GENERAL INTRODUCTION

Introduction

Obsessive Compulsive Disorder (OCD) often has a deleterious impact on quality of life of patients and their relatives. Treatment is available, however the effectiveness of it is moderate. This might be because knowledge of this disorder is still limited. The literature is inconsistent or incomplete on many factors that might be crucial for development of the best possible treatment of OCD.

This thesis focusses on some of these gaps in knowledge, that is on chronic OCD, on the relationship between adverse childhood experiences and OCD severity, on the impact of poor insight on the natural course of OCD and lastly on the effectiveness of the Inference Based Approach to treating patients with OCD with poor insight versus the effectiveness of Cognitive Behavioural Therapy.

The results of the Netherlands Obsessive Compulsive Disorder Association (NOCDA) study were used to explore the first 3 of these topics. The NOCDA study is an ongoing longitudinal study in which several psychological and social variables are measured repeatedly among 419 patients with OCD. To study the latter topic a multicentre randomized controlled trial in which 90 patients with OCD with poor insight participated was performed.

Before proceeding to these issues a general introduction will be given into OCD, its clinical picture and the classification of OCD.

Obsessive-Compulsive Disorder

Obsessions and compulsions are the essential symptoms of Obsessive Compulsive Disorder (OCD). Obsessions are repetitive thoughts, urges or images, with an unwanted and frightening or disgusting content. Compulsions are mental or behavioural acts which are performed over and over again, often ritually. In general, having an obsession means being insecure about something and performing a compulsion means trying to gain certainty by doing something ritually.

Although the source of doubt and response to it is often about certain themes like compulsive handwashing for fear of contamination, and checking electrical devices for fear of fire, there is no limit to the number of topics obsessions and compulsions can refer to. Some patients avoid speaking in the past tense about their husband in order to keep their love alive, walk funny walks to prevent killing ants, or sing a song about strawberries while filling their toddlers cub in order not to pour chlorine in it. Others are afraid to change into Hitler by hearing his name, get pregnant by hugging their dog, or develop paedophile tendencies by listening to Michael Jacksons ‘Billy Jean’. There are others obsessed by the endlessness of the universe, by the question whether they find their partner attractive, or by the fact that they accidently accepted 3 cents to much change in the supermarket 10 years ago. Still others telephone the undertaker again and again to ask whether their grandmother was not buried alive, avoid trimming fingernails without wearing safety glasses, or count to 4 while putting a bottle of coca cola in the refrigerator in order to prevent an explosion. Nevertheless, despite the diversity in expression, an essential commonality of OCD themes concerns being insecure and the need for certainty.

Clinical picture

Patients with OCD spend excessive amounts of time with being insecure and trying to gain certainty, sometimes up to more than 8 hours a day, at the expense of valuable personal-, social-, or occupational goals. Often relatives get involved, sometimes in a subtle way, for example by not mentioning specific topics, but often by reassuring, performing rituals and giving up their personal goals. Many patients feel guilty and ashamed and try to hide their symptoms because they do realize to some extent that their worries are excessive and unreasonable. And even if they do not, patients still might feel ashamed because of the horrific content of obsessions, or because ritualizing leads to embarrassing situations.

Spontaneous recovery hardly ever occurs, on the contrary, OCD typically waxes and wanes and regularly takes decades. Worrying and ritualizing at the expense of valuable personal goals for so many years, often goes hand in hand with depressive symptoms and a low quality of life. Indeed, health related quality of life was found to be lowest in OCD cases as compared to those with any other mental disorder or physical disorders. Notwithstanding the obvious suffering of patients with OCD, many of them postpone seeking treatment for many years.

Prevalence and age of onset of OCD

The lifetime morbid risk of OCD (i.e. the proportion of people who will eventually develop the disorder at some time in their life) found in a recent epidemiologic inquiry in the US was 2.7% and the 12 month prevalence was 1.2%. However, in a review on epidemiologic inquiries performed in several countries, lifetime prevalence rates of OCD (i.e. the proportion of people who ever had a diagnosis of OCD during their life) ranged from 0.7% to 2.5%. In a Dutch study the lifetime prevalence of OCD was 0.9%. These differences are mostly due to the use of different instruments and different...
inclusion criteria in epidemiological enquiries. No great differences have been found between countries\(^5\). OCD affects approximately as many men as women\(^7\).

