Looking for mediators: cognition, perceived control and coping in the treatment of anxiety-disordered children
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Chapter 8
General discussion
The studies presented in this dissertation aimed at two main goals: 1) To improve the measurement of potential mediators in children by developing two types of instruments (an indirect measure and a repeated measure) that are currently underrepresented in research with children, and 2) To examine mediators of evidence-based, cognitive behavioral treatment of anxiety disordered youth. In this final chapter, the findings from the studies presented in Chapters 2 through 7 are summarized and discussed. Furthermore, strengths and limitations of the studies are described and clinical implications of the results are discussed, followed by recommendations for future research.

It is interesting to note how the focus and goals of a study can change over time due to changing insights in methodological and statistical issues. When our study described in this dissertation began in 2005, we set out to measure several moderators and potential mediators in both direct (questionnaires) and indirect (computer tasks) ways. The question was whether changes in specific constructs (e.g. perceived control) were reflected in direct and indirect measures simultaneously or successively, and whether mediators could be identified in both a direct and indirect way. However, while keeping up with the quickly expanding literature on implicit measures, we discovered that the development of those measures, when applied to children, was still largely in its infancy. It appeared that indirect measures might become useful as a diagnostic tool in the future, but are currently still in an experimental phase. Our goal to use indirect measures in an analysis of potential mediators therefore had to be adjusted to the goal to develop valid and developmentally sensitive indirect measures for use with children. In this dissertation we report on the development of one of these measures, the Perceived Control IAP. Vervoort (2010) in her dissertation, has described several other instruments that we developed to assess response inhibition in neutral and threatening situations (the emotional Stop Task), automatic stimulus evaluations (a pictorial Extrinsic Affective Simon Task, EAST) and threat-related attentional processes (pictorial dot probe detection task, see also Wolters et al., 2012).

A second change in our plans concerned the analysis of mediators. Initially, the method to evaluate mediators as described by Baron and Kenny (1986) and later refined by Kraemer, Wilson, Fairburn, and Agras (2002) was used as a frame of reference for the statistical analyses. We therefore decided to include a waitlist control group which had to wait sufficiently long, but not too long for ethical reasons. A waitlist period of eight weeks was considered acceptable and had been employed in other studies (e.g. Kendall, 1994; Kendall et al., 1997). As the waitlist condition was eight weeks, we decided to plan the in-treatment assessment in the treatment group between session eight and nine (i.e. after approximately eight weeks of treatment). However, what holds for the literature about indirect measures, also holds for the literature about statistical mediation analysis: quite a number of studies conducting mediation analyses have been published between 2005 and 2010. Many different and advanced statistical methods with regard to mediation analysis have become available next to the use of regression analysis, as is described in depth by MacKinnon (2008). We decided that Latent Difference Score (LDS) Modeling was the optimal method to examine our research question: does a change in
the putative mediator precede a change in the outcome variable. Choosing the LDS method meant that it was not possible to include the waitlist condition anymore, as this condition and the treatment condition were of unequal length. However, we were still able to establish the efficiency of CBT relative to a waitlist condition in our particular sample.

**Summary of the Findings**

In Chapter 2 and 3 we described the development and use of the Perceived Control IAP, a computer task to indirectly measure perceived control in children. The rationale for developing an indirect measure of perceived control was that indirect measures are generally less sensitive to social desirability or introspective abilities and might be an aid to predict relapse. We showed that the IAP was able to discriminate between non-referred children with higher and lower anxiety levels (Chapter 2) and between anxiety disordered and non-anxious children (Chapter 3). Higher anxious non-referred children or anxiety disordered children reported less perceived control on both the direct measure (questionnaire) and indirect measure (IAP). However, the effect on one of the IAP scores was only found for children younger than twelve years old: in older children we did not find a difference on indirect perceived control between either non-referred children with higher and lower anxiety levels (Chapter 2), or between anxious and non-anxious children (Chapter 3). In both studies, the direct and indirect measures were weakly associated. This is in line with previous research and the notion that direct and indirect measures assess related, but distinct constructs. The internal reliability of the IAP proved to be weak to moderate and test-retest reliability was moderate. We conclude that the IAP can become a valuable supplement to understand perceived control in children, but the task is not sensitive enough yet to measure intraindividual changes.

