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

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Citation for published version (APA):

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Download date: 25 Apr 2020
Anxious phenomena such as fear and worry are common in childhood and adolescence. In most cases, these phenomena are part of normal development and most children 'grow out' of these fears [e.g., Gullone, 2000; Muris, Merckelbach, Gadet, & Moulauter, 2000]. A substantial number of children, however, suffer from high levels of chronic and impairing anxiety, making anxiety disorders the most prevalent forms of youth psychopathology [e.g., Cartwright-Hatton, McNicol, & Doubleday, 2006] often lasting into adulthood [e.g., Muris, 2006a; Weiss & Last, 2001]. This fact has raised research interest, resulting in a wealth of empirical studies and the formulation of numerous theories describing the etiology of childhood and adolescent anxiety disorders [e.g., Vasey & Dadds, 2001].

An important theory on psychopathology with clear implications for the study of anxiety disorders was formulated by Jeffrey Gray [e.g., 1982, 1987] in what has become known as the Reinforcement Sensitivity Theory (RST). RST has greatly inspired psychopathology research, both in adults [for review, see Bitttebier, Beck, Claes, & Vandereycken, 2009] and in youth [e.g., Chorpita, 2001; Lonigan & Phillips, 2001; Quay, 1988]. Gray stated that all behavior originates from activity in three major brain systems: the Behavioral Approach System (BAS), the Behavioral Inhibition System (BIS), and the Flight/Fight System (FFS). Stable individual differences in the activity of the systems are assumed to be related to different personality dimensions. For example, individuals with a highly active BIS are thought to have an anxious personality. Furthermore, overactivity in one of the systems is thought to be the core component of psychopathology. For example, an overactive BIS is thought to be involved in anxiety disorders [e.g., Gray, 1982; Gray & McNaughton, 2000].

Quay (1988, 1997) used Gray's BIS and BAS concepts to develop a theoretical framework for externalizing and internalizing problems in children. With regard to childhood anxiety disorders, Quay (1988, p. 120) stated: 'It is abundantly clear that the broad-band internalizing disorder of Anxious/Withdrawn involves an overactive BIS - almost by definition'.

I Introduction
In this dissertation, I will elaborate on the proposed link between an overactive BIS and childhood anxiety disorders. Before doing so, a more extensive background of Gray's Reinforcement Sensitivity Theory is provided. Because the aim of my dissertation is to describe the role of BIS in childhood and adolescent anxiety disorders, reference to FFS and BAS will be made sparingly and only if necessary for the understanding of how BIS is involved in anxiety disorders. Gray's RST is a neuropsychological theory, describing behavior at both a neurological and a psychological level. The discussion in the present dissertation focuses on the psychological component of the model, without reference to the specific neural structures and neurological processes that mediate the psychological processes.

**GRAY'S REINFORCEMENT SENSITIVITY THEORY**

**The original model (1982)**

Gray's original account of the Reinforcement Sensitivity Theory (RST; 1970, 1982) describes how all human behavior follows from activity in three major neuropsychological systems: the Fight/Flight System (FFS), the Behavioral Inhibition System (BIS) and the Behavioral Approach System (BAS). These three systems are sensitive to different types of stimuli. The FFS reacts to unconditioned aversive stimuli, indicative of an immediate threat. The BIS reacts to conditioned aversive stimuli, to novel, unknown stimuli, to highly intense stimuli and to innate fear stimuli. Being conditioned stimuli, they are warning signals for potential threat and punishment. Gray calls these BIS-activating stimuli 'adequate stimuli for anxiety'. The BAS reacts to appetitive stimuli. Activity in the systems gives rise to different affective states. FFS and BIS give rise to negative affect, whereas BAS underlies positive affect. As such, FFS-activity is related with feelings of fear, panic and anger, BIS-activity with feelings of anxiety and BAS-activity with hope and joy. Next to these affective responses, activity in the three systems has behavioral consequences. Activity in the BAS is related to impulsivity and approach behavior. Activity in the FFS is related to escape from and aggression towards a present threat, whereas activity in the BIS is related to inhibition and avoidance from a potential threat. More specifically, the BIS has three functional outputs: activity in the BIS (1) immediately inhibits ongoing motor behavior (behavioral inhibition), (2) is associated with an increment of arousal level, resulting in a more negative evaluation of the environment (stimulus evaluation) and (3) is concerned with
orienting-investigative behavior, increasing and focusing attention to the activating stimuli (selective attention). These three BIS-outputs are more or less automatic responses to signals of threat.