OCD has a bimodal distribution of age of onset with a peak of incidence in childhood and another in mid adulthood. It is suggested that 20 years is the recommended cut-off age for the determination of early versus late age of onset in OCD\(^8\).

**Classification**

A classification of OCD (code 300.3) conform the currently most frequently used version of the Diagnostic and Statistic Manual of Mental Disorders\(^9\) requires presence of time consuming (at least 1 hour a day) obsessions or compulsions that cause marked distress, or interfere significantly with the person's normal routine, occupational (or academic) functioning, or usual social activities or relationships.

With respect to these specific criteria little has changed in the DSM-5\(^10\). However, a major change concerns the role of insight in OCD, which already changed markedly from DSM-III to DSM-IV. In the eighties of the past century, during DSM-III, in order to be diagnosed with OCD, patients had to be able to recognize their symptoms as nonsensical (criterion B). At that time insight was understood as intrinsic to the diagnosis. A decade later, when the fourth version of the DSM came out, this criterion was weakened but not abandoned; patients still had to recognize, at some point during the course of the disorder, that the obsessions or compulsions are excessive or unreasonable. In this fourth version the specifier ‘with poor insight’ was added. Now, after the launch of the DSM-5 the criterion regarding recognition of excessiveness and unreasonableness of the obsessions and compulsions is abandoned. The fourth-version specifier ‘with poor insight’ is in DSM-5 replaced by 3 specifiers:

I. ‘with good or fair insight’, which is applicable if the individual recognizes that obsessive-compulsive disorder beliefs are definitely or probably not true or that they may or may not be true

II. ‘with poor insight’, meaning that the individual thinks obsessive-compulsive disorder beliefs are probably true

III. ‘with absent insight/delusional beliefs’, which is applicable if the individual is completely convinced that obsessive-compulsive disorder beliefs are true

The DSM-5 Anxiety, Obsessive-Compulsive Spectrum, Post-Traumatic and Dissociative Disorders Work Group has recommended deleting the DSM-IV criterion B requiring recognition of the excessiveness or unreasonableness of obsessions or compulsions, because these terms have different meanings that could easily be misinterpreted by clinicians and researchers, and because studies have shown that some patients with OCD lack insight completely\(^11\).

The specifiers of DSM-5 describe insight rather unidimensional in terms of the extent to which patients recognize the incorrectness of their beliefs. However, as described more detailed in the literature on psychotic disorders, insight has been widely regarded as a multidimensional construct that comprises patients' awareness of having a mental illness, the need for treatment, and the ability to distance themselves from distortions and to relabel their symptoms\(^12\). In the case of impaired insight aberrant beliefs are thought to be sufficiently intense to override the normal processes of reality testing\(^13\).

It is important to understand the phenomenon insight in OCD because poor or absent insight is fairly common\(^14-23\) and the clinical condition of these patients is worse than that of patients with good insight. Poor insight appears to be associated with higher OCD symptom severity\(^14-24\), lower quality of life\(^27\), more chronicity\(^24,25\) and suicidal ideation\(^26\). Furthermore a worse response to psychotropic medication\(^15,17,27\) and cognitive behaviour therapy (CBT)\(^22,28-31\) was found for patients with OCD with poor insight than for their good insight counterparts, however the literature is not entirely consistent on these points. Furthermore, the prevalence rates of poor insight and the clinical profile of patients with OCD and poor insight has not been established firmly. Also, knowledge on the impact of insight on the natural course of OCD is marginal. The natural course of insight itself is understudied as well.

More knowledge about insight in OCD might help to comprehend the relevance of insight for OCD and its prognosis, and the possible necessity to specifically target insight in OCD treatment. In the NOCDA study insight was measured, whereby the
clinical profile of OCD with poor insight, and the impact of insight on the course of OCD can be studied. Insight in OCD is discussed in more detail in chapter 4.

