The behavioral inhibition system in childhood and adolescent anxiety: an analysis from the information processing perspective

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**STUDY 2: BOO! INCREASED THREAT-RELATED RESPONSE INHIBITION IN CHILDHOOD ANXIETY**

**Abstract** Deficient inhibition underlies different types of childhood psychopathology. Numerous studies support the idea of underinhibition in externalizing problems. Less evidence exists for overinhibition in internalizing problems. The present study investigates behavioral inhibition in clinical anxiety. Sixty-nine children and adolescents [aged 8-18] with at least one DSM-IV anxiety disorder completed two versions of a Stop Signal Reaction Time Task: one with neutral and one with anxiety-relevant stop stimuli. General task performance [mean reaction time, within-subject standard deviation of reaction times, and percentage correct responses] 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. These results are consistent with the idea of threat-related overinhibition in anxiety.

Deficiencies in inhibition are a central theme in several theories about childhood psychopathology (e.g., Nigg, 2000; Oosterlaan & Sergeant, 1996; Oosterlaan, 2001). Quay (1988, 1997) developed a theoretical framework for internalizing and externalizing behavior in children, based on Gray's (1982, 1987) model of behavioral inhibition and activation. Gray posits that behavior originates from activity in two different neurobiological systems: the Behavioral Inhibition System (BIS) and the Behavioral Activation System (BAS). The BIS is activated by signals of punishment (i.e., warning signals for potential negative affective events or threat). In addition, the BIS reacts to novel, unknown stimuli, to highly intense stimuli and to innate fear stimuli (including stimuli involved in social interaction). The BAS is activated by signals of reward and by appetitive stimuli. BIS-activity can lead to feelings of anxiety and initiates behavioral inhibition. BAS-activity is linked with positive feelings and contributes to impulsivity and approach behavior. Quay (1988, 1997) links childhood emotional and behavioral problems to inadequate activation of the BIS, the BAS or both systems. Overactivity of the BIS (overinhibition) is assumed to be responsible for internalizing problems (e.g., anxiety disorders) and their accompanying pattern of avoidant and inhibited behavior. Underactivity of the BIS and overactivity of the BAS (or a combination of both) are thought to underlie externalizing problems (e.g., Attention Deficit Hyperactivity Disorder and Conduct Disorder) and their accompanying impulsive and uninhibited behavior.

The most extensively used paradigm to study behavioral inhibition is the Stop Signal Reaction Time Task (Logan & Cowan, 1984; Logan et al., 1984). In the Stop Task, participants have to respond to a primary task, which consists of a two-choice reaction time task. On presentation of a go signal, participants have to press one of two response buttons as quickly and accurately as possible. On some trials, a stop signal is presented, which indicates that participants have to withhold their response to the go signal. Ability to inhibit is indexed by the latency of the stop process with shorter latencies indicating enhanced inhibitory capacities.

In contrast to the large number of stop task studies on inhibitory deficits in externalizing problems (for recent reviews see e.g., Alderson et al., 2007; Lijffijt et al., 2005), stop task studies on inhibition in anxiety are scarce and have yielded virtually no support for the hypothesized increased behavioral inhibition in childhood anxiety. Although comorbid anxiety problems seem to decrease the inhibition deficits typically found in ADHD, anxious children [with or without ADHD, aged 6-14] showed no enhanced inhibition compared to control children (Korenblum et al., 2007; Manassis et

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2Gray also described a third system, the Fight-Flight System (FFS) that is activated by unconditioned aversive stimuli and initiates fight or flight, but this system was not incorporated in Quay's model (1988).
There are several possible explanations, both methodological and theoretical, for the failure to find firm evidence for increased behavioral inhibition in anxiety (e.g., Oosterlaan et al., 1998). Most studies focus on deficient inhibition in externalizing problems, and include participants with emotional problems only as pathological controls for participants with ADHD (e.g., Korenblum et al., 2007). In addition to that, stop task studies typically involve only small samples (e.g., Manassis et al. 2000), and thus may have been underpowered to detect possible group differences between anxious and non-anxious participants. Consistent with this, a dimensional perspective on psychopathology and inhibition revealed that inhibition was increased in children (aged 6-12) with increasing levels of internalizing problems (Kooijmans et al., 2000). Next to these methodological issues, there is a more theoretical explanation for the lack of evidence for increased inhibition in anxiety, directly related to Gray's suggestion that the BIS gets activated by anxiety-relevant stimuli (Gray, 1982; 1987). Therefore, the hypothesized increased inhibition in anxiety would only become apparent in threatening situations (Oosterlaan et al., 1998). Consistent with this, increased inhibition in youth with anxiety disorders is found in a study using the Change Task, a more complex variant of the Stop Task. In the Change Task, participants are instructed not only to inhibit their response in reaction to a stop signal, but also to immediately re-engage in another response (Oosterlaan & Sergeant, 1998). It can be assumed that participants experience this more difficult task as more threatening, especially when they are anxious. Surprisingly, the idea that inhibition in anxious participants would only be enhanced in threatening situations was never tested directly.