Repeated assessment is not only valuable to determine temporal relations between variables in mediation studies, but it can also be valuable in individual treatments. In Chapter 4 the development of the Anxiety Severity Interview for Children and Adolescents (ASICA) is described. We developed this instrument to sensitively and repeatedly assess components of the anxiety response (physiological, cognitive, and behavioral) over the course of treatment. The ASICA fits in "patient-oriented research", which is more focused on individual than group differences. The ASICA proved to be sensitive to treatment change and was able to effectively discriminate between anxious and non-anxious children. We believe that the use of the ASICA by therapists can help them to monitor treatment progress and provide their clients with an insight into their treatment progress.

Chapter 5 and 6 dealt with the role of positive thoughts in theoretical and treatment models of anxiety. So far, too little attention has been paid to the role of positive thoughts in childhood anxiety. We expanded an existing questionnaire (the CATS), which measures negative thoughts, with items developed to measure positive thoughts. We chose the CATS
because this questionnaire was developed using children’s self-statements, contains items that measures thoughts rather than anxiety symptoms, and has good psychometric properties. The resulting questionnaire, the CATS-N/P, proved to have factorial validity and good reliability in a non-anxious sample (Chapter 5) and was able to discriminate between anxious and non-anxious children (Chapter 6). Anxious children reported more negative, but also less positive thoughts than non-anxious children. Further, using the CATS-N/P, we showed that both the amount of negative and positive thoughts was predictive of anxiety level, indicating that a relative shortage of positive thoughts may contribute to anxiety disorders in children.

In Chapter 7 we evaluated several putative mediators in the treatment of anxiety disorders using state of the art statistical analysis. The main characteristic that distinguished our design from other studies was the longitudinal approach with an in-treatment assessment point. By modeling the interaction between change in the putative mediators and change in anxiety symptoms, we showed that a change in positive thoughts and several coping strategies preceded change in anxiety level. Surprisingly, our model did not support a role of negative thoughts as a mediator. We found a reciprocal effect for perceived control where an increase in perceived control both preceded and followed upon a decrease in anxiety. Finally, an avoidant coping style turned out to be a consequence rather than a cause of change in anxiety level.

Strengths and Limitations

Strengths
The main strength of our study is that, as far as we know, we are the first to investigate multiple putative mediators of the treatment of anxiety disordered children in a temporal design. This is an important step forward from the usual cross-sectional designs. Although we are well aware that ascertaining true causality is very difficult and that we only investigated one of the requirements to establish mediation, a longitudinal design provides more insight into cause-and-effect relations than pre-post designs where temporal relations between variables cannot be established (Nock, 2007). The use of a longitudinal design distinguishes our study from earlier studies that examined possible mediators of the treatment of anxiety in children (Alfano et al., 2009; Kendall & Treadwell, 2007; Lau, Chan, Li, & Au, 2010; Maric, Heyne, MacKinnon, Van Widenfelt, & Westenberg, 2012; Treadwell & Kendall, 1996). These studies used a pre-post design (Alfano et al., 2009; Kendall & Treadwell, 2007; Lau et al., 2010, Treadwell & Kendall, 1996) or a longitudinal design without an in-treatment assessment (Maric, Heyne et al., 2012) and were therefore unable to examine temporal relations between possible mediators during treatment and outcome.

Additionally, with the statistical analysis used, not only did we model inter individual differences, but also intra individual changes and differences in intra individual change. This is important, as individuals’ time courses can differ substantially from each other. Another
advantage of our design is that we were able to examine reciprocity and reverse causality, in which change in the outcome secondarily produces change in the putative mediator. In fact, we did find evidence for reciprocity in the case of perceived control and evidence for reverse causality for avoidant coping strategies.