**Course**

OCD typically takes many years. A mean duration of the disorder of 22 years was found in a study among 293 patients with OCD who were referred to healthcare\(^2\). Results of another study, examining the course of 113 referred patients with OCD, show that the probability of OCD remission (defined as: 8 consecutive weeks being symptom-free) is relatively low, namely 16% after 1 year, 25% after 5 years, 31% after 10 years and 42% after 15 years\(^3\). For those who remitted from OCD the probability of recurrence (defined as: 4 consecutive weeks meeting diagnostic criteria of OCD after remission) was 25% after 5 years\(^2\).

**Chronicity of OCD**

Based on findings like the above mentioned, it seems obvious to state that OCD generally runs a chronic course. However, researchers, so far, used dissimilar definitions of chronic OCD, which hampered understanding chronicity in OCD. Indeed, conflicting results were found, not only in terms of frequency of chronicity, which ranged from 24%\(^4\) up to 98%\(^5\), but also in terms of associated severity, illness burden and socio-demographic and clinical characteristics. Understanding of chronicity in OCD and factors underlying it, may improve classification and treatment of OCD. In the NOCDA study an instrument was used that measures the course of OCD, whereby the issue of chronicity in OCD could be examined. Chronicity of OCD is discussed in chapter 2.

**Co-morbidity**

Presence of co-morbid disorders is the rule rather than the exception in OCD. A recent Dutch study found, consistent with the existing literature, that 55% of the patients with OCD reports current comorbidity and as much as 78% reports comorbidity during life-time\(^6\). Most common are comorbid depressive and anxiety disorders, which in general follow rather than precede OCD. Especially when multiple comorbid disorders are present, higher OCD symptom severity, more chronicity of OCD and lower quality of life are found\(^7\).

This impact of comorbidity on clinical correlates of OCD is relevant in several ways, one of which is that putative predictors of (severity or chronicity) of OCD, might in fact be merely predictors of comorbid disorders.

**Adverse childhood experiences**

One domain of research in which the question remains unanswered whether established relationships with OCD hold for pure OCD as well as, or as much as for OCD with comorbid disorders, is the domain of adverse childhood experiences (ACEs). In the DSM-5, referring to one specific study\(^8\) childhood physical abuse and sexual abuse are mentioned as environmental factors associated with an increased risk for developing OCD. However, in this study, and other studies on this topic and on the relationship between ACEs and severity of OCD, the role of comorbidity was not taken into account. This topic needs examination because the presence or absence of a relationship between ACEs and severity or chronicity in (pure) OCD might have implications for the relevance of addressing ACEs in OCD treatment.

In the NOCDA study ACEs were assessed, as were co-morbid Axis-I disorders and severity and chronicity of OCD, whereby the relationship between these factors could be studied. This topic is discussed in chapter 3.

**Treatment**

Effective treatments for OCD include Cognitive Behaviour Therapies, like Exposure with Response Prevention (ERP) and Cognitive Therapy (CT)\(^9\), and Serotonine Reuptake Inhibitor (SRI) Pharmacotherapy\(^10\). A recent meta-analysis revealed that CBT is more effective than SRIs, and that the combination of CBT and an SRI is more effective than an SRI alone\(^11\). Only a part of the patients with OCD receives adequate CBT, because approximately 25% of the patients refuses CBT\(^12\) and 30% of the patients that do start CBT drops out prematurely\(^13\). Furthermore, of the patients that do complete treatment with CBT, approximately 40-50% does not reach at least 35% symptom reduction\(^14,15\). At five year follow up after treatment with both CBT and pharmacotherapy 46% of the patients still fulfils DSM-IV criteria for OCD\(^16\).

A notorious predictor of poor treatment outcome in OCD is poor insight\(^17\). At the beginning of this century a psychological treatment for OCD was developed that specifically targets insight: the Inference Based Approach (IBA). In a small study IBA appeared to be not more effective than CBT, however a post-hoc analysis in a subsample of patients with poor insight suggested that IBA was more effective\(^18\). Given the severe impact of OCD with poor insight on patients’ lives, there is an urgent need for effective treatments. Therefore a randomized controlled trial was set to identify the superiority of IBA compared to CBT. In chapter 5 this topic will be discussed in detail.
AIMS AND OUTLINE OF THIS THESIS