Activity in the different systems is thought to not only have short term effects on affective state and immediate behavior, but also to have more long term, trait-like consequences. Activity in the BIS and the BAS are linked to the personality dimensions Anxiety and Impulsivity respectively. Individuals who are highly susceptible to aversive stimuli and signals of punishment (i.e. individuals with a high reactive BIS) can be seen as having an anxious personality, whereas high susceptibility to appetitive stimuli or signals of reward (i.e. high reactive BAS) constitutes an impulsive personality. Gray's BIS/Anxiety and BAS/Impulsivity are comparable to Watson and Clark's (1984) Negative Affect (BIS) and Positive Affect (BAS). BIS and FFS seem to be the two components [anxiety and anger] of a general distress temperamental trait that Rothbart (2004) labeled as Negative Affectivity and Buss and Plomin (1975, 1984) as Emotionality.

Gray linked activity in the BIS, FFS and BAS [and their related personality types] to psychological disorders. He proposed that individuals with a certain personality type are more likely to manifest psychopathological symptoms consistent with the activity in the related system. Adding to this idea that personality characteristics are important risk factors for psychopathology, hypersensitivity of or overactivity in one of the systems is suggested to be the core factor of a certain psychological disorder. As such, individuals with a highly active BIS are thought to be anxiety-prone and particularly at risk for anxiety disorders. Pathological anxiety is assumed to be caused by an extremely sensitive, hyperactive BIS [e.g., Gray, 1982, 1987].

Some important revisions

Although the core assumption formulated in the 1982 model still holds - i.e. overactivity in the BIS causes pathological anxiety - several adaptations have been made to the original model by Gray [e.g., Gray & McNaughton, 1996, 2000] and others [e.g., Corr, 2001, 2002].

Updating the 1982 model with new experimental data, Gray and McNaughton (1996, 2000) reconsidered the role of BIS and FFS (from then on called Freeze Flight Fight System, FFFS) in anxiety disorders. Other than in the original model, the FFFS is hypothesized to be activated not only by unconditioned, but also by conditioned aversive stimuli. The FFFS gives rise to feelings of fear and FFFS-responses are aimed at reaching safety by removing oneself from the source of the threat. The BIS is also
activated by the aversive stimuli (both conditioned and unconditioned), but only when there is conflict, for example when the subject’s ‘... primary purpose is to achieve some goal which requires it to move towards a source of danger – that is, when it has concurrent conflicting goals’ (Gray & McNaughton, 2000, p.84) of approaching something rewarding (e.g. working on a PhD-dissertation in order to obtain a degree) and at the same time wanting to avoid something threatening (e.g. failure and negative evaluation). Apart from this approach-avoidance conflict due to simultaneous activation of BAS and FFFS, conflict can arise from concurrent BAS-BAS or FFFS-FFFS activation. While overactivity in the BIS is assumed to be the causal factor for all anxiety disorders (as it was in the original model), overactivity in the FFFS is thought to be additionally involved in panic disorder, social phobia and specific phobia (Gray & McNaughton, 1996, 2000; Kimbrel, 2008; Zinbarg & Yoon, 2008). Research testing this new perspective is still scarce, partly because most instruments used to test Gray’s theory are based on the original 1982 model. As such, they do not yield separate scores for BIS-sensitivity and FFFS-sensitivity. In Chapter 3 of this dissertation, it will be tested whether a frequently used instrument to assess BIS/BAS-sensitivity captures both BIS and FFFS.