The present study compares behavioral inhibition in neutral and threatening situations using two versions of the Stop Signal Task: a neutral task and an anxiety-relevant task. We aimed at limiting the influence of the threat only to the inhibitory process and not on other aspects of task performance. Therefore, instead of administering the task in a threatening situation, we chose to manipulate the emotional valence of the stop stimulus. In the neutral task, stop stimuli were emotionally neutral pictures. In the anxiety task, they were threatening (for detailed description of the tasks and the stop stimuli, see method section). Usually, a single stop stimulus is used throughout the task. In the present study, instead of just one single stop stimulus, ten neutral and ten anxiety-relevant stop stimuli were used. The use of different stop signals may prevent habituation that could attenuate the emotional impact of the stimuli.

Behavioral inhibition was examined in a large sample of clinically referred children...
and adolescents diagnosed with a DSM-IV diagnosis of anxiety disorder (for inclusion criteria, see method section). It was hypothesized that these anxious participants would show increased inhibition in the anxiety-relevant compared to the neutral task. Furthermore, to test the prediction based on Gray's model [1982, 1987] that activity in the BIS is related to the behavioral output of behavioral inhibition, the association between inhibitory control and sensitivity of the BIS as measured with a self-report questionnaire was examined. It was predicted that high BIS-sensitivity would be associated with increased inhibition compared to low BIS-sensitivity.

Method

Participants
Sixty-nine 8 to 18 years old ($M=12.70$, $SD=2.87$) anxiety disordered children and adolescents (28 boys) were included in the study. They were referred to one of two child psychiatric outpatient units in the Netherlands (de Bascule, Amsterdam and Accare, Groningen). Anxiety diagnoses according to the DSM-IV criteria were based on a semi-structured diagnostic interview, the Anxiety Disorders Interview Schedule for DSM-IV – Child and Parent Version (ADIS-IV:C/P, Silverman & Albano, 1996; Siebelink & Treffers, 2001). Children and parents were interviewed separately. Based on both interviews, a clinical diagnosis with clinician severity rating (CSR, ranging between 1 and 8) was derived. Children were included in the study when their CSR was 4 or more (which is indicative of clinical anxiety diagnosis) on a least one anxiety disorder. Primary diagnoses included Social Phobia (SP, 42.86%), Separation Anxiety Disorder (SAD, 12.33%), Specific Phobia (14.29%), Generalized Anxiety Disorder (GAD, 12.24%) and Panic Disorder with or without Agoraphobia (PD, 14.29%). There was considerable anxiety comorbidity: 50% of the anxious participants received two or more anxiety diagnoses or an additional mood disorder diagnosis. Although ADHD-symptoms were frequently reported, they did not reach clinical levels, so none of the participants suffered from comorbid attention deficit hyperactivity disorder.

All participants were free of anxiolytic medication and had not received cognitive behavioral therapy for their anxiety disorder in the past 6 months prior to inclusion in the study. Before treatment, children and parents were asked to participate in a study on mediators and moderators of CBT for anxiety disorders. Children completed the questionnaire and the tasks during an individual pre-treatment test session, in the presence of one of the researchers. The study design was reviewed and accepted by the medical ethics committee of both participating clinics. Written informed consent
was obtained from both children (aged 12 and older, \(n=44\)) and their parents. After participating in the present study, children received cognitive behavioral therapy for their anxiety problems.

