetic factors contributing to this stability (Van Grootheest *et al.*, 2007b). Knowledge about the stability of the individual symptom dimensions over time in adults is particularly important when considering different aetiologies underlying the symptom dimensions. Preliminary research supports the validity and clinical usefulness of a multidimensional approach (Mataix-Cols *et al.*, 2002) but large-scale research is vital to an understanding of the differential characteristics and course of the symptom dimensions of OCD and their relevance to the clinical management of the disorder.

Methods

The NOCDA Consortium

The NOCDA consortium consists of researchers from both academic and non-academic research centres and mental health care settings with a longstanding history of collaborative efforts in studying the epidemiology, biological and psychosocial determinants and treatment of OCD and other anxiety disorders. To ensure the formation of an adequate sample, a nation-wide multicentre association was formed in November 2006, within which seven mental health care centres have joined forces to perform the baseline measurements (GGZ inGeest, Amsterdam; Marina de Wolf Centre for Anxiety Research, Ermelo; Centre for Anxiety Disorders "Overwaal", Lent; Dimence, GGZ Overijssel; LUMC Department of Psychiatry, Leiden University Medical Centre; the Mental Health Care Institute Noord- en Midden-Limburg, Venray; and the Academic Anxiety Centre, PsyQ Maastricht). Data is being archived in a safe, confidential and enduring system, and will be disclosed and made available to researchers. Specific publication protocols have been developed to regulate access to the database.

Study design

This study is a multicentre naturalistic cohort study on the course and outcome of OCD in patients referred to a mental health care centre for evaluation and treatment. We included 419 OCD patients within an integrated multicentre research infrastructure. Participants are contacted five times within a six-year period for clinical measurements: at baseline and after one, two, three and six years. The programme aims to follow a large representative sample of OCD subjects in different stages of the disease and with different degrees of illness severity. Comprehensive measurements will be performed at baseline and after two, four and six years at one of the participating mental health care centres by a trained and experienced research nurse or psychologist. At one-year follow-up, a short self-report questionnaire is sent to participants to be completed at home and sent back to the research centre.

Sampling and recruitment issues

The present study included persons aged 18 years and over with a lifetime diagnosis of OCD, as determined by the administration of the 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 patients diagnosed with OCD who were referred to one of the participating mental health care centres were asked permission to be contacted for research purposes during the intake procedure. All OCD patients who consented were contacted and invited to participate in the study, irrespective of the stage of the disorder, the OCD subtype, the presence of co-morbidity and the stage of chronicity.

Sample size, attrition and power

The central aim of our study is to identify variables (measured at baseline) that are prognostically important for chronicity in OCD. We powered the study to detect relative risks (RRs) of at least 1.50 because effects of this size are deemed to be clinically relevant. An effect of this size would occur, for example, when we find a predictor of chronicity associated with a risk of 0.60 of becoming chronic in the exposed group versus 0.40 in the non-exposed group. Power analyses with conventional levels of Alpha (0.05) and Beta (0.80) revealed that the sample size needed to detect such a predictor is $n = 107$ in each (exposed/non-exposed) group. We also need to take into account loss-to-follow-up and have estimated this quite liberally at 20% over each two-year follow-up period, based on previous experience with similar studies [Netherlands Study of Depression and Anxiety (NESDA); Penninx *et al.*, 2008]. This means that at six-year follow-up you would expect to have retained at least $0.80^3 = 51.2\%$ of the original sample. Therefore, we needed to start our study with a sample size of at least $(2 \times 107)/0.512 = 418$ at baseline.

Over a period of four years, 687 adult OCD patients underwent an intake assessment. One hundred and ninety-seven participants refused to participate (28.7%), 32 participants were not able to participate for mental or physical reasons (4.7%) and 39 participants could not be contacted (5.7%). Consequently, 419 participants (60.9%) were included and took part in the baseline measurements.

Measures used at baseline

Both the baseline measurements and the complete follow-up measurements (at two, four and six years after baseline) involve existing and validated semi-structured interviews and self-report questionnaires to gather information on the symptoms and severity of OCD and its co-morbidity as well as information on general wellbeing, quality of life, daily activities, social factors such as socio-economic status, social network, social support, family composition and other possible prognostic factors such as life events, medical consumption (the use and costs of medical care and medication) and alcohol and drug use. The five-hour baseline assessment also includes sampling of DNA and material for biobanking, data on demographic and biographical factors and personality variables. Table 1 provides an overview of all the instruments used for the baseline measurements.