In the 1982 model, Gray stated that the BIS and the BAS were two functionally separate systems, exerting an independent influence on behavior. This separable subsystems hypothesis (SSH) suggests that responses to BIS-activating stimuli should depend on an individual’s BIS-sensitivity but not on one’s s level of BAS-sensitivity, while responses to BAS-activating stimuli should depend on one’s BAS-sensitivity, independent of one’s BIS-sensitivity. The same holds for the sensitivity and activity of the system: individuals with high BIS-levels are more reactive to BIS-activating stimuli than to BAS-activating stimuli, while individuals with high BAS-levels demonstrate an opposite reactivity pattern. The SSH leads to the assumption that, at any moment, behavior is controlled by the one system that is most active at the time, be it due to activating stimuli or to an individual’s sensitivity. Evidence for such dominance of one system over the other is provided by empirical studies showing that high anxiety (i.e. a highly reactive BIS) is associated with stronger reactions to aversive stimuli than to appetitive stimuli. For example, in some studies physiological reactions to aversive stimuli are found to be strongest in clinically anxious children (e.g., Waters, Henry, & Neumann, 2009). However, other studies yielded inconsistent results. For example, children with anxiety disorders are sometimes found to react indifferently to aversive and non-aversive stimuli (e.g., Craske et al., 2008) or to allocate attention towards both aversive and appetitive stimuli (e.g., Waters, Lipp, & Spence, 2004). This last finding is consistent
with Corr’s joint subsystems hypothesis (JSH, 2001, 2002, 2004) suggesting that there can be a joint influence of the BIS and BAS on behavior. Such functionally interdependent effects of BIS and BAS are expected in case of moderately aversive and appetitive stimuli or in individuals with normal levels of BIS/BAS-activity. However, when strong aversive or appetitive stimuli are used, effects consistent with the SSH are expected. So, in case of very strong BIS-activating stimuli, behavior is predicted to be mediated only by the BIS, with no influence of the BAS. Comparable effects assumingly occur in individuals with hyperactive BIS. Therefore, in individuals with extreme BIS-activity, as in clinically anxious individuals, the overactive BIS is predicted to exclusively control behavior, overruling the effects of the individuals’ BAS-activity. In Chapter 3, the separable subsystems hypothesis (SSH) will be tested against the joint subsystems hypothesis (JSH) in a sample of clinically anxious and non-clinical children and adolescents. In the experimental studies of the present dissertation (Chapters 4-6), predictions of the SSH are tested. Therefore, it will be investigated whether anxious children react stronger to BIS-activating than to neutral, positive or negative stimuli and whether BIS-activating stimuli yield stronger effects in anxious than in non-anxious participants.

LINKING BIS WITH ANXIETY DISORDERS

The link between the BIS and anxiety disorders as described in the RST, is rather straightforward: hyperactivity in the BIS underlies all anxiety disorders (e.g., Gray, 1982, 1987; Gray & McNaughton, 2000). So, there is no fundamental difference between normal and pathological anxiety: in this dimensional view, anxiety is always connected to activity in the BIS. Anxiety disorders ‘are extreme manifestations of aspects of normal anxiety’ (Gray & McNaughton, 2000, p.285).

A hierarchical model of anxiety and emotional disorders

Overactivity in the BIS is thought to be common to all anxiety disorders, but each disorder is associated with its own specific features (e.g., Gray & McNaughton, 2000). For example, social phobia is thought to be related not only to BIS, but also to FFFS (Kimbrel, 2008). Evidence for such a hierarchical structure in childhood anxiety can be found in factor-analytic studies describing a general second-order factor underlying all
anxiety disorders and several first-order factors associated with each disorder (e.g., Nauta, et al., 2004).

