The behavioral inhibition system in childhood and adolescent anxiety: an analysis from the information processing perspective
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In the present dissertation, Reinforcement Sensitivity Theory (RST) provided a framework to study anxiety disorders in children and adolescents. RST developed out of the seminal work of Jeffrey Gray (1982). RST describes how activity in three brain systems (the BAS, the BIS and the (F)FFS) has immediate behavioral and affective consequences. Individual differences in the sensitivity and activity of these systems are assumed to be related to individual differences in temperament or personality. Overactivity in one of the systems is thought to be central to psychological disorders. As such, one of the main hypotheses that follows out of RST relates clinical anxiety to overactivity in the BIS (Gray, 1982; Gray & McNaughton, 2000). Previous research using self-report questionnaires provided evidence for the relation between BIS-sensitivity and anxiety in adults. In the present thesis, a more diverse methodology was used to test whether the hypothesis of an overactive BIS in clinical anxiety applies to children and adolescents. A self-report questionnaire was used to measure sensitivity to the input of the BIS (i.e. anxiety relevant stimuli), while computer tasks were used to measure the output functions of the BIS (i.e. inhibition, evaluation, attention). Computer tasks have been used previously to assess reactivity to BIS-input but few studies adopt an information processing perspective to investigate BIS-output (for an exception, see Field, 2006).

SUMMARY OF THE STUDIES

Evidence for the role of the BIS in childhood and adolescent anxiety

**BIS-sensitivity**

The child version of the Carver and White (1994) BIS/BAS-scales (Muris et al., 2005) was used to assess BIS-sensitivity in clinically anxious and non-anxious youth [Chapter 3]. Results supported the hypothesis that clinical anxiety is associated with overactivity in the BIS (Gray, 1982). BIS-scores were higher in the anxious sample than
in the non-anxious sample and higher BIS-levels were related to the presence of more symptoms of anxiety. Factor analysis revealed that the BIS-scale consists of two subscales. Following Heym et al. (2008), these subscales were labelled BIS_Anxiety and FFFS_Fear. Results are consistent with the idea formulated by Corr [e.g., 2001] that in cases of extreme BIS-sensitivity [i.e. in clinically anxious individuals] the BIS dominates the BAS [separable subsystems hypothesis: anxiety symptoms are only predicted by BIS-scores], while in cases of moderate BIS-sensitivity [i.e. in the general population] BIS and BAS have a joint influence [joint subsystems hypothesis: anxiety symptoms are predicted by both BIS and BAS-scores].

**BIS-activity: Inhibition**

Two versions of the Stop Signal Reaction Time Task were used to investigate inhibition in neutral and threatening situations one with neutral and one with anxiety-relevant pictorial stop stimuli (Chapter 4). In Study 1, validity of both pictorial versions of the Stop Task was established in a community youth sample. General performance and inhibition were comparable with results of studies using more traditional Stop Tasks. In Study 2, the neutral and anxiety-relevant versions of the task were used to assess the inhibition output of the BIS in clinically anxious children and adolescents with at least one DSM-IV anxiety disorder. General task performance did not differ between tasks. However, the stop signal reaction time (SSRT), measuring the speed of the inhibitory response, was shorter in the anxiety-relevant than the neutral task. In addition to that, high BIS-sensitivity was associated with increased response inhibition. Because results support the idea that inhibition is increased when clinically anxious children are confronted with threatening situations, they provide preliminary evidence for the role of BIS-activity in clinical anxiety. Furthermore, in the clinically anxious sample, reactions to BIS-activating stimuli were stronger than reactions to neutral stimuli. As such, results are consistent with the separable subsystems hypothesis suggesting that individuals with extreme BIS-levels are more sensitive for BIS-activating stimuli than for other types of stimuli.

**BIS-activity: Evaluation**

The Extrinsic Affective Simon Task [EAST] was used to assess the evaluation output of the BIS [Chapter 5]. Although the EAST has been used successfully in studies investigating automatic evaluations in adult fear and anxiety as well as in addiction and obesitas in youths, the paradigm was not previously used to assess automatic evaluations in childhood and adolescent anxiety. In Study 1, the development of a child
friendly version of the pictorial EAST is described. Although the task had some minor
drawbacks [e.g. the automatic evaluation of positive stimuli seems to be neutral in the
sample included in this study], results indicate that it is suitable to investigate automatic
evaluations in both children, adolescents and adults. In Study 2, the task was used to
compare automatic evaluations of positive, neutral, negative and anxiety-relevant stimuli
between clinically anxious and non-clinical youth. Automatic evaluations of positive,
neutral and negative stimuli did not differ between anxious participants and matched
controls. Anxious participants, however, showed a negative threat-related evaluation
bias. Compared to controls, anxious youth had stronger negative evaluations of anxiety-
relevant stimuli (not of other types of stimuli). Furthermore, in anxious participants
evaluations of anxiety-relevant stimuli were more negative than those of negative
stimuli, whereas this difference was not found in controls. Increased [parent-reported]
anxiety was associated with a stronger threat-related negative evaluation bias. Because
results support the idea of a threat-related evaluation bias in clinically anxious youth,
they provide preliminary evidence for increased BIS-activity in anxiety disorders.
Furthermore, because in the clinically anxious sample, reactions to threatening stimuli
were stronger than reactions to neutral or generally affective stimuli, results are
consistent with the separable subsystems hypothesis.