Diagnosis of OCD and co-morbid mental disorders

The presence of OCD and co-morbid Axis I disorders was determined by the administration of a Dutch version of the SCID-I (First *et al.*, 1999) prior to recruitment to the study. The SCID-I has been shown to have high interrater reliability and diagnostic accuracy (Ventura *et al.*, 1998).

Assessment of course and severity of OCD and co-morbid symptomatology

The Y-BOCS severity scale (Goodman *et al.*, 1989a, 1989b) and the Y-BOCS symptoms questionnaire are both widely accepted as the golden standard for the assessment of OCD severity and course. Both measures have been shown to have excellent internal consistency, test-retest reliability and convergent validity with other OCD measures. The Y-BOCS severity scale is a clinician-rated measure of obsessive compulsive symptom severity, with documented reliability and validity (Goodman *et al.*, 1989a, 1989b; Anholt *et al.*, 2009). This measure has a total of 10 items with a range from 0 to 40. The Y-BOCS symptom checklist is an 80-item questionnaire with a repeatedly replicated four-factor structure providing information on overall OCD symptom severity as well as the presence of the following symptom dimensions (Leckman *et al.*, 2007; Summerfeldt *et al.*, 1999): an aggression/checking factor, a symmetry/ordering factor, a contamination/washing factor and a hoarding factor.

The Padua Inventory-Revised (PI-R) (Sanavio 1988; Van Oppen *et al.*, 1995) was used to assess both the overall severity of OCD symptoms as well as the presence and severity of specific OCD subtypes. This self-report questionnaire has been proven to have a robust factor structure across samples. The PI-R consists of 41 self-rated items, which are rated on a five-point scale from 0 (not at all) to 4 (very much). The total score ranges from 0 to 164. The reliability and validity of the PI-R are well established (Anholt *et al.*, 2009). Research on the internal structure revealed a five-factor solution (Van Oppen *et al.*, 1995). These factors are: (I) impulses, (II) washing, (III) checking, (IV) rumination and (V) precision. The reliability for the five subscales was found to be satisfactory to excellent.

The onset and fluctuation of OCD symptoms prior to baseline was established by administration of the Life Chart (Eaton *et al.*, 1997), an interview which uses reported life events in order to help the respondent to envision a timeline. The interviewer then uses this timeline to assess the course of OCD symptoms over the past five years.

Co-morbid depressive symptoms were measured with the Beck Depression Inventory and the Hamilton and Montgomery–Åsberg depression rating scale (Montgomery and Asberg, 1979). Anxiety and panic symptoms were measured with the 21-item Beck Anxiety Index (Beck *et al.*, 1988). The presence and severity of co-morbid tic symptoms were measured with the Yale Global Tic Severity Scale (Leckman *et al.*, 1989). As recent interest in OCD spectrum disorders has indicated a possible relatedness with attention deficit hyperactivity disorder (ADHD) and autism (Anholt *et al.*, 2010), the 18-item ADHD-rating scale IV (DuPaul *et al.*, 1998) and 50-item Autism-Spectrum Quotient questionnaire (AQ) (Baron-Cohen *et al.*, 2001; Hoekstra *et al.*, 2008) were administered to establish the presence of ADHD and autism symptomatology.

OCD cognitions

The Interpretation of Intrusion Inventory (Triple I) (Steketee *et al.*, 2001) was administered to assess the specific appraisals of responsibility, over-importance of thought intrusions and control of intrusions. These cognitive aspects of intrusions are believed to be of importance with respect to the persistence of obsessions and compulsive behaviour. The Triple I consists of 31 statements that reflect appraisals or interpretations of intrusive thoughts, images or impulses; for example, "Having this thought means it might be true". These appraisals are scored according to the strength of belief, from 0 ("I did not believe in this idea at all") to 100 ("I was completely convinced this idea was true").