The general factor underlying anxiety disorders (i.e. overactivity in the BIS) is also thought to be underlying major depressive disorder (e.g., Fowles, 1988, Tellegen, 1985). The idea of a general distress factor underlying both anxiety and depressive disorders is articulated in Clark and Watson’s tripartite model (1991). Based on the evidence of substantial overlap between anxiety and depression, Clark and Watson proposed a non-specific generalized distress component, i.e. Negative Affect (NA), underlying both types of emotional problems. To explain the evidence of meaningful differentiation between anxiety and depression, they proposed two specific factors, each relating to either anxiety or depression. They hypothesized that anxiety is uniquely related to Physiological Hyperarousal (PH) while depression is uniquely related to low Positive Affect (PA). Although the evidence for PH in childhood anxiety is less convincing than in adult anxiety (e.g., Chorpita, 2002; Chorpita, Plummer, & Moffit, 2000; Ollendick, Seligman, Goza, Byrd, & Singh, 2003), there is increasing support for applicability of the tripartite model in childhood anxiety and depressive disorders (e.g., Chorpita, Albano, & Barlow, 1998; Joiner, Catanzaro, & Laurent, 1996; Yang, Hong, Joung, & Kim, 2006).

Zinbarg and Yoon (2008) related RST constructs to the tripartite model. They proposed that BIS is comparable to NA and BAS to PA. As thus, high BIS-reactivity is the common factor in anxiety and depression, while BAS-reactivity distinguishes between both emotional disorders. Anxiety is hypothesized to be associated with average levels of BAS, whereas depression is characterized by low levels of BAS. In Chapter 3, the anxiety part of this hierarchical RST-model (high BIS and low to moderate BAS levels in all anxiety disorders, FFFS in social phobia, panic disorder and specific phobias) will be tested in children and adolescents with and without anxiety disorders.

THE ROLE OF COGNITION IN ANXIETY:
AN INFORMATION PROCESSING PERSPECTIVE ON BIS-ACTIVITY

Within his dimensional view on anxiety, Gray emphasized the role of cognitive factors in both normal and pathological anxiety: 'it is not the stimulus as such which gives rise to anxiety, but rather the interpretation placed on the occurrence of that stimulus by the individual’ (Gray & McNaughton, 2002, p. 278; Corr, 2008). Activity in the BIS is thought to have cognitive consequences involving stimulus evaluation and
attentional allocation. Hyperactivity in the BIS produces 'exaggerated' cognitive outputs, leading to an excessive negative bias that results in increased threat perception. The affective consequence of this bias results in excessive feelings of anxiety. RST thus implies that anxiety not only depends on the activation of a neural system (i.e. the BIS), but also on cognitive information processing, sharing the acknowledgment of the important role of cognitions in the etiology of anxiety disorders with cognitive theories of anxiety (e.g., Beck & Clark, 1997; Beck, Emery, & Greenberg, 1985; Kendall, 1985; Mogg & Bradley, 1998). Cognitive theories of anxiety emphasize the adaptive qualities of normal anxiety. Normal anxiety forms an innate survival and safety mechanism by alerting an individual to possible threat and by preparing one for adaptive behavior. However, anxiety becomes pathological when reactions to threat are inappropriately intense and prolonged due to overactive threat schemas. These dysfunctional threat schemas involve the overestimation of the likelihood and the severity of threat and the underestimation of one's personal coping capacities. As such, they give rise to cognitive biases relating to attention, evaluation and interpretation (e.g., Daleiden & Vasey, 1997; Muris & Field, 2008).

The information-processing paradigm has proven to be a fruitful approach to investigate the cognitive biases and distortions relevant for psychopathology, in both adults (e.g., Mogg & Bradley, 1998) and children (e.g., Bjittebier, Vasey, & Braet, 2003; Daleiden & Vasey, 1997; Muris & Field, 2008; Vasey & McLeod, 2001). A frequently used information-processing model to describe cognitive biases in childhood anxiety was proposed by Crick and Dodge (1994). In their model, there are six subsequent information-processing stages (encoding, interpretation, goal clarification, response construction, response selection, enactment). Although Crick and Dodge presented their stages as unities, different behavioral and cognitive processes take place in each stage. For example, the outcome of the encoding stage involves the activation of several processes aimed at the selection of stimuli for further processing. In this stage, the three output modalities of the BIS can be identified. The inhibition output prepares for the orienting-investigating behavior necessary for the scanning of the environment. The evaluation output assigns valence to stimuli. Based on this evaluative outcome, processing resources are assigned to relevant stimuli. As such, the attentional outcome determines which stimuli are retained for further processing.