**BIS-activity: Attention**

The dot probe detection task was used to assess the attentional output of the BIS in
clinically anxious and non-anxious adolescents [Chapter 6]. Although there is strong
evidence for biased attentional processing in anxious [not in non-anxious] adults, results
from previous studies with children and adolescents are far less consistent. In the study
in Chapter 6, both anxious and non-anxious adolescents showed an initial attentional
bias towards threat. This bias disappeared in both groups when strategic control of
attentional allocation was possible. Although threatening [i.e. BIS-relevant] stimuli did
initiate BIS-output [initial attentional bias] consistent with RST, the study provided no
evidence for overactivity of the BIS in anxious youth. Furthermore, attentional processes
were not associated with BIS-sensitivity.

**LINKING BIS WITH ANXIETY DISORDERS**

Gray proposed the BIS as the underlying factor in a continuum ranging from normal
behaviour and personality over subclinical traits to clinical syndromes [i.e. anxiety
disorders]. Following such a dimensional approach, there is a direct link between
personality and psychopathology (spectrum hypothesis). There are, however, several other models describing the association between personality and psychopathology. In Chapter 6, we tested a model proposing an indirect link between BIS and anxiety (Lonigan et al., 2004). According to the model, regulative temperament (i.e. effortful control) is assumed to moderate the effect of temperamental reactivity (as a manifestation of BIS) on anxiety. In addition to that, cognitive processes (i.e. attentional bias towards threat) are thought to mediate the relation between reactive temperament and anxiety. In our sample, reactive temperament (thus BIS) predicted internalizing problems, with no role of effortful control in low-anxious and extremely high anxious youth, but a protective role of effortful control in anxious youth in the medium range of clinical anxiety. This suggests that the moderating role of regulative temperament only applies in the medium ranges of temperamental reactivity, but not when reactivity is low (as in non-clinically anxious youth) or extremely high (as in clinically anxious youth with severe problems). Our results, however, did not provide evidence for the indirect link between temperament and anxiety trough attentional processes. Although (strategic) attentional processes were related with temperament, we did not find a significant correlation between attentional bias and anxiety.

IMPLICATIONS FOR ASSESSMENT AND TREATMENT

Implications from the RST-framework

At first look, the dimensional approach of RST in which psychopathology symptoms are seen as extreme manifestations of personality traits suggests a rather pessimistic prognosis regarding treatment of anxiety disorders. This negative point of view is based on the idea that personality traits tend to remain relatively stable across time (e.g., McCrae & Costa, 1996). However, at closer look, there is room for more optimism. Temperamental traits (i.e. the childhood precursors of personality traits) are found to be less stable than adult personality traits (e.g., Roberts & DelVecchio, 2000). Furthermore, not all young adults who were temperamentally vulnerable as a child develop internalizing problems (e.g., Asendorpf, Denissen, & van Aken, 2008). Temperamental factors and personality traits seem to be mutable, for example due to intelligence, social competence, personal success and satisfaction (e.g., Asendorpf, 1994; Roberts, Caspi, & Moffit, 2003). That temperament or personality traits can change implies that they can be changed, which opens up the possibility that they can be changed by psychotherapy. As such, a dimensional view on the link between personality and psychopathology, does not necessarily imply a pessimistic prognosis on
the possibility of symptom change through psychotherapy.

