Towards improving treatment for childhood OCD: Analyzing mediating mechanisms & non-response

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Citation for published version (APA):

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Introduction
Introduction

A few years ago I explained the present study to a 13-years-old boy who came to our centre to be treated for an obsessive-compulsive disorder (OCD). I told him that we were conducting a study into the treatment of OCD. Not because we wanted to know whether this treatment is effective – we know that already – but because we wanted to know how treatment works and why it is effective. The boy listened quietly. Then he nodded thoughtfully and concluded ‘So, actually, treatment is just arbitrary.’ And, in a way, he was right. We treat OCD in children and adolescents1 with so called evidence-based strategies, while the mechanisms of change are still unknown.

If a treatment strategy is effective, why should we want to know the mechanisms of change? The most important reason is that for most evidence-based interventions there is room for improvement. Cognitive behavioral therapy (CBT) is the evidence-based treatment for childhood OCD. Several studies, meta-analyses and reviews have demonstrated the efficacy of CBT (e.g., Abramowitz, Whiteside, & Deacon, 2005; Freeman et al., 2007; O’Kearney, Anstey, Von Sanden, & Hunt, 2010; Olatunji, Davis, Powers, & Smits, 2013; The Pediatric OCD Treatment Study (POTS) Team, 2004; Watson & Rees, 2008). However, CBT proved to be only moderately effective; mean improvement rates for childhood OCD varied between 40–65% (e.g., O’Kearney et al., 2010). Moreover, there are large individual differences in treatment response. CBT leads to substantial improvement for the majority of patients, but not for all. As OCD often significantly interferes with children’s psychosocial development (e.g., Valderhaug & Ivarsson, 2005), the need to improve treatment is obvious.

Surprisingly, despite the amount of studies reporting the efficacy of CBT, the theoretical models on which CBT is based are hardly examined in children and mechanisms of change are unknown. Furthermore, partial and non-response receives little attention in the literature. We are not able to predict for whom CBT will be effective, and for whom alternative options should be considered. Moreover, little is known about effective treatment strategies for partial and non-responders.

What are mediating mechanisms in CBT? For whom does CBT work and for whom is CBT less effective? What should be recommended for those children

1 Throughout this thesis, the term ‘children’ is used to refer to both children and adolescents, unless otherwise mentioned.
who do not sufficiently benefit from this treatment? This thesis is a search for an answer to these questions.

**OCD in children and adolescents**

A substantial number of children suffer from OCD, with prevalence estimates around 1–2% (Geller et al., 2012). OCD is characterized by obsessions and/or compulsions, and patients often avoid situations, actions or objects that may trigger obsessions or compulsions. Most children report both obsessions and compulsions, but some have compulsions without obsessions, or obsessions without compulsions. The obsessions and/or compulsions are time-consuming or significantly interfere with daily functioning (American Psychiatric Association, 1994). Untreated, OCD often leads to substantial impairment in family, academic and social functioning (e.g., Piacentini, Bergman, Keller, & McCracken, 2003; Valderhaug & Ivarsson, 2005). An eleven-year-old boy with a severe OCD, for example, was so afraid of becoming contaminated, that he spent whole days with showering, washing hands, and avoiding contaminated objects. He refused to touch anything that was related to school, and avoided all contact with objects or persons that had been outside the house without cleaning. He sat on his own, very clean chair (his mother had to clean this chair every time he wanted to sit on it), and ate from a special plate (after it was cleaned very well). He didn’t go to school anymore. His parents and sister had to conform to strict rules concerning cleaning rituals, touching objects, and putting their stuff at specific places. Nobody was allowed to enter his room, and only his mother could touch him. He fell asleep holding his hands up, cautious not to touch anything.

Obsessions are persistent repetitive, intrusive thoughts, images or impulses which cause marked distress. Compulsions are recurrent behaviors, rituals or mental acts which are performed to prevent or reduce distress (American Psychiatric Association, 1994). The majority of children perceive their obsessions and compulsions as senseless, excessive or inappropriate, but nonetheless they can’t stop them. Insight into the senseless or excessive nature of symptoms is not required to meet the diagnostic criteria for OCD. Obsessions in children typically concern disasters, harm, accidents, and sickness or death of the child or family members. Other common themes are fear of contamination, unpleasant and unwanted thoughts about immorality, aggression or sexuality, thoughts of doing awful, improper or embarrassing things against their will,
and transformation obsessions (thoughts about turning into someone else or taking over unwanted characteristics; Volz & Heyman, 2007). The content and nature of the obsessions may change over time. Not all children report obsessions. Some children perform rituals because they ‘have to’, or ‘until it feels just right’, so-called ‘just-right experiences’ (Coles, Heimberg, Frost, & Steketee, 2005; Leckman, Walker, Goodman, Pauls, & Cohen, 1994).