In the present dissertation, I will adopt the information-processing paradigm to study the three functional BIS-outputs (inhibition, attention, stimulus evaluation). This approach, with focus on cognitive components of the RST, complements experimental performance-based studies focusing on conditioning and motivational components of
RST. Although studies investigating cognitive processes in anxiety are not primarily designed to test RST-related hypotheses (for an exception, see Field, 2006), they can provide valuable information on the functional aspects of BIS-activity (Avila & Torrubia, 2008). For example, studies on threat-related attentional bias and automatic evaluations suggest that anxious individuals (i.e. individuals with high BIS-activity) show a negative cognitive bias, consistent with the attention and stimulus evaluation output of the BIS (for reviews, see Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Huijing, 2006; Puliafico & Kendall, 2006; Yiend, 2010).

THE PRESENT DISSERTATION: 
BIS IN CHILDHOOD AND ADOLESCENT ANXIETY

The present dissertation aims to further our knowledge on the link between activity in the BIS and childhood and adolescent anxiety. In the second chapter, I will provide a brief overview of different methods to assess sensitivity and activity of the BIS. First, I will evaluate different self- and parent-report questionnaires measuring BIS-sensitivity. Following that, I will introduce the information-processing perspective when discussing the possibility of using cognitive performance-based measures as indicators of BIS-activity. The empirical part of this dissertation (Chapters 3-6) will mirror this overview. In the first study, data on self-reported BIS and BAS-sensitivity in a sample of clinically anxious children and adolescents are presented (Chapter 3). The child version of the Carver and White (1994) BIS/BAS-scales (Muris, Meesters, de Kanter, & Eek Timmerman, 2005) was used to assess sensitivity of the Behavioral Inhibition and the Behavioral Activation System. Relations of BIS/BAS-sensitivity with trait anxiety, as well as with symptoms of anxiety and depression are investigated. Following this, there will be three chapters describing cognitive processes related to the functional outputs of the BIS, i.e. inhibition (Chapter 4), stimulus evaluation (Chapter 5), and attention (Chapter 6). In Chapter 4, response inhibition in neutral and threatening situations is studied. We developed two pictorial versions of the Stop Signal Reaction Time Task (Logan, Cowan, & Davis, 1984): one with neutral and one with anxiety-relevant stop stimuli. In a first study, the validity of both Stop Tasks versions was tested in a community sample. In a second study, it was tested whether inhibition of clinically anxious children was increased in threatening compared to in neutral situations. Relations between response inhibition and self-reported BIS-sensitivity are investigated. Chapter 5 deals with stimulus evaluation. In a first study, the development of a child-
friendly assessment tool to measure automatic evaluations is described, i.e. a pictorial version of the Extrinsic Affective Simon Task [De Houwer, 2003a]. In a second study, this task is used to compare automatic evaluations in a sample of clinically anxious children and adolescents with those of a community youth sample. Relations of automatic evaluations with self-reported trait-anxiety [as an index of BIS-sensitivity] and parent-reported anxiety severity are reported. In Chapter 6, threat-related attentional processes in clinically anxious and non-clinical adolescents are studied using a pictorial dot probe detection task [Vasey, Daleiden, Williams, & Brown, 1995]. The original paradigm was adapted to study initial and strategic attention by presenting stimuli at different stimulus durations (500 ms for initial attention, 1250 ms for strategic attention). Links with Negative Affectivity [as a proxy of BIS-sensitivity], regulative capacities and severity of internalizing problems are studied. Finally, in the conclusion and discussion section of my dissertation [Chapter 7], I will provide a summary and evaluation of the main findings, I will describe implications for treatment and formulate suggestions for further research.