Public health consequences and health care use

In order to establish both the individual as well as the socioeconomic impact of OCD, information on health

Table 1. Overview of measurement instruments in the NOCDA study

Topic	Measurement instrument	Reference	Method
Course of psychopathology			
Axis I diagnosis	Structured Clinical Interview for mental Disorders	First *et al.*, 1999	Int
Severity: - OCD	Yale Brown Obsessive Compulsive Scale-severity	Goodman *et al.*, 1989a	Int
- Depression	Beck Depression Inventory	Beck *et al.*, 1961	SR
	Hamilton and Montgomery Åsberg depression rating scale	Montgomery and Asberg, 1979	Int
- Anxiety	Beck Anxiety index	Beck *et al.*, 1988	SR
- Tics	Yale Global Tic Severity Scale	Leckman *et al.*, 1989	Int
- ADHD	ADHD rating scale IV	DuPaul *et al.*, 1998	Int
Presence and severity of OCD	Padua Inventory-Revised	Sanavio, 1988	SR
subtypes/symptom dimensions	Yale-Brown Obsessive Compulsive Scale Symptom Checklist	Goodman *et al.*, 1989a	SR
History OCD	LIFE CHART	Eaton *et al.*, 1997	Int
Autism	Autism-spectrum Quotient questionnaire	Baron-Cohen *et al.*, 2001	SR
OCD cognitions	Interpretation of Intrusion Inventory	Steketee *et al.*, 2001	SR
Patients' perspective			
Health care use/need for care	Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness-health care	Hakkaart-van Roijen, 2002	Int
Public health consequences			
Disability	EuroQol	The EuroQol Group, 1990	SR
Work/loss of productivity/content	Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness	Hakaart-van Roijen, 2002	Int
Demographic information and personality characteristics			
Demographic and biographic info	Standard questions	n/a	SR
Personality characteristics	Five-Factor Personality Inventory	Hendriks *et al.*, 1999	SR
Psychosocial functioning			
Recent life events	Standard questions	n/a	Int
Childhood abuse	Structured Trauma Interview	Draijer and Langeland, 1999	Int
Expressed emotion	Level of Expressed Emotion	Cole and Kazarian, 1988	SR
Daily Hassles	Daily Hassles	Kanner *et al.*, 1981	SR
Attachment	Self-reported general attachment style	Griffin and Bartholomew, 1994	SR
Social support/activity	Social Support Inventory	Brown *et al.*, 1987	SR
Loneliness	Loneliness Scale	De Jong, Gierveld and Kamphuis, 1985	SR
Affiliation	The need for affiliation scale	Van Tilburg, 1988	SR
(Physiological) health indicators			
Presence of chronic illness	Standard questions	n/a	SR
Alcohol and drug use	Standard questions	n/a	SR
Smoking	Standard questions	n/a	SR
Body composition	Weight, height, waist + hip circumference	n/a	ME
Blood pressure	Systolic and diastolic BP Assessment	n/a	ME

(*Continues*)

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Table 1. (Continued)

Topic	Measurement instrument	Reference	Method
Genetic determinants			
DNA/lymphocytes	Full blood/buccal swabs	Boomsma *et al.*, 2008	Blood
Family history	Family tree inventory	Fyer and Weissman, 1999	Int
Estimation of patients' time for the specific baseline measurements		INTERVIEW	180 min.
		SELF-REPORT	120 min.

Note: SR = self-report; Int = interview; ME = medical examination; Blood = data collection via fasting blood sample; n/a, not available.

care use, daily functioning, work productivity and costs is indispensable. Therefore, measurements include validated instruments to establish disability (EuroQol Group 1990) and loss of productivity and health care use (Hakkaart-van Roijen, 2002).

Physiological health indicators

Anxiety and health have a reciprocal relationship. Anxiety and related avoidance behaviours can lead to an exacerbation of existing health problems (de Voogd *et al.*, 2010; Huffman *et al.*, 2008; Mehta *et al.*, 2007). In turn, somatic illness (such as diabetes and COPD) and realistic health concerns can contribute to the onset and aggravation of anxiety symptoms (Khuwaja *et al.*, 2010; Muller *et al.*, 2005). The presence of specific chronic somatic conditions was established by providing an inventory of 21 common chronic illnesses and asking the respondent if they ever suffered from any of these conditions. In addition, smoking, alcohol and drug use, and gambling were measured by means of a series of structured questions that were previously constructed and used in other clinical surveys, such as NESDA (Penninx *et al.*, 2008) and the Longitudinal Aging Study Amsterdam (Deeg *et al.*, 1993). Body composition was established by objective, standardized assessments of height, weight and hip and abdominal circumference. Systolic and diastolic blood pressure were measured in lying and standing position using an electronic omron phygmomanometer.

