Children's behavioral inhibition and anxiety disorder symptom severity: The role of individual differences in respiratory sinus arrhythmia

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ABSTRACT

Although behavioral inhibition (BI) is clearly identified as a temperamental risk factor for childhood anxiety psychopathology, much less is known about whether the strength of this association may vary as a function of parasympathetic nervous system regulation in children with anxiety disorders. To build upon extant research in this area, the present study examined whether respiratory sinus arrhythmia (RSA) can explicate the conditions in which BI is linked to increased symptom severity among anxiety-disordered children ($N = 44$; $M = 9.61$ years, $SD = 1.63$; 52% female and African American, respectively). We examined RSA responding both during a basal period and during a stressor ("challenge" RSA): interacting with a "mystery guest" who was wearing a mask. As hypothesized, the interaction between BI and both basal and challenge RSA was significantly related to anxiety disorder symptom severity, even after controlling for depressive symptoms. The form of the interaction indicated that highest levels of anxiety disorder symptoms were found among children with high levels of BI and low basal and challenge RSA, respectively. These data provide novel empirical evidence of a clinically-relevant interplay between RSA and BI in relation to anxiety disorder symptom severity among clinical youth. Future work is needed to expand on the specific mechanisms that may be responsible e for the interplay between temperamental and psychobiological risks for childhood anxiety.

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Behavioral inhibition (BI) is a potent risk factor in the development of childhood anxiety psychopathology (Kagan & Snidman, 1991; Kagan, 2008). Theorized to be a highly heritable temperament trait, BI is characterized by increased arousal in response to novel stimuli, social reticence, and withdrawal even in situations where the potential for reward is high (Fox & Helfinstein, 2013; Kagan, 1994). In fact, Rapee and Jacobs (2002) argued that BI is the most crucial factor in the development of anxiety, given considerable behavioral, affective, and physiological overlap between BI and clinical levels of anxiety (Kagan, 2008; Weems & Silverman, 2008). Research has also shown moderate stability of BI across development (Kagan, Reznick, Snidman, Gibbons, & Johnson, 1988) as well as longitudinal associations with later anxious symptoms (Kagan & Snidman, 2004; Muris, 2006).

Notably, the construct of BI differs from other biobehavioral models of temperament that underscore the neurobiological systems implicated in approach and withdrawal behavior (Davidson, 1992; Gray, 1994). Specifically, Gray (1994) model described a behavioral approach system (BAS) that regulates approach behavior in response to reward cues, and a behavioral inhibition system (BIS) that encourages withdrawal in the face of stimuli or situations that signal punishment, unfamiliarity, and non-reward. Although there is conceptual overlap between BI (Kagan, 1994) and BIS (Gray, 1994), non-reward signals should not elicit BI in Kagan's model, which is comparatively more developmental in scope and emphasis (Zentner & Bates, 2008). The focus of the current investigation is thus on Kagan's concept of BI.

Not all behaviorally inhibited children go on to develop an anxiety disorder, however (Clauss & Blackford, 2012; Degnan & Fox,

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2007). One study found that children classified as behaviorally inhibited as toddlers were significantly more likely to meet criteria for social anxiety at age 13 than children classified as uninhibited (Schwartz, Snidman, & Kagan, 1999), but no differences were found between inhibited and uninhibited groups for other forms of anxiety. In a separate study, 17% of inhibited children met criteria for social anxiety disorder, versus only 5% of uninhibited children (Biederman et al., 2001). These findings suggest that there are other factors that explain why some behaviorally inhibited children go on to develop an anxiety disorder while others do not, and underscore the need for additional research on *moderators* of the BI-anxiety association (White, McDermott, Degnan, Henderson, & Fox, 2011), such as *when, for whom*, and *under what conditions* BI relates to increased anxiety. Investigations in this area have found that attentional biases (Pérez-Edgar et al., 2010), variations in amygdala-insula connectivity (Hardee et al., 2013), and greater incentive-related striatal activation (Guyer et al., 2006; Helfinstein et al., 2011) among BI children may be associated with higher internalizing symptoms such as anxiety. However, because extant studies have focused on at-risk groups (by virtue of their BI levels), the conditions in which BI may be linked to increased clinical severity among children already diagnosed with an anxiety disorder are relatively unknown. Research among clinical samples is needed to identify precise mechanisms implicated in more severe presentations of the disorder.

One potential moderator of the BI-anxiety relationship is respiratory sinus arrhythmia (RSA)—a psychophysiological indicator of parasympathetic nervous system (PNS) control. The PNS system is involved in processes such as rest, healing, self-regulation, and growth (Porges, 2007) while RSA is defined as the rhythmic fluctuations in heart rate associated with the respiratory cycle. RSA is modulated by the PNS through the myelinated vagal nerve (Grossman & Taylor, 2007). In the absence of internal or external threats, RSA functions akin to a 'brake,' to slow down the heart and maintain baseline heart rate levels. Under conditions of threat (e.g., a child who is afraid of elevators is asked to ride one), the brake is released (vagal suppression, also known as RSA suppression) to increase heart rate and prepare sympathetic modulation (fight or flight; Berntson et al., 1994; Hinnant & El-Sheikh, 2009). Thus, high basal RSA corresponds with greater PNS control (i.e., a stronger "brake") and is thought to allow for increased physiological flexibility and adaptability to environmental demands and potential threats (Beauchaine, 2001).