Typical compulsions in children are cleaning rituals, checking, repeating, counting, touching, ordering, and reassurance seeking. Compulsions can include overt behaviors, such as cleaning, touching or asking for reassurance, as well as covert behaviors, such as counting, thinking good thoughts, silent praying, or rewinding memories. Children often perform magical rituals to prevent harm, such as specific movements, avoiding bad numbers, or a bedtime ritual. It is not unusual that parents become actively involved in the rituals. They have to say neutralizing words or phrases, repeatedly answer questions or provide reassurance following strict rules (e.g., saying the same sentence over and over again with the right intonation, at the right time, and with the right expression), assist the child in avoidant behaviors, etc. The parents often comply with these demands, as protest usually results in panic or tantrums. When children are disturbed while performing a ritual, the ritual often starts over from the beginning.

Childhood OCD is associated with high rates of co-morbidity. Anxiety and depression are the most common co-morbid disorders, but tics, pervasive developmental disorders and eating disorders are also frequently reported (e.g., Turner, 2006).

Treatment
The treatment that was examined in the present thesis consisted of 16 weekly sessions of individual CBT as described in the Dutch treatment manual ‘Bedwing je dwang’ (‘Control your OCD’; De Haan & Wolters, 2009). The treatment involved psychoeducation, an inventory and hierarchy of symptoms, exposure with response prevention (ERP), cognitive interventions, and relapse prevention. The primary aim of psychoeducation is to help the child and family to understand OCD. It includes information about obsessions and compulsions, causes of OCD, prevalence, maintenance factors, and treatment. Most children are very ashamed of their OCD, and develop detailed strategies to hide their rituals. In the first treatment session, children learn that they are not the only ones
with OCD and OCD does not mean that they are becoming mad. It is explained that most people recognize OCD-related behaviors, such as checking the door for a second time before leaving, straightening picture frames on the wall, or using lucky numbers by taking decisions. Because it is not unusual that family members have to accommodate themselves to long-lasting, interfering rituals, OCD is often associated with a high degree of familial conflict and frustration. In an attempt to alter the negative beliefs and attitudes that may arise in the child and the family members, an alternative view is provided. It is argued that OCD is better understood as too much of something good, like being clean, neatly and orderly, careful, and considerate, rather than something which is bad. However, in an excessive rate positive characteristics can become troublesome. Therefore, the treatment is aimed to stop the excessive behavior and retrieve the good habit.

In ERP, the child is confronted with anxiety-evoking situations (exposure), such as touching contaminated objects, or leaving the room without stepping back and forth over the doorstep several times. The child is not allowed to perform compulsions or avoidant behavior to reduce anxiety, such as washing hands afterwards or touching the object with their hands covered with sleeves (response prevention). Even without performing compulsions the anxiety will decrease, an effect known as habituation. Repeating the exposure over and over again makes that the situation becomes less distressing. Consequently, the urge to perform compulsions will diminish. To keep the anxiety within a tolerable level, ERP is performed in a gradually fashion. At the start of the treatment a detailed inventory of all OC symptoms is made, and a graded symptom hierarchy from ‘less distressing’ to ‘very distressing’ is composed. Usually, ERP starts with the least distressing complaint, unless there are strong arguments to start with more difficult exercises (for example, when complaints lead to unbearable situations at home). The selection of ERP exercises proceeds in mutual agreement between the therapist and the child. Exercises are prepared and practiced during the treatment sessions and are further practiced at home.

Cognitive interventions rely on the assumption that patients with OCD interpret unwanted intrusive thoughts in a dysfunctional way. The primary focus is to teach the child to change the dysfunctional interpretation into a functional one, such as ‘thinking about something bad, does not mean it will really happen’. Cognitive interventions can be used as separate interventions
Towards improving treatment for childhood OCD

or to assist and facilitate compliance with ERP. Several cognitive interventions are described in the manual, ranging in complexity from simple (e.g., helping thoughts, like ‘when I do my best, it is good enough,’ or ‘my mother can take care of herself very well’), to more sophisticated cognitive techniques (e.g., probability estimates and an inventory of pros and cons). The manual provides guidelines for selecting those interventions that would most likely fit with a particular child depending on age, intellectual level, interest/motivation, and insight in their complaints.