Assessment of demographic and personality characteristics

Sociodemographic characteristics were measured using a structured questionnaire involving questions regarding age, gender, ethnicity, living arrangements, religion, composition of family of origin and current household composition. Socioeconomic information was gathered on the level of education, occupation and income. As basic dimensions of temperament and personality have often been found to be related to the onset and course of anxiety in general and OCD in particular, personality characteristics according to the Big Five were established with the 100-item Five-Factor Personality Inventory (Hendriks *et al.*, 1999).

Psychosocial functioning

Trauma exposure, both during childhood and in adulthood, and certain life events such as pregnancy and parenthood have been linked to the course and onset of OCD. Two subscales of the Structured Trauma Interview (Draijer and Langeland, 1999) regarding physical and sexual abuse in childhood were administered to establish trauma exposure during childhood. The occurrence of trauma and life events in the year prior to baseline measurements was established by interviewer-administration of 23 standardized questions on life events. The Daily Hassles questionnaire was included to measure stress arising from daily circumstances such as work, arguments or financial problems (Kanner *et al.*, 1981). Other indicators of psychosocial functioning believed to be of interest to the course of anxiety and OCD are social support, expressed emotion, loneliness and attachment. Validated measures of these constructs were included in the baseline measurements using the Social Support Inventory (Brown *et al.*, 1987); Level of Expressed Emotion scale (Cole and Kazarian, 1988); Loneliness Scale (De Jong Gierveld and Kamphuis, 1985); the need for affiliation scale (Deeg *et al.*, 1993); Self-reported general attachment style questionnaire (Griffin and Bartholomew, 1994).

Genetic determinants

In $n = 382$ participants (91.2% of the total population) DNA was isolated, either from blood sampling or, in the case of refusal, through buccal swab sampling. DNA from buccal swabs was collected using four swabs taken at the outpatient clinics and in the home setting. The swabs were processed and stored using a salting out procedure (Miller *et al.*, 1988). The blood samples were collected from

subjects using standard phlebotomy procedures and using sterile vacutainer tubes. After taking 20 ml of blood, DNA was directly extracted, isolated using a chlorophorm/isopropanol extraction procedure (Meulenbelt *et al.*, 1995) and stored. Also, 6 ml ACD tubes were stored in liquid nitrogen as a source to establish EBV transformed cell lines. Finally, 10 ml of heparinized blood was collected to measure biochemical and immunological parameters at a later stage.

Procedures

Staff training and supervision

The NOCDA study is coordinated by the academic department at VU Medical Centre/GGZ inGeest and the EMGO + Institute in Amsterdam. The fieldwork coordinator at this site is responsible for the training and supervision of research assistants in all of the participating mental health care centres. Newly appointed research assistants receive a two-day course, and regular follow-up one-day training sessions are held to address questions and problems raised by the research assistants. The first two interviews are audiotaped and monitored by the fieldwork coordinator in order to address any misunderstandings or errors in performing the measurements. All subsequent interviews are audiotaped for future reference. The monitoring of these audiotapes is continuously performed randomly on about 10% of all taped interviews, as well as on the basis of questions raised by the research assistants and the fieldwork coordinator. Every mental health care centre has appointed one local research coordinator as the primary contact. The local research coordinator facilitates the logistics of measurements on site.

Data management and control

Data management is conducted by the Department of Psychiatry at VU University Medical Centre/GGZ inGeest and the EMGO + Institute in Amsterdam. The data manager provides electronic data collection programs, processes and prepares the data for research, monitors and updates administrative data from participants and provides back-up procedures.

Ethical issues

The Medical Ethical Committee VUmc gave their approval for the current study in October 2005 and all of the participating centres have acquired permission to cooperate in this study from their own local Medical Ethical Committees, some in 2006 and some in 2007. All participants received verbal and written information with regard to the objectives and procedure of the study, with specific attention drawn to their right to refuse or stop participating at any time during the study, as well as specific information on the investment required from the participant. Separate informed consent forms were provided to link respondent information in an anonymous fashion to external data banks (such as mortality or hospitalization databases). The confidentiality of data is ensured by keeping separate files linking personal information such as name and address to a unique research ID number, which can only be accessed by the principal investigator, data manager and fieldwork coordinator.