However, a patient's personality might limit the range of his or her potential therapeutic improvement. If the aim of therapeutic intervention is to lower one's clinical symptom scores (preferably back into the normal, non-clinical distribution) then one's position on a personality dimension might constrain the range in which this reduction can occur (i.e. the therapeutic range hypothesis; Zinbarg, Uliaszek, & Adler, 2008). As such, there might be a threshold value for BIS above which it becomes more difficult to obtain clinically significant decreases in posttreatment symptom scores. This idea relates to the finding in Chapter 6, that an increase in regulative temperamental (EC) loosens its protective value when reactive temperament is too high. This suggests, that therapeutic techniques aimed at boosting effortful control might not be that beneficial with extremely anxious (i.e. highly reactive) children or adolescents. However, when a reduction in temperamental reactivity has reached (for example after CBT or exposure), training of regulative strategies might have additional therapeutic value. Furthermore, several aspects or correlates of the child's personality might have an impact on treatment progress and treatment outcome. For example, children with high BIS-levels might try to avoid failure and therefore they might be less inclined to fulfil exposure exercises. At the same time, they might want to avoid critique and punishment for this non-compliance. The FFFS-FFFS conflict that thus arises might increase anxiety with a detrimental effect on the therapeutic process. As thus, personality seems to limit the amount of therapeutic effect that can be expected when treating anxiety disorders. However, because BIS is involved in all emotional problems (both anxiety and depression), treating the primary diagnosis might lead to the reduction of other emotional problems. As such, the dimensional perspective of RST with the hierarchical model of emotional disorders implies an optimistic view on the range of therapeutic benefits.

Implications from the information processing framework

The information processing framework and the performance-based measures that are developed herein have several clinical implications for the assessment and treatment of anxiety.

Concerning the assessment of anxiety, it is frequently advocated that the indirect, implicit performance-based measures have 'incremental validity' over more direct measures as questionnaires and interviews. This claim does not mean that implicit measures reveal some sort of 'true cognition or attitude' underlying behaviour. Rather, implicit measures are complementary ways to obtain information that can not be
revealed using techniques that call for introspection. Implicit instruments are indeed the appropriate way to assess automatic, sometimes unconscious, threat-related processes (De Houwer, 2006).

A large amount of studies using performance-based measures to investigate automatic processes related to psychopathology optimistically suggest that in the future, those measures might become useful as a diagnostic tool. At the moment, however, we are far from reaching this goal. One important factor that stands in the way is the use of several different versions of the instruments. Instead of using standardized instruments, most researchers develop tailor-made versions with minor or major adaptations to the original task to study their specific research questions. Additionally, there exist no implicit instruments with norm scores, so cut-off-scores for clinical functioning cannot be determined. Related to this, at the moment, there are no data on the ability of implicit instruments to correctly identify the majority of individuals suffering from anxiety disorders [sensitivity] or correctly exclude most people without pathological problems [specificity]. In the present dissertation (Chapter 5, Study 2), it was found that not all children with anxiety disorders show a threat-related evaluation bias [sensitivity], and not all children showing a threat-related evaluation bias suffer from pathological anxiety problems [specificity]. Furthermore, although we were able to find group differences in automatic evaluations, it is difficult to establish strong associations between individual differences in automatic evaluations and self-reported anxiety [sensitivity]. Additionally, the predictive validity of automatic biases for anxiety severity is unsatisfactory to approve of the use of implicit instruments as diagnostic tools. Moreover, poor psychometric qualities of the present implicit instruments such as low internal reliability and low test-retest reliability also impede their use as diagnostic tools. Still another hindrance for the diagnostic use of implicit instruments relates to their lack of discriminant validity. At the moment, there are no automatic processes known to be specifically related to only one disorder. For example, attentional bias [at least in adults] has been found in both anxiety and depression. As such, instruments assessing automatic processes are not valid for the discrimination between disorders. Taken together, at the present moment, the conclusion is that more research has to be done aimed at improving the diagnostic utility of implicit instruments.