ERP is introduced early in treatment (second session), followed by and combined with cognitive interventions (second or third session). Treatment is round off with relapse prevention. Parents are involved in the therapy process. Parent involvement, varying from attending part of some sessions to fully attending each session, is dependent on the child’s developmental level, preferences of the child and the parents, and clinical considerations.

This thesis
Before the study into the effect of CBT and mediating mechanisms could be conducted, some preparatory work had to be done. We selected measures, translated questionnaires, and developed a version of the dot probe task to measure selective attention for (OCD-specific) threat. Next, we evaluated the reliability and validity of these measures. The results are described in Part I of this thesis. Part II of the thesis addresses the questions concerning mediating mechanisms in CBT, predictors of treatment outcome and non-response.

Part I. Candidate mediating mechanisms:
Dysfunctional cognition and selective attention for threat
Cognitive models are prominent in the OCD literature. According to cognitive theories of the development and maintenance of OCD, the core problem in OCD is the meaning patients ascribe to unwanted, intrusive thoughts. It is assumed that patients with OCD interpret intrusions – which are in fact innocent thoughts – as potentially harmful or bad, resulting in anxiety and distress. Consequently, compulsive behaviors are performed as an attempt to reduce anxiety. The idea that dysfunctional beliefs about normal intrusions are the core problem in OCD has become widespread since the publication of Salkovskis (1985), and from that time on research and treatment for OCD has been strongly influenced by cognitive models. Although there is some
evidence for cognitive theories in adults (see Frost & Steketee, 2002), little is known about the role of dysfunctional beliefs in childhood OCD.

Research into cognitive models of OCD is hindered by several methodological shortcomings and inconsistencies across studies. To improve research into cognitive models, an international group of researchers started the Obsessive Compulsive Cognitions Working Group (OCCWG). This group reviewed the literature and made an inventory of all available cognitive measures. Based on consensus ratings six belief domains were described expected to be relevant in OCD: inflated responsibility, overestimation of threat, perfectionism, intolerance of uncertainty, overimportance of thoughts, and beliefs about the importance of controlling one’s thoughts (OCCWG, 1997, 2001). Next, a measure was developed that provides an overview of these belief domains. This measure, the Obsessive Beliefs Questionnaire (OBQ), originally was developed for adults, but has been adapted for children (OBQ-CV; Coles et al., 2010). The aim of the first study of this thesis, described in Chapter 1, was to examine the psychometric properties of the Dutch version of the OBQ-CV in a community sample of 8-to-18-years-old children and a clinical sample of children with OCD. Furthermore, we examined whether children with OCD reported more dysfunctional beliefs than typically developing children, and whether dysfunctional beliefs were related to OC symptoms.

Strongly related to cognitive models advocated by members of the OCCWG, is the meta-cognitive model of OCD (Wells, 1997, 2000). While all models ascribe a key role to the dysfunctional appraisal of unwanted intrusive thoughts, the meta-cognitive model more strongly emphasizes the role of meta-cognitive beliefs such as thought-event fusion (‘thinking about an event means it has really happened or will happen’), thought-action fusion (‘if I have a bad thought, that means I really want to do it’), thought-object fusion (‘things can become contaminated with other people’s characteristics and I could catch it’), beliefs that harm can be averted by performing rituals, and beliefs that negative thoughts or feelings will become unbearable, dangerous or permanent. Based on this model, several meta-cognitive treatments have been developed for adults (Fisher & Wells, 2008; Rees & van Koesveld, 2008) as well as for children (Simons, Schneider, & Herpertz-Dahlmann, 2006).

The Meta-Cognitions Questionnaire (MCQ; Cartwright-Hatton & Wells, 1997; Wells & Cartwright-Hatton, 2004) has been developed to examine
Towards improving treatment for childhood OCD

meta-cognitive beliefs. The MCQ contains five belief domains: 1) positive beliefs about worry; 2) beliefs about uncontrollability of worrying and about the dangers of failing to control worrying; 3) cognitive confidence; 4) beliefs about superstition, punishment and responsibility associated with worry; and 5) cognitive self-consciousness. Similar to the OBQ, the MCQ originally was developed for adults, but an adapted version for adolescents has been made (MCQ-A; Cartwright-Hatton et al., 2004). To our knowledge up to now this questionnaire has never been used in clinical samples of youth with OCD. Therefore, we examined the psychometric properties of the Dutch version of the MCQ-A in a clinical sample of adolescents with OCD and a non-clinical sample of adolescents. Similar to the validation study of the OBQ-CV, we examined whether children with OCD reported more meta-cognitive beliefs than non-clinical adolescents, and whether these beliefs were linked to OCD severity. This study is described in Chapter 2.