Another strength of our study was that we paid extra attention to the use of valid and reliable measurement instruments. This is important in any study, but especially when employing complex statistical models where unreliable instruments can have a large impact on the outcome. We used existing measures (e.g. the ADIS-IV CP or CCSC-R1) when psychometric properties of the Dutch versions were satisfactory. In other cases we were not satisfied with the existing measures and decided to make adaptations (e.g. CATS-N/P) or a translation (ACQ-C; Hogendoorn et al., 2011). Psychometric properties of all developed and translated measures were examined in both a large sample (over 550 children) of non-referred children and in a clinically anxious sample. Further, we also developed and investigated an indirect measure that provided an alternative way to measure perceived control in children. In the future this measure might be used to examine whether indirectly assessed perceived control might mediate treatment outcome.

Finally, we included a clinically representative group of anxious children. Some studies recruit children via advertisements in papers, which is an effective way, but the anxiety level of children recruited that way is often low to moderate. Other studies employ very strict inclusion- or exclusion criteria, limiting their generalizability. Our sample consisted of children who were referred to the outpatient clinics of either one of two academic centers for child and adolescent psychiatry. Many children had severe anxiety disorders, including 19% that did not attend school anymore. Some of these children only rarely left their house and were severely impaired in their social and academic life. More than 50% of the children in our sample reported more than one (anxiety) disorder. The therapists differed in time of experience: some just graduated and others had more than ten years of experience. We therefore think that our results generalize to common clinical practice.

Limitations
Our study had several limitations. Although we included a clinically representative group of anxious children in our study, it should be noticed that there was essentially no cultural diversity in our sample, as most children were of Dutch origin. Further, although our initial sample size was satisfactory, attrition rates were fairly high. Some children dropped out due to the severity of their disorder and they needed more than the outpatient treatment we could offer them. Another reason for parents and children to drop out was burden of time involved: assessments sometimes took up three to four hours. Although the attrition rate was fairly high, it was comparable to the attrition rates in other studies (e.g. Kolko, Brent, Baugher, Bridge, & Birmaher, 2000). Further, the drop out or the timing of drop out (e.g. at mid-treatment or at follow-up) did correspond to pre-treatment characteristics (e.g. anxiety level, age, gender).
A major limitation was that some children received further treatment during the follow-up period. Originally we planned a treatment-free period for three months after the twelve sessions of the treatment protocol. However, it turned out that this was not always possible, because some children still had serious complaints. When this was the case, the preferred option was to continue with the Coping Cat protocol and continue the use of exposure exercises and previously learned skills. In some instances it was necessary to add medication or to even refer to inpatient treatment. As a result, the follow-up period was not as “pure” as the treatment period. However, most mediating effects occurred during the first treatment period and were most likely the result of the initial treatment.

So far, we stressed the importance of a longitudinal design. However, the timing of the in-treatment assessment (after session 8) might not have been optimal and too late to capture early changes. This idea is supported by studies in adults, which have found that changes can occur very early in therapy and sometimes quite suddenly (e.g. Penava, Otto, Maki, & Pollack, 1998; Wilson, 1999). However, other studies report that changes can also occur in the final phases of treatment (Maric, Wiers, & Prins, 2012). For future studies we recommend more and earlier assessment points, preferably at every session or every other session.

Although we examined several mediators in our study, the model used in our study is most likely still oversimplified. The mediators that we incorporated were chosen for their importance in theories about the development and treatment of anxiety disorders. However, many more mediators could have been examined, for example interpretation bias, anxiety sensitivity, self-efficacy, etc. Additionally, although we assessed several possible moderating variables – such as age, gender, number of diagnoses, behavioral inhibition, and executive functioning – we did not include these in the model (moderated mediation). In earlier studies, it has been found that higher levels of child- and parental psychopathology (especially parental anxiety and depression) and older age of the child were associated with less favorable treatment response (e.g. Silverman, Pina, & Viswesvaran, 2008; Southam-Gerow, Kendall, & Weersing, 2001), although in other studies age has not proven to be a significant moderator (e.g. Rapee, Schniering, & Hudson, 2009). On the other hand, other factors do not seem to predict treatment response, for example child ethnicity, gender, therapeutic relationship, family income or family composition (Rapee et al., 2009; Silverman et al., 2008; Southam-Gerow et al., 2001). In future studies we recommend to combine mediators and moderators in the same model to be able to investigate possible moderated mediation or mediated moderation. For example, it is conceivable that negative or positive thoughts are mechanisms of change, but perhaps only in older children.