Timeline and follow-up assessments

Recruitment took place from September 2005 to November 2009. The one-year follow-up assessment consists of a series of self-report questionnaires containing repeated assessments of core self-report instruments in order to establish the course of OCD symptoms and other psychological symptoms as well as recent events and health care utilization. The two-year and four-year follow-up assessments are similarly as extensive as the baseline assessment, including a face-to-face interview in which virtually all baseline measures are repeated. At two-year follow-up some additional measures were included, such as measures of motivation and insight, schizotypal symptomatology and prenatal and perinatal complications. One-year, two-year and four-year assessments are presently taking place and the six-year assessment is being developed.

Results

Characteristics of the study sample

Of the total sample, 91.2% ($n = 382$) met full one-month DSM-IV-TR criteria for OCD at the time of recruitment to the study, while the remaining 8.8% had met full criteria for OCD in the past ($n = 37$). The female ratio of the total sample is 55.8% ($n = 234$). Age at recruitment varies from 18 to 79 years, the mean age is 36.6 years [standard deviation (SD) = 10.92). Of the sample, 95.7% were of Dutch nationality, 37.6% had a higher vocational or university degree (Master's) and 49.8% of the sample were living with a partner.

Characteristics of non-respondents versus respondents

We compared basic demographic characteristics between those who refused or were unable to participate ($n = 267$) in the study with those who participated ($n = 419$). No significant differences were found with regard to distribution of the sexes ($\chi^2 = 0.71$, df = 1, $p = 0.75$), age ($t = 0.96$, df = 684, $p = 0.34$) or number of years of education received

($t = -0.03$, df = 610, $p = 0.98$). A comparison based on clinical characteristics cannot be provided as these data were unavailable for those who refused.

Clinical characteristics

As can be seen from Table 2, the mean severity of OCD symptoms as established by the administration of the Y-BOCS severity scale (Goodman *et al.*, 1989a) fell in the moderate range (total score between 16–23). The vast majority of our sample suffered from moderate to severe OCD symptoms (reflected by a Y-BOCS total score between 16 and 31). The mean duration of illness (as established by the age at onset of the OCD item in the SCID-I; First *et al.*, 1999) at the time of baseline measurements was approximately 17.9 years, with a range from 0 to 64 years. Mean age at onset of minor symptoms (as established by administration of the Y-BOCS) was 15.7 years.

As can be seen from Table 3, both current and lifetime co-morbidity with affective disorders is high, at 23.4% and 63.7% respectively. The same holds true for anxiety disorders other than OCD (36% current co-morbidity and 46.5% lifetime). Other common co-morbid disorders are eating disorders (10.5% lifetime) and substance use disorders (including alcohol abuse and dependence; 12.6% lifetime).

Most participants reported multiple current and lifetime obsessions. The obsession subtypes most frequently present in our sample are aggressive obsessions (81.6% lifetime), contamination obsessions (59.3% lifetime), religious obsessions (53.7% lifetime) and somatic obsessions (52% lifetime). The compulsion subtypes most frequently present in our sample are checking compulsions (84.1% lifetime), cleaning compulsions (64.0% lifetime) and repeating compulsions (63.0% lifetime).

Table 2. Clinical characteristics of participants ($n = 419$)

Variable	Mean	SD	Range	Missing (*n*)
Age at recruitment	36.60	10.92	17–79	0
Age at onset OCD	18.44	9.63	4–59	42
Age at onset first minor symptoms	15.72	8.75	3–58	37
Y-BOCS severity	19.89	8.10	0–40	5
OCD severity categories	*n*	*Valid %*		
Subclinical (0–7)	33	8.0		
Mild (8–15)	90	21.7		
Moderate (16–23)	140	33.8		
Severe (24–31)	121	29.2		
Extreme (32–40)	30	7.2		

Table 3. Prevalence of lifetime and current co-morbid DSM-IV Axis I Disorders ($n = 419$)[1]

DSM-IV diagnosis	Lifetime		Current	
	n	%	*n*	%
OCD only	93	22.2	172	41.1
Any affective disorder	267	63.7	98	23.4
Any psychotic disorder	18	4.3	10	2.4
Any anxiety disorder	194	46.3	150	35.8
Any substance use disorder (incl. alcohol)	53	12.6	20	4.8
Any somatoform disorder	22	5.3	22	5.3
Any eating disorder	44	10.5	19	4.5

[1]There were no missing data for any of these variables.