Although cognitive theories have dominated the OCD literature for decades, criticism on these models is increasing (e.g., Julien, O’Connor, & Aardema, 2007; Longmore & Worrell, 2007). In Chapter 3 and 4 we focus on an alternative model concerning increased selective attention for threat.

Several investigators have suggested that increased selective attention for threatening information may be an underlying mechanism in OCD. Patients with OCD may show facilitated detection of potential sources of danger (Foa & McNally, 1986), which is referred to as increased vigilance for threat. This is for example shown by a patient with fear of contamination who becomes anxious because he immediately detects a very small red spot on the table which might be blood. In addition, difficulties with disengaging attention from potential threat may explain the repetitive character of obsessions and compulsions (e.g., Bannon, Gonsalvez, Croft, & Boyce, 2002; Bannon, Gonsalvez, & Croft, 2008; Chamberlain, Blackwell, Fineberg, Robbins, & Sahakian, 2005; Enright & Beech, 1993a, 1993b; Hartston & Swerdlow, 1999; Muller & Roberts, 2005). Only a small number of studies into selective attention for threat in OCD has been conducted, and to our knowledge selective attention for OCD-specific threat in childhood OCD has not been studied yet.

In general, selective attention is measured by computer tasks based on response times. We selected the dot probe task (Mogg & Bradley, 1998). This task is often used, it provides a more direct measure of attentional bias than
the Stroop task (which also is often used), and several attentional processes can be distinguished (e.g., vigilance and difficulty to disengage; Koster, Crombez, Verschuere, & De Houwer, 2004). Subsequently, we adapted the dot probe paradigm to the demands of the present study. We selected neutral, OCD-specific and general threat stimuli, and used pictorial instead of lexical stimuli to make the task appropriate for children. Most dot probe studies in children have used a single, quite long presentation duration of threatening stimuli (≥ 1250 ms; e.g., Taghavi, Neshat-Doost, Moradi, Yule, & Dalgleish, 1999; Vasey, Daleiden, Williams, & Brown, 1995). This only allows a snapshot of attention and provides little information on early, automatic processes versus later, more controlled processes. Attentional biases can result from automatic as well as controlled processes, and vigilance for threat may occur in an early stage of information processing whereas difficulty disengaging from threat may occur in a later stage. Therefore, we used several stimulus exposure durations (17 ms masked, 500 ms, and 1250 ms) to examine the time-course of attentional processes. Following the normal procedure we included congruent as well as incongruent threat trials (threat-neutral picture pairs). To examine whether an attentional bias for threat results from vigilance or difficulty to disengage, we also included neutral trials (neutral-neutral picture pairs) (Koster et al., 2004). Finally, we compared neutral trials with threat trials to examine whether there was a slowing effect of threatening information in general (interference).

However, before we could evaluate increased selective attention for threat in children with OCD, we had to examine the time-course of selective attention in typically developing children. Therefore, we conducted a study in a community sample. The main objective of the first dot probe study was to examine whether typically developing children show an automatic attentional bias to threatening scenes and whether this attentional bias can be controlled with longer presentation durations. Furthermore, we examined behavioral interference by threat over time. This study is described in Chapter 3.

After this first dot probe study, we made some adaptations to the task. With the adapted version we performed a second study to examine whether increased selective attention for threat may be an underlying mechanism in childhood OCD. The aim of this study, described in Chapter 4, was to examine the time-course of selective attentional processes in children with OCD, a matched clinical control group of children with another anxiety disorder, and a non-clinical control group.
Part II. Mediating mechanisms and non-response
In Part II we focus on our primary research questions. The study described in Chapter 5 was aimed to answer the question: What are mediating mechanisms in CBT for childhood OCD? The study described in Chapter 6 addresses the questions: For whom does CBT work and for whom is CBT less effective?; and, What should be recommended for children who do not sufficiently benefit from CBT?

We had selected two potential mediating mechanisms: changing dysfunctional OCD-related beliefs and a decrease of selective attention for OCD-related threat. Based on the findings in Part I we rejected our hypothesis concerning increased selective attention for (OCD-related) threat in childhood OCD. Consequently, selective attention for threat was not further tested as a potential mediator. We proceeded with one potential mediator: changing dysfunctional OCD-related beliefs. Dysfunctional beliefs were measured with the OBQ-CV, because the studies described in Chapter 1 and 2 showed that the relation between dysfunctional beliefs and OC symptoms was less consistent for the MCQ-A than for the OBQ-CV. Moreover, the OBQ-CV was available for a larger sample as this questionnaire covered a broader age range.