**Two versions of the Stop Task**

In the Stop Task, participants have to respond to a primary task (go task), as quickly and accurately as possible after presentation of a go signal. In the present study, the go signal was a picture of an airplane, presented in the middle of the screen (Kooijmans et al., 2000). Participants were instructed to press the left response button if the nose of the airplane pointed to the left and the right response button if the nose pointed to the right. On 25% of the trials, a stop signal was presented. On appearance of the stop signal, participants were instructed to inhibit their response to the go signal. The delay between the go signal and the stop signal influences the probability of successful inhibition. The longer the stop signal delay, the more difficult it becomes to inhibit responses. In the present study, this interval was determined by a tracking algorithm based on the participant’s stopping performance (e.g., Logan et al., 1997). The initial delay between go and stop signal was set at 250 ms. If participants failed to inhibit on a stop trial, the stop signal delay for the next stop trial was shortened by 50 ms, increasing the probability of successful inhibition. After successful stopping, the stop signal delay was lengthened by 50 ms, decreasing the probability of successful inhibition. The tracking algorithm converges on the delay at which the chance of inhibition is 50%.

Two versions of the Stop Task (i.e. a neutral and an anxiety task) were administered. Both versions differed regarding the stop signals. Stop signal stimuli were pictures selected from the IAPS (Lang et al., 2005), based on normative scores. IAPS-numbers, description, and mean valence and arousal ratings from the IAPS manual are shown in Table 4.1 (p.48). The IAPS has been validated for use in Dutch adolescents (Kolman, 2009). All selected stimuli were considered suitable for use with children according to experienced child therapists. Neutral stimuli had a medium valence and a low arousal score. Anxiety relevant stimuli were related to the five factors of the 'Fear Survey Schedule for Children – Revised': Failure/Criticism, the Unknown, Minor Injury/Small Animals, Danger/Death, and Medical Fears (Ollendick et al., 1989). Because the IAPS contains no suitable picture covering Failure/Criticism, one was custom made (a school report card with low grades).

Participants were told that withholding or stopping a response is difficult and that sometimes they would be able to stop and sometimes they would not, so they should
not worry if they would not succeed. They were explicitly instructed to respond immediately when the go stimulus appeared and not to wait for the stop signal. To optimize performance, extensive feedback was provided throughout the tasks. Standardized instructions were used.

Prior to administration of the neutral and the anxiety stop tasks, there were two practice tasks of 40 trials each. In the first practice task, participants practiced the go task. In the second practice task, the stop task was introduced. Stop stimuli in the practice task were neutral pictures selected from the International Affective Picture System (IAPS; Lang et al., 2005; IAPS numbers: 5531, 7002, 7053, 7096, 7205). Following the practice tasks, the neutral and the anxiety task were administered. Task order was counterbalanced over participants. Both tasks consisted of two experimental blocks of 80 trials. The 60 go trials and 20 stop trials of each block were presented in a fixed-randomized order. Each experimental block was preceded by 20 trials used for establishing the tracking algorithm. Those 20 trials were not included in the data analysis.

Task performance was indexed by mean reaction time (MRT), within-subject standard deviation of reaction times (SDRT) and percentage correct responses (%C) on go trials. Ability to inhibit was indexed by the stop signal reaction time (SSRT) reflecting the latency of the response to the stop signal. Since the response to the stop signal is a covert response (i.e. withholding the response to the go signal), SSRT cannot be observed, but has to be estimated by subtracting the mean delay between go and stop signal from the mean RT on go trials \( \text{SSRT} = \text{MRT} - \text{mean delay} \) (Logan et al., 1984).

**BIS/BAS-scales**

Sensitivity of the Behavioral Inhibition and the Behavioral Activation System was indexed by the Carver and White (1994) BIS/BAS-scales (Dutch child version: Muris et al., 2005). This self-report questionnaire consists of 20 items that have to be scored on a 4-point scale (1=not true, 2=somewhat true, 3=true, 4=very true). Seven items make up the BIS-scale, and include statements such as 'I worry about making mistakes'. Thirteen items make up the BAS-scale, and include statements such as 'I often do things for no other reason than that they might be fun'. Scores on the BIS/BAS-scales are meaningfully related to symptom measures and personality traits in both community (Muris et al., 2005) and clinically anxious youth samples (Vervoort et al., 2010). In the present sample, internal consistency indexed by Cronbach’s \( \alpha = .70 \) for BIS-scores and \( \alpha = .83 \) for BAS-scores. Data for the BIS/BAS-scales were missing for
two participants (1 girl aged 8 and 1 boy aged 13).