A final remark is that our conclusions are based on just a single measurement instrument for most variables. In future studies we recommend using multiple questionnaires for the same construct (e.g. positive thoughts) to see whether the effects are stable. Of course, different modalities (e.g. indirect measures, behavioral observation) may be included as well (see also Maric, Wiers et al., 2012).
Implications

Theoretical Implications

The results of the described studies have implications for the cognitive model of anxiety disorders. Our findings raise, for example, questions about the validity of the "Power of Nonnegative Thinking" hypothesis and the Tripartite model of anxiety and depression in children. The Power of Nonnegative Thinking hypothesis states that only negative thoughts play a role in anxiety and suggests that it is not necessary to change positive thoughts during treatment (Kendall & Chansky, 1991). Contrary to this hypothesis, in our study positive thoughts did seem to play a role in the treatment of anxiety disorders: anxious children reported less positive thoughts than non-anxious children, the amount of positive thoughts predicted anxiety level, and a change in positive thoughts preceded a change in anxiety symptoms in the treatment of anxiety disorders. The theoretically proposed role of negative thoughts was only partially supported by our studies. Anxious children reported more negative thoughts than non-anxious children (Chapter 5); the amount of negative thoughts was predictive of anxiety level (Chapter 6) and negative thoughts decreased during and following treatment (Chapter 7). However, a decrease in negative thoughts did not temporarily precede a change in anxiety symptoms (Chapter 7). Note that methodological issues (late in-treatment assessment) might have precluded finding an effect for negative thoughts. Our results add to other studies which have found that higher anxious children report less positive thoughts than less anxious children (Calvete & Cardenoso, 2002; Ronan & Kendall, 1997; Zatz & Chassin, 1985).

The Tripartite model of anxiety and depression assumes that both anxiety and depression share a heightened negative affect, but that physiological hyperarousal is specific for anxiety while a lack of positive affect is specific for depression (Clark & Watson, 1991). So far, the Tripartite model has not been examined frequently in children, but results from previous studies seem to indicate that a lack of positive affect is associated with both depression and social phobia (e.g. Anderson & Hope, 2008; Hughes & Kendall, 2009). Our study adds to these findings and although some children reported comorbid mood disorder, this was only a small part of the sample (16%) and will not explain the effect. Exploratory analysis of our data revealed however, that children with comorbid mood disorder or children with social phobia or panic disorder reported even less positive thoughts than children with a single anxiety disorder, no social phobia or no panic disorder, respectively. To summarize, adult models of the role of cognition in anxiety may not be readily applicable to children, as was also mentioned before by Field, Cartwright-Hatton, Reynolds and Creswell (2008). Especially the role of positive thoughts in childhood anxiety needs more attention. Note that we only investigated parts of the cognitive model and did not look at other components of the model such as interpretation or attention biases.