Mediating mechanisms in CBT for childhood OCD: the role of dysfunctional cognition
It generally is assumed that restructuring dysfunctional cognitions is an important step in treating OCD, and cognitive restructuring procedures form a significant part of most treatment packages. However, the exact role of dysfunctional cognitions in OCD is unclear. This would be less problematic had CBT been a very effective treatment, but unfortunately it is not. As there is considerable room for improvement, it would be worthwhile to evaluate the role of cognitive restructuring in treatment for OCD. So far, hardly any study has addressed the question whether changing dysfunctional cognitions indeed is a mediator in CBT for OCD. The small number of available studies mainly concern adult patients and have yielded inconsistent results.

The aim of the study described in Chapter 5 was to examine whether changing dysfunctional beliefs is a mediator of treatment outcome in CBT for childhood OCD. Participants were 58 children (8–18 years) who were referred to an outpatient clinic for treatment for OCD. They received sixteen weekly sessions of CBT. Dysfunctional beliefs and OCD severity were measured pre-
treatment, mid-treatment, post-treatment and at 16-week follow-up. It was examined whether changes in dysfunctional beliefs preceded changes in OCD severity, were a consequence of changes in OCD severity, or whether the relation was bidirectional. Based on the cognitive model, we expected cognitive changes to precede changes in OC symptoms. Whether this hypothesis was supported by the results, is discussed in Chapter 5.

Partial and non-response to CBT for childhood OCD
To improve treatment and prevent non-response, knowledge is needed about predictors of treatment effect. Research on predictor variables in childhood OCD is scarce. In the study described in Chapter 6 we investigated several potential predictors for the effect of CBT. Severity of OCD was examined as previous studies have suggested that this variable may be predictive of treatment outcome (Garcia et al., 2010; Ginsburg, Kingery, Drake, & Grados, 2008). In addition, we selected two other variables that are assumed to be predictive of treatment outcome in clinical practice, but hardly or never have been examined. These variables are rate of improvement during the first treatment sessions, and co-morbid autistic traits. Improvement during the first treatment phase is often considered a predictor for further success. If there is hardly any symptom reduction during the first sessions, not only patients and parents but also therapists may lose their faith in the treatment and often treatment policy is changed (i.e., adding medication or referring to inpatient treatment). It is questionable whether a change of treatment strategy is justified in this early stage. In addition, autistic traits are a common co-morbid condition of OCD in children (Ivarsson & Melin, 2008). CBT is generally assumed to be more difficult to deliver to children with autistic traits due to poor emotion understanding and cognitive rigidity (Krebs & Heyman, 2010). However, patients with co-morbid autism are often excluded from randomized controlled clinical trials (e.g., The POTS Team, 2004), and it is unclear whether co-morbid autistic traits are predictive of CBT outcome.

Predicting partial or non-response to CBT is just a first step. We also need to know what would be more effective treatment strategies for these patients. According to the AACAP guideline, patients with moderate to severe OCD should be treated with the combination of CBT and medication (an SSRI), instead of with CBT monotherapy. Furthermore, the combination of CBT and medication is recommended for patients who do not sufficiently respond to
Towards improving treatment for childhood OCD

CBT (usually 12–20 treatment sessions) (Geller et al., 2012). It should be noted that the effectiveness of these guideline has never been established. Although it may intuitively be sensible to combine treatment modalities (CBT and medication) for patients with severe complaints and for patients who do not sufficiently benefit from standard CBT, the decision to add medication to CBT should be well-founded because of possible adverse effects of medication and unknown effects in the long term (e.g., Geller et al., 2012; Storch et al., 2010). We wondered whether patients with severe OCD can be effectively treated with CBT without medication, and whether continuation of CBT monotherapy (i.e., extending the number of treatment sessions) will lead to further improvement for partial and non-responders.

Participants were 58 children (8–18 years) who were referred to an outpatient clinic for treatment for OCD. Participants were randomly allocated to either an active treatment condition (CBT), or an eight-week waitlist control condition followed by CBT. Severity of OCD, problem behavior, symptoms of anxiety and depression, and quality of life were measured during treatment and follow-up. Assessments were performed pre-waitlist (if applicable), pre-treatment, mid-treatment, post-treatment, at 16-week follow-up, and at one-year follow-up. In Chapter 6 the findings are discussed. We conclude this chapter with several clinical implications.

Finally, in the section Summary & General discussion the main findings of the studies are summarized and discussed.