Statistical Analysis

Prior to statistical analysis of the stop task data, we checked whether the tracking algorithm successfully established the chance of inhibition at 50%. Two boys (aged 9 and 10) were excluded from further analyses because they inhibited in less than 45% of the stop trials. Two girls (aged 8 and 13) were excluded because they were outliers on total SSRT over both tasks (SSRT > M + 2SD, SSRT=463 and SSRT=520). Two girls (aged 9 and 14) were excluded because they were outliers on total %C (%C < M-2SD, %C=47.08 and %C=73.33). Consequently, analyses were run with 63 participants.

Go task performance was studied by three separate one-way repeated measures ANOVAs with task (neutral task vs. anxiety task) as within-subject variable and MRT, SDRT and %C as dependent variables. Differences between both tasks in term of inhibitory control as measured by SSRT were tested with a one-way repeated measures ANOVA with task (neutral task vs. anxiety task) as within-subject variable. Two-tailed significance is reported ($p<.05$), unless otherwise specified. Generalized eta squared ($\eta^2$) is used as index of effect size for significant effects (Bakeman, 2005; Olejnik & Algina, 2003). In addition to that, Pearson correlation coefficients describe relations between SSRT and BIS/BAS-scores. Because a directional hypothesis was formulated (inhibition increases with higher BIS), one-tailed significance is reported ($p<.05$) when describing the relation between SSRT and BIS-scores.

Results

Sensitivity of the Behavioral Inhibition and Behavioral Activation System

In the present clinical sample, BIS-scores were higher ($M=10.89$, $SD=3.83$) than in the community sample of Muris et al. (2005, $M=6.90$, $SD=3.87$, $t(351)=7.69$, $p<.001$). BAS-scores ($M=16.81$, $SD=6.20$) were comparable to those reported by Muris et al. ($M=16.85$, $SD=6.39$, $t(351)=0.05$, $p=.96$).

Go Task Performance and Inhibition in the neutral and the anxiety task

Table 4.4 shows the major dependent variables, separately for both tasks. There were no differences between both the neutral and anxiety task on indices of go task performance. We also performed repeated measures ANOVAs with task as within-subject variable and task order (neutral - anxiety versus anxiety - neutral) as between-subject variable. Results showed no effects of task order. There were no practice effects on %C and SSRT, but MRT and SDRT decreased from the first to the second task.
performance. Response inhibition was enhanced when stop signals were anxiety-relevant compared to when stop signals were neutral, as indicated by the small significant main effect of task on SSRT, $\eta^2_g = .04$.

Table 4.4 Go task performance and Inhibition in the neutral and the anxiety task

<table>
<thead>
<tr>
<th></th>
<th>neutral task</th>
<th>anxiety task</th>
<th>repeated measures ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRT (ms)</td>
<td>436.71 (94.22)</td>
<td>437.58 (92.25)</td>
<td>$F(1,62) = 0.01, p = .91$</td>
</tr>
<tr>
<td>SDRT</td>
<td>88.63 (37.45)</td>
<td>85.11 (36.51)</td>
<td>$F(1,62) = 1.20, p = .28$</td>
</tr>
<tr>
<td>%C</td>
<td>92.04 (3.33)</td>
<td>91.35 (3.62)</td>
<td>$F(1,62) = 2.62, p = .11$</td>
</tr>
<tr>
<td>SSRT (ms)</td>
<td>232.59 (72.41)</td>
<td>212.74 (44.94)</td>
<td>$F(1,62) = 6.89, p = .01$</td>
</tr>
</tbody>
</table>

Note. MRT: mean reaction time; SDRT: within-subjects standard deviation of reaction times; %C: percentage correct responses on go trials; SSRT: stop signal reaction time.

Response Inhibition and BIS-sensitivity

High BIS-sensitivity was associated with increased response inhibition, as shown by the negative correlations between BIS-scores and SSRT (neutral: $r = -0.23$, $p = .04$, anxiety: $r = -0.21$, $p = .05$, both one-tailed). Response inhibition was not related with BAS-sensitivity (neutral: $r = -0.02$, anxiety: $r = -0.13$, both $p > .05$).

Discussion

The present study tested the hypothesis with regard to overinhibition in children and adolescents with anxiety disorders. Consistent with models describing the role of the Behavioral Inhibition System in anxiety (e.g., Gray, 1982; Quay, 1988), the present sample of clinically anxious youth reported higher sensitivity of the BIS than a community sample (Muris et al., 2005). In addition, behavioral inhibition as measured with the Stop Task was increased in a threatening situation compared to in a neutral situation, as indexed by a faster SSRT in the anxiety-relevant than in the neutral version of the task.