Perceived control. Perceived control was examined as a mediator because it is supposed to play a central role in the development of anxiety disorders (Chorpita & Barlow, 1998),
because anxious children have been found to report lower levels of perceived control (Weems, Silverman, Rapee, & Pina, 2003) and because perceived control has been found to increase after treatment (Muris, Mayer, den Adel, Roos, & Van Wamelen, 2009). Although we replicated the findings of Muris et al. (2009), perceived control did not act as a mediator in treatment. We found evidence for a reciprocal effect in which an increase in perceived control both preceded and followed upon a decrease in anxiety. This is interesting, as it is generally assumed, but as far as we know not yet experimentally or longitudinally examined, that low perceived control contributes to heightened anxiety and not vice versa. Although perceived control generally increases after treatment, it could also be a consequence of mastery experiences in successful coping and exposure exercises and follow upon a decrease in anxiety. Our results suggest that the association between perceived control and anxiety might be more complex than has been thought so far. Evidently, our results should be replicated and future studies could examine the temporal relationship between, for example, increased active coping strategies, perceived control and symptom reduction. Finally, the experimental status of the perceived control IAP precluded an examination of the role of indirectly assessed perceived control in treatment. It would be interesting to examine whether perceived control as measured by the IAP increases after treatment and whether this change precedes or follows a change in anxiety level.

Clinical Implications

In this study we found an indication that a change in positive thoughts and coping strategies mediate treatment effects in the treatment of anxiety in children, and seem to contribute to a decrease in anxiety symptoms. However, we want to stress again that we investigated mediators, but not the treatment components that bring about this change. Because different therapeutic techniques, like cognitive restructuring and exposure, were not studied separately, we cannot identify which technique caused the change. Although a change in positive thoughts turned out to precede symptom improvement, we still do not know why the amount of these thoughts increased. Thoughts can change for example due to cognitive restructuring, due to changed coping strategies, due to mastery experiences during exposure, or due to (a combination of) all three. Additionally, we do not know which techniques brought about the change in coping strategies. Based on our results we cannot advise to omit or increase the use of certain therapeutic techniques such as cognitive restructuring in the treatment of childhood anxiety. However, we can advise therapists to specifically pay attention to the amount and function of positive thoughts a child reports, or to the used coping strategies.

The measurement instruments we developed in this study can be used by clinicians to assess components of anxiety disorders and the progress of treatment. The ASICA proved to be a reliable and clinically useful instrument to monitor treatment progress. Therapists can use the ASICA to identify specific problems of the child pre-treatment and to plan treatment. Some children will report many anxiety-related physiological responses, while others will report many anxious thoughts. Some children may report that they never try to do anything about their fears,
while others do try to resist their avoidant behavior or fears, but do not manage yet to control them. The repeated assessment of the ASICA during treatment can be used to set and evaluate treatment goals. For example, some children cannot report any negative or positive thoughts pre-treatment. In this case, a first goal can be to learn to distinguish thoughts from feelings, and a second goal to change these thoughts and feelings. The repeated assessment of the ASICA can help to monitor this process. Finally, we know from clinical practice that the plotting of ASICA scores in a graph can be a real incentive for children: they report to be motivated to "see the lines go down". Due to the amount of other variables we used to investigate putative mediators in this study, we did not incorporate the ASICA in our LDS models. However, the ASICA could be used to examine mediation in future studies and could be especially relevant in n=1 designs which incorporate multiple repeated assessments.

The other developed or translated instruments (e.g. the CATS-N/P, ACQ-C) can also be used to inform therapists about the status of the patient at the start of treatment or to evaluate treatment progress. For example, when a child does not report many negative self-statements in the beginning, the therapist can decide to invest less time in cognitive therapy, but more in exposure. On the other hand, when a child is not able to report any anxious thoughts, the CATS-N/P can be used to give examples of negative and positive self-statements.

Directions for Future Research

Although both researchers and therapists who work in the field of clinical psychology have the same goal, namely to treat emotional and behavioral disorders rapidly, effectively and efficiently, their interests may differ. Researchers want to control as many external influences as possible, ask therapists to strictly adhere to the treatment protocol and generally examine treatment changes in groups rather than in individuals, requiring large sample sizes. On the other hand, therapists want to know which treatment or what treatment components are most effective for a particular individual and want to be able to flexibly deliver treatment protocols. In the future we would ideally be able to screen a referred child for certain characteristics and offer it a tailor-made treatment with the highest chance of fast and enduring success. There are several ways to reach this goal, for example by further examining mediators or by investigating treatment components.