This prudent statement on the clinical utility of performance-based implicit measures does not imply, however, that performance-based instruments and the information-processing perspective lack practical utility. On the contrary, the information-processing perspective on anxiety clearly points to possible targets for
intervention. Cognitive behavioral therapy (CBT) techniques are aimed at changing maladaptive cognitions, both strategic and automatic. Changing biases in early stages of information processing (as the biased RST-outputs in the encoding stage) might be a highly powerful approach, since they determine how further processing will occur. A complicating factor in such approach, however, is that the processes involved in early stages of information processing are mostly automatic, and therefore relatively difficult targets. There is, however, some support for the idea that automatic processes can be altered through therapy. Although a one-session exposure in vivo treatment (1x150 minutes) failed to change threat-related automatic evaluations (Huijding & de Jong, 2009), a more extensive exposure treatment (3x90 minutes) did result in altered threat-related automatic processes (Teachman & Woody, 2003). Evidence that CBT indirectly results in actual change of automatic processes is confined to studies with adults (e.g., Gamer, Schmukle, Luka-Krausgrill, & Egloff, 2008; Teachman, Marker, & Smith-Janik, 2008). At the University of Amsterdam and the University of Groningen, in a collaboration with the BasCule, Amsterdam and Accare, Groningen, there is an ongoing research project on CBT for childhood and adolescent anxiety disorders. One of the aims of the project involves indirectly changing automatic processes (attention, automatic evaluations) with the Coping Cat protocol (Kendall, 1990). To change anxiety-related automatic and strategic processes in a more direct way, cognitive bias modification (CBM) trainings have been developed (e.g., Koster, Fox, & MacLeod, 2009). Outcomes of attentional retraining and interpretation modification programs are promising and suggest that CBM has clinical potential in the treatment of anxiety disorders in adults (Amir, Beard, Burns, & Bomyea, 2009; Beard & Amir, 2008). Interpretation training was also found to successfully alter children's conscious interpretations of ambiguous scenarios (Muris, Huijding, Mayer, & Hameetman, 2008; Muris, Huijding, Mayer, Remmerswaal, & Vreden, 2009) and to reduce children's social anxiety symptoms (Vassilopoulos, Banerjee, & Prantzalou, 2009). These studies provide preliminary evidence that therapeutic strategies aimed at reducing cognitive biases in various stages of the information processing sequence and at various points of the automatic-strategic continuum might have beneficial effects on anxiety symptoms. However, no studies have so far shown that these positive outcomes of CBM programs are actually mediated by the modification of automatic processes, which is an important remaining question that needs to be addressed.
SUGGESTIONS FOR FUTURE RESEARCH

RST-research

In this dissertation, I aimed to provide answers for research questions that developed out of an RST-account on childhood and adolescent anxiety. However, as ever, interesting and inspiring questions remained unanswered. Therefore, I will point to some unresolved issues and make suggestions for future RST-research.

Most RST-research to date was based on the original theory, and only few studies adopted the new perspective developed in the revised RST. This seems mainly due to the fact that most RST-instruments have been developed out of the original RST-account. New tailor-made instruments should be developed to test the predictions of the revised theory.

Although I tried to incorporate themes from the revised RST into my studies (e.g. the attention for the joint vs. separable subsystems hypothesis), the research questions were mainly based on the original theory. For example, the new conceptualisation of the BIS in terms of conflict is largely ignored in the present dissertation. Although Gray and Newman (2000) defined ‘conflict’ in terms of the simultaneous activation of BAS and FFFS, other RST-researchers (e.g., Corr, 2008) suggested that conflict could arise from two competing BAS activations [e.g. having to choose between going to a party of a class mate or going to the movies with a friend] or from an avoidance-avoidance conflict [e.g. wanting to stay in bed to avoid the monsters under the bed or wanting to go downstairs to mum and dad but then having to cross the dark stairway]. Future research should aim at identifying conditions in which BIS-activation conflict occurs. Once there is more clarity on this issue, it might be worthwhile to investigate whether different types of conflict (i.e. BAS-FFFS, BAS-BAS, FFFS-FFFS) are related to different types of anxiety disorders. For example FFFS-FFFS conflicts might be more related to panic disorder and specific phobias, while BAS-BAS conflicts might be underlying generalized anxiety disorder.

Furthermore, even when I focused on the differences between the original and the revised theory and tried to distinguish between BIS_Anxiety and FFFS_Fear in Chapter 3, the FFFS-concept remained somewhat cloudy. Although factor analysis revealed two factors that were interpreted earlier as BIS_Anxiety and FFFS_Fear, this interpretation can be called into question. Consistent with the hierarchical model, FFFS_Fear items were related to social phobia, specific phobia and panic disorder, yet they were also related to generalized anxiety disorder (GAD) and depression. Thus, the two factors
found in the factor analysis might not differentiate very well between BIS and FFFS. Indeed, the content of alleged FFFS-factor is a mixture of BIS and FFFS items, referring to potential threat (BIS) and fear (FFFS). Thus, interpretation of the second factor in terms of FFFS seems unjustifiably given the item content and the associations with GAD. Future questionnaire research should therefore be aimed at developing theoretically sound FFFS_Fear items, and more generally, to instruments that measure constructs that pertain to revised RST.

An important feature of the present dissertation is that it looks at RST from an information processing perspective. As such, the cognitive aspects of the BIS received the attention they deserve. However, research suggests that anxiety is related not only to the processes discussed in the present dissertation, but also to other cognitive distortions, as biased strategic interpretations and memory biases. Future research should investigate how those biases are related to RST-concepts. As such, the information-processing model of RST can be expanded to include later stages of information processing.