Discussion

Strengths

The NOCDA study is one of the first two ongoing research efforts (Pinto *et al.*, 2006) with a sufficiently large sample size to adequately determine the influence of psychological and social determinants, and more specifically, the different symptom dimensions, on the long-term prognosis of OCD. Moreover, the NOCDA study is the first study on the long-term course of OCD to incorporate biological and genetic parameters in its design. The creation of a nation-wide network of mental health care centres devoted to the advancement of knowledge about the prognosis and treatment of OCD and the establishment of an expansive high-quality database will give rise to numerous studies into the nature and characteristics of OCD.

The present study has been developed in close collaboration with a large-scale naturalistic study on the course of depression and anxiety disorders other than OCD, the NESDA (Penninx *et al.*, 2008). As NESDA is aimed at identifying the determinants of the long-term outcome of depression and anxiety disorders (other than OCD), the methodological similarities between the two studies create a unique window of opportunity for the comparison of the characteristics, course and economic ramifications of OCD and those of other anxiety disorders and depression, as well as health controls.

Limitations

Although a sample of 419 OCD subjects for a longitudinal prospective study is a singular event in the research literature to date, one might wonder whether it is sufficiently large for the purposes of our investigation, especially considering the fact that the current state of knowledge does not permit us to limit ourselves to the testing of very

specific hypotheses regarding the prognosis of OCD. The central aim of our study is to identify variables (measured at baseline) that are prognostically important for chronicity in OCD. Although our study is powered to detect clinically relevant effects, other less prominent associations may be more difficult to discern. Therefore, we consider it of the utmost importance that our data be made accessible to other research groups involved in the study of OCD, in the hope that pooled data from different studies might ultimately provide us with more definitive answers.

Representativeness of our OCD sample

In any study on the natural course of a specific disorder, representativeness and comparability to other samples in other countries are key issues. A comparison between non-respondents and respondents on basic demographic characteristics yielded no significant differences between both groups. However, a comparison based on clinical characteristics could not be presented here, as the data were unavailable for non-respondents. In order to discuss the representativeness of our sample, we need to compare our baseline characteristics to those of other large surveys of OCD patients. We focused our study on the natural course of OCD in clinically referred patients (rather than OCD in the general population). Pinto and colleagues (Pinto *et al.*, 2006) are carefully working on a similar longitudinal study on the natural course of OCD in the United States in a large clinically referred OCD sample (The Brown Study, n = 293).

All demographic and clinical characteristics described in the present study sample, such as severity of OCD symptoms, co-morbidity patterns and duration of illness strongly resemble their sample. Distribution of Y-BOCS severity ratings are comparable to other large surveys of OCD samples and adequately reflect the entire spectrum of OCD severity in referred patients, ranging from subclinical to extreme, with most patients scoring in the moderate to severe range. Demographic characteristics (such as age, education, gender, percentage married, low rates of minorities) and co-morbidity ratings in the NOCDA sample also closely resemble other OCD study samples (Samuels *et al.*, 2006; LaSalle *et al.*, 2004; Franklin *et al.*, 2000; Eisen *et al.*, 2010; Foa *et al.*, 1995). Lifetime co-morbid Axis I disorders are present in the vast majority of OCD patients, with high co-morbidity ratings for affective disorders and anxiety disorders other than OCD.

However, when looking closely at specific co-morbidity patterns across studies, a few differences are apparent. We find lower rates of substance use disorder (including alcohol) than most other studies on similar OCD samples (Pinto *et al.*, 2006; LaSalle *et al.*, 2004; Eisen *et al.*, 2010). It is possible that due to a stringent division between anxiety clinics and alcohol and drug clinics in the Netherlands, OCD patients with co-morbid substance use disorders are in fact underrepresented in our sample.

The most frequently recorded specific obsession subtypes across different study samples appear to be aggressive and contamination obsessions, although differences are found in the exact distribution of subtypes between studies (Pinto *et al.*, 2006; Samuels *et al.*, 2006; Foa *et al.*, 1995; Rasmussen and Tsuang 1986). The most frequently recorded subtypes of compulsions were checking, cleaning and to a lesser extent repeating and ordering. Overall, we can conclude that our sample roughly mirrors other large OCD study samples from Europe and the United States.

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Declaration of interest statement

The authors have no competing interests.

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