The aims of this thesis were, first, to determine the magnitude of chronicity in OCD and to examine whether chronic OCD is different from non-chronic OCD in terms of severity, illness burden and socio-demographic variables, vulnerability factors and clinical characteristics. Because the results of earlier studies on this topic are rather inconsistent an explorative approach was chosen, that is: no hypotheses were pre-specified. An observational cross-sectional design was used. Participants of the NOCDA study that fulfilled the DSM-IV criteria of OCD at baseline and of whom data on the course of OCD were available (N=379), were divided into a group of patients with chronic OCD and a group of patients with non-chronic OCD, using a definition of chronicity that closely resembles the definition of chronicity in depression, namely continuous presence of at least moderately severe OCD symptoms during at least two consecutive years. Their scores on a comprehensive set of clinical and demographic measures were compared using straightforward logistic regression analyses. Multivariate statistical techniques were used to examine which factors are independently associated with chronic OCD, that is: appeared to be related to chronic OCD after controlling for the effect of all other factors that were measured. (This study is presented in chapter 2).

The second aim of this thesis was to better understand the relationship between Adverse Childhood Experiences (ACEs) and severity and chronicity of OCD, taking into account the role of comorbidity. More specifically the following issues were examined: 1) Are specific categories of ACEs associated with severity of OCD symptoms? 2) Is there a dose-response relationship between ACEs and severity of OCD? 3) Are specific categories of ACEs associated with chronic OCD? 4) Is there a dose-response relationship between ACEs and chronic OCD? 5) Are ACEs related to comorbidity in patients with OCD? To study this, again because of conflicting earlier findings or because of the lack of empirical findings, an explorative approach was chosen, no hypotheses were pre-specified. ACEs, OCD symptom severity, chronicity and comorbidity were measured among the participants of the NOCDA study that fulfilled the DSM-IV criteria of OCD at time of enrolment (N=382). In this observational cross-sectional design regression analyses were performed to find answers to the postulated questions. (This study is described in chapter 3).

The third aim of this thesis was to better understand the role of insight in OCD. An observational cross-sectional design was used to i) establish the range of insight in a clinical sample of patients with OCD and ii) characterize the clinical profile of OCD with poor insight. An observational cohort design was used to iii) study the natural course of insight and its correlation with the natural course of OCD severity and iv) study the impact of poor insight on the natural two-year course of OCD. No hypotheses were pre-specified because of the inconsistency in existing data on the prevalence of poor insight and its correlates and the sparsity of data on the impact of insight on the natural course of OCD. Participants of the NOCDA study with OCD complaints at time of insight measurement (N=253), were divided into four groups, namely into participants with good-, fair-, poor- and absent insight. At the same measurement time clinical and demographic factors were assessed. The scores on these factors were compared among the insight groups. At follow-up (two years later), insight into OCD and severity of OCD were measured again. The correlation between changes in insight and changes in OCD was calculated. Finally, a linear mixed effects model was used to determine whether patients with poor insight at the first measurement had a different outcome at follow-up than patients who had good or fair insight at the first measurement, given that they had the same OCD severity at the first measurement. And whether this difference was independent of other factors known to predict the course of OCD (This study is described in chapter 4).

The final aim of this thesis was to compare the effectiveness of a relatively new psychotherapy that specifically targets insight in OCD, the Inference Based Approach (IBA), to the gold standard Cognitive Behaviour Therapy (CBT) in patients with OCD with poor insight. We hypothesized that IBA would be more effective than CBT. Therefore a parallel-group multisite randomized controlled trial was set to identify the superiority of 24 sessions of IBA compared to 24 sessions of CBT in a sample of patients with OCD with poor insight. Ninety adult patients with a primary diagnosis of OCD with poor insight that were referred for treatment in one of the three participating highly specialized anxiety disorder departments participated in the study. The primary outcome measure of the study was severity of OCD symptoms. Secondary outcome measures were insight into OCD, severity of depressive and anxiety symptoms and quality of life. All outcome measures were repeated at pre-test, mid-test (after 14 sessions of treatment), post-test (after 24 sessions of treatment) and follow-up (three months after post-test). (A full description of this study is given in chapter 5).

The results of the studies conducted are summarized, discussed and integrated with recent findings in chapter 6.
REFERENCES