One of the most attractive features of RST is that it is a neuropsychological theory. I focused on the psychological components of the theory. Future research might benefit from incorporating both the psychological and biological components, and study for example the associations between psychological (e.g., evaluation bias) and neurological or psychophysiological (e.g., cortisol secretion) manifestations of the BIS.

In my dissertation, I made an attempt to elucidate the link between personality and psychopathology. The model tested in Chapter 6 assumed that attentional bias mediates the association between reactivity and anxiety, while allowing for moderation by regulative control. Future research should test other potential cognitive (e.g. evaluation bias) or non-cognitive (e.g. parenting-style, peer relations) mediators and moderators (e.g. cultural and ethnic factors). Future research should also study other personality-psychopathology models. Although there is evidence for the idea that psychopathological symptoms can be seen as extreme poles of normal personality traits, it might be that certain moderating factors (e.g. regulative capacities) have a different influence on the personality-psychopathology link at different points of the trait dimension. As was suggested by our data, it might be that above some threshold value of a personality trait, some moderating factors loose their protective capacities, whereas below some threshold value there is no need for protective moderation. As such, future research should consider the possibility of diverging links between personality and psychopathology in subclinical versus clinical populations.
Research on automatic processes in anxiety

With its information processing perspective, my dissertation fits into the recently developed but rapidly growing research field studying automatic processes in psychopathology. In the past decade, evidence has shown that disorders are related not only with distortions in conscious, strategic cognitions, but also with dysfunctional automatic processes (e.g., Huijding, 2006; Muris & Field, 2008). However, it remains a question whether such automatic biases are merely a cognitive by-product of anxiety or whether they are a causal factor in the etiology of psychopathology. Including indirect instruments to assess automatic processes in longitudinal prospective studies might provide preliminary information on the predictive validity of automatic biases for the onset of anxiety problems. However, in order to draw causal conclusion, experimental manipulation of automatic processes are necessary. In adult anxiety research, it has been shown that the modification of attentional bias results in symptom relief suggesting that automatic biases in attention are indeed causally involved in anxiety (Amir et al., 2009; Schmidt, Richey, Bruckner, & Timpano, 2009). In studies with children, it seems more difficult to establish this causal link. Some studies succeed in experimentally changing automatic cognitions but this change was unrelated to anxiety (e.g., Askew & Field, 2007; Lawson, Banerjee, & Field, 2007). Therefore, the causal role of automatic processes in childhood and adolescent anxiety (and other disorders) remains an important issue for future research.

Several paradigms have been developed to assess automatic processes. For example, different attentional tasks are used each tapping into different aspects of the attentional process (Yiend, 2010). An individual’s ability to suppress irrelevant distractor information is, for example, studied in filtering tasks (e.g., the emotional Stroop task), while the ability to detect relevant information is studied with visual search tasks (e.g., the face-in-the-crowed paradigm). Cueing tasks (e.g., the dot probe task) investigate how well participants can detect a target when their attention was drawn to a particular location (traditionally a threatening vs. neutral stimulus). A large body of studies using those paradigms have greatly enhanced the knowledge on attentional processes in childhood and adolescent anxiety (Puliafico & Kendall, 2006). However, up until now, less is known on what happens when anxious children and adolescents have to allocate their attentional resources to meet multiple demands. The ability to flexibly allocate processing resources to meet multiple demands is adaptive and important in everyday life because ‘getting stuck’ in, for instance, something threatening, means that ongoing behaviour is interrupted as other pieces of the environment cannot be
processed. For example, the attentional blink paradigm investigates how well participants can fulfil two demands (i.e. reacting to two sequential targets). When attending to one target takes too long, the processing of the second target is hindered, meaning that the second demand is often not fulfilled. As such, the attentional blink paradigm can provide an ecologically valid index of attentional processing in daily life. Future research might endeavour studying this multiple task aspect of anxiety-related attention in children and adolescents.

Although psychopathology researchers enthusiastically adopted the information processing paradigm to study relevant automatic processes, it has since become clear that we must remain critical with respect to the instruments we use. For example, whereas the EAST is frequently used to assess automatic evaluations, it is clear that EAST-effects can be interpreted in multiple ways. For example, EAST-responses only partly depend on the automatic activation of the stimulus valence, but also on more strategic response options (Stahl & Degner, 2007). Indirect instruments used as assessment tools for automatic processes often suffer from poor psychometric characteristics. For instance, measurement error in indirect instruments is often high, resulting, among other things, in a weak correspondence to direct, self-report instruments and in low internal reliability (Hofmann et al., 2005). Furthermore, information on test-retest reliability of indirect instruments is often lacking, as are normative data. These measurement issues point to the importance of future research into the development and optimization of reliable and valid instruments for the assessment of automatic processes.