Although inhibitory performance of anxious youth has been studied in previous studies (e.g., Korenblum et al., 2007; Manassis et al., 2000), this was done mainly to compare the performance of participants with ADHD with the performance of another clinical group. The present study is the first to focus explicitly on inhibition in children and adolescents with anxiety disorders. Most studies comparing inhibitory performance between anxious youth and normal controls failed to find firm evidence for increased behavioral inhibition in anxious youth (for review, see Oosterlaan et al., 1998). In this present study, inhibition in clinically anxious children and adolescents is found to be
increased when stop signals are threatening stimuli. This finding is consistent with BIS-models of anxiety (Gray, 1982, 1987; Quay, 1988).

Self-reported sensitivity of the Behavioral Inhibition System was associated with increased inhibition as measured with the Stop Task. The negative correlation between BIS-scores and SSRT suggests that the high sensitivity in the BIS, characteristic of clinically anxious youth, is associated with a faster inhibition process. It remains unclear, however, which mechanisms are responsible for the increased threat-related inhibition found in the present study. Research on attentional processes in anxiety suggests that anxiety is associated with a faster detection of threat stimuli (for reviews, Bar-Haim et al., 2007; Puliafico & Kendall, 2006; Yiend, 2010). This faster detection of threatening stimuli compared to neutral stimuli could lead to earlier initiation of the inhibition process. Alternatively, the faster inhibition process in the anxiety-related task might be the result of the combination of the use of threatening stimuli and the hyperactivity of the BIS, which is thought to be characteristic for anxiety disorders (e.g., Gray, 1982, 1987; Quay, 1988). Future studies should clarify this issue, by investigating whether the link between inhibition and anxiety is mediated by attentional processes.

In previous studies, measures of BAS-sensitivity were positively correlated with SSRT (e.g., Avila & Parcet, 2001), indicating that overactivity in the BAS was associated with poorer inhibition. The absence of this relationship in the present study could be due to the stronger BIS-sensitivity in the anxiety-disordered sample overruling possible effects of BAS-sensitivity. This finding is consistent with ideas formulated by Corr (2001; 2002) concerning the relations between BIS and BAS. Corr stated that under normal conditions BIS and BAS jointly influence behavior. In extreme cases, as with the hyperactive BIS associated with anxiety disorders, however, Corr expected that the systems would act independently as separate systems, because the hyperactive BIS-system would be dominant, neutralizing the effect of BAS-activity.

Although results of the present study clearly suggest that threat-related inhibition is enhanced in a clinically anxious, the present work has some limitations. First, inhibitory functioning of the clinically anxious sample was not compared directly with that of a normal control sample. In a pilot study administrating the neutral and the anxiety-relevant version of the Stop Task a community sample of children and adolescents (aged 7-18), we found no differences between both versions (Vervoort, 2009). Future studies should complement the within-group comparison from the present study by investigating between-group differences in a case-control design, with large samples of carefully selected clinically anxious participants and participants not diagnosed with anxiety. Second, although the stop signal paradigm is a valid and reliable measure of
inhibition (e.g., Kindlon et al., 1995), it measures only one form of response inhibition, i.e. behaviorally withholding a prepotent, but discrete response. The paradigm, however, provides no information of other types of response inhibition, such as interrupting continuous responses. Related to this issue, the stop signal task measures response inhibition, so it remains to be tested whether our results can be generalized to other forms of inhibition, as interference control, cognitive inhibition and oculomotor inhibition (Nigg, 2000). Research on oculomotor inhibition, for example, shows decreased inhibitory efficiency in anxious adolescents (e.g., Jazbec, McClure, Hardin, Pine, & Ernst, 2005). Since both response and oculomotor inhibition are affected, it can be speculated that there is a central inhibition problem in anxiety. The exact nature of the inhibition problem in anxiety, however, remains unclear and awaits further investigation.

In spite of its limitations, the present research provides empirical evidence for increased threat-related behavioral inhibition in childhood and adolescent anxiety. It thus supports models of anxiety that associate activity in the Behavioral Inhibition System with anxiety (e.g., Gray, 1982, 1987; Quay, 1988). Knowledge of threat-related processes increases our understanding of the development, maintenance and reduction of anxious psychopathology. Ultimately, instruments assessing anxiety-related processes, like the anxiety-relevant Stop Task, might become useful in the detection of individuals at risk for anxiety disorders.