RSA is consistently related to emotion regulation abilities and psychopathology among children and adults (Beauchaine, 2001; Beauchaine, Gatzke-Kopp, & Mead, 2007), where high RSA is thought to serve as a protective factor (see Beauchaine, Neuhaus, Brenner, & Gatzke-Kopp, 2008). For instance, children with *higher* RSA exposed to negative family environments (e.g., martial conflict, problem drinking) are at lower risk of developing both internalizing and externalizing behaviors (El-Sheikh, 2005; El-Sheikh, Harger, & Whitson, 2001; Katz & Gottman, 1995, 1997). Among children ages 8–12 with social anxiety disorder, *lower* levels of basal RSA have been found in comparison to matched controls, as well as limited RSA reactivity in response to a social stressor (Schmitz, Krämer, Tuschen-Caffier, Heinrichs, & Blechert, 2011). Taken together, children with lower basal RSA (higher arousal at rest) are thought to be overly vigilant and attentive to potential threats in the environment, exhibit restricted autonomic flexibility, and, when confronted with actual challenges, may be less able to cope and regulate their responses, resulting in increased anxiety (Thayer & Lane, 2000).

Despite the buffering effect of RSA on psychopathology symptoms (Beauchaine, 2001; Beauchaine et al., 2007), research has yet to examine RSA as a moderator of the BI-anxiety relationship,

especially among children who already have an anxiety disorder. This research is scientifically and clinically important for at least three reasons. First, RSA assessment may help to identify subgroups of children with anxiety disorders for whom BI is tied to increased anxiety symptom severity. Second, significant moderation of the BI-anxiety relationship would support the clinical utility of psychobiological assessments among clinically anxious children who do not respond to traditional treatment approaches (Kupper et al., 2005). Lastly, data with children suggest that physical activity and regular training may increase PNS control of cardiac function (Gutin, Owens, Slavens, Riggs, & Treiber, 1997; Gutin et al., 2005; Nagai, Hamada, Kimura, & Moritani, 2004), pointing to novel intervention opportunities to increase vagal tone among children with anxiety disorders.

The aim of the current study was to answer the following research question: *in the context of clinical anxiety, does RSA moderate the association between BI and anxiety disorder symptom severity?* In an attempt to provide a more detailed examination of this question, we examined RSA responding both during a basal period and during a stressor task: interacting with a "mystery guest" who is wearing a mask (see Method for details; van Brakel, Muris, & Bögels, 2004; Vreeke & Muris, 2012; Vreeke et al., 2012). We hypothesized that both basal RSA and RSA during the stressor (hereafter referred to as "challenge RSA") would moderate the association between BI and anxiety disorder symptom severity. Specifically, we hypothesized that increases in BI would be associated with concomitant increases in anxiety disorder symptom severity among children with low (but not high) RSA.

1. Method

1.1. Participants

Forty-four children between 8 and 12 years of age ($M = 9.61$ years, $SD = 1.63$; 52% female) and their mothers participated in this study. Their mothers' age ranged from 26 to 50 years ($M = 38.48$ years, $SD = 6.86$; 57% married). Fifty-four percent of the mothers were African American and 46% were White. Fifty-two percent of the children identified as African American, 39% as White, and 9% of mixed race. The mean annual income of families ranged from $50,000 - $60,000 (overall range = < $10,000 - > $150,000), with 34% reporting an annual income of < $30,000. Fourteen percent of mothers had a high school diploma or GED, Thirty percent of mothers had some college education, 18% a 2-year college degree, 16% a 4-year college degree, 2% had completed some graduate level courses, 11% had a master's degree, and 9% had a doctoral degree. Fifty-one percent of mothers worked full-time.

Children met *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text revision; DSM-IV-TR; American Psychiatric Association, 2000) criteria for at least one anxiety disorder diagnosis based on results from semi-structured interviews conducted (separately) with both the child and the mother. Specific phobias were the most common anxiety disorder (43%), followed by generalized anxiety disorder (20%), social anxiety disorder (20%), separation disorder (11%), post-traumatic stress disorder (2%), and obsessive compulsive disorder (2%). The majority of the sample (75%) had comorbid diagnoses, with specific phobias and attention deficit/hyperactivity disorder as the most common forms of comorbidity. Children were excluded if they had (a) a physical disability impairing ability to use a computer, (b) borderline or extremely low intellectual functioning (estimated full scale IQ < 80; see Procedure), (c) below average reading comprehension (standard score < 85; see Procedure), (d) psychosis, and/or (e) suicidality.