Mechanisms of Change

There are still many steps to take in the study of the active mediators of treatment. Our study was one of the first to investigate change over time in the treatment of anxiety in children. The results suggest that a change in positive thoughts and coping strategies precede a change in anxiety level. However, important questions remain to be answered. First, we only investigated part of the requirements that are needed to establish whether a certain variable is a mediator,
or mechanism of change (see Kazdin & Nock, 2003). In this study we focused especially on
temporal precedence and possible reciprocal effects between putative mediators and treatment
outcome, and did not include a control condition in the analysis. This precludes definitive
conclusions about whether the investigated variables are mediators. Future studies could at least
combine a temporal design with the use of an experimental and control condition. Second, the
results of our study should be replicated in another sample. Third, the generalizability of the
results to other treatment packages or other treatment modalities (e.g. group delivery, internet
delivery, etc.) should be examined. Fourth, the specificity of our results is unclear and we do
not know if we would find the same or other results for positive thoughts and coping in, for
example, childhood depression. Fifth, we advise to investigate the role of both positive and
negative thoughts and perceived control more thoroughly by longitudinal designs with more
assessment points. Sixth, other possible mediators should be studied in a longitudinal design,
for example interpretation bias, social skills (see Alfano et al., 2009) or self-efficacy (see Maric
Heyne et al., 2012). Additionally, putative mediators (e.g. positive thoughts) and moderators
(e.g. age, kind of anxiety disorder) could be combined in future studies.

**Treatment Components**

As we mentioned before, we only studied temporal precedence of putative mediators
and could not link them to specific treatment components. A next step is to implement so
called “dismantling” studies where specific treatment components are investigated. Specific
components that can be identified in most CBT programs for anxiety problems are relaxation
exercises, cognitive restructuring, teaching problem solving skills and exposure exercises.
Although it is sometimes very difficult to disentangle the components, a dismantling study could
for example compare “cognition free” treatment with “exposure free” treatment. Subsequently,
the changes in cognition, coping and perceived control in both conditions could be monitored.
In this way it could be determined whether a change in thoughts is a mediator in both or in
only one condition. Of course, other components such as social skills training, targeting parent
anxiety or the inclusion of parents could be examined. Dismantling studies are not new, but they
often do not measure mediators (Hudson, 2005). Most dismantling studies show that different
components can bring about change in the same variables or that the same component can
bring about change in different variables. Further, underlying mechanisms might be different
for different anxiety disorders (Davis III, May, & Whiting, 2011). Therefore we recommend
combining dismantling studies with the examination of treatment mediators.
General Conclusions

In this dissertation several putative mediators in the treatment of anxiety disorders in children were examined. Parallel to this, two additional instruments were developed to improve the measurement of mediators. The main conclusions are: 1) An increase in positive thoughts and coping strategies precedes a decrease in anxiety level during the treatment of childhood anxiety disorders; 2) Both positive thoughts and negative thoughts are related to anxiety disorders in children, which has implications for the use of the Power of Nonnegative Thinking hypothesis and Tripartite model in children; 3) A decrease in negative thoughts does not seem to precede a decrease of anxiety level during the treatment of anxiety disorders in children; 4) Changes in perceived control do not only precede, but also follow upon a change in symptom level during the treatment of childhood anxiety; 5) A change in an avoidant coping style does not precede a change in symptom level in the treatment of childhood anxiety, but instead follows upon a change in anxiety level; 6) The Perceived Control Implicit Association Procedure (IAP) can be used to indirectly assess perceived control in children, but it cannot be applied yet to measure intraindividual change; 7) The Anxiety Severity Interview for Children and Adolescents (ASICA) can be used to repeatedly assess anxiety severity during treatment and its use is valuable both for the clinician and the client; 8) The Children's Automatic Thoughts Questionnaire-Negative/Positive (CATS-N/P) is a valid and reliable instrument to measure both negative and positive thoughts in children; 9) Further research is needed to establish which treatment techniques bring about change in putative treatment mediators.