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The tell-tale heart: physiological reactivity during resolution of ambiguity in youth anxiety

Michelle Rozenman, Allison Vreeland, Marisela Iglesias, Melissa Mendez, and John Piacentini

Division of Child & Adolescent Psychiatry, UCLA Semel Institute for Neuroscience & Human Behavior, Los Angeles, CA, USA

Abstract

In the past decade, cognitive biases and physiological arousal have each been proposed as mechanisms through which paediatric anxiety develops and is maintained over time. Preliminary studies have found associations between anxious interpretations of ambiguity, physiological arousal, and avoidance, supporting theories that link cognition, psychophysiology, and behaviour. However, little is known about the relationship between youths' resolutions of ambiguity and physiological arousal during acute stress. Such information may have important clinical implications for use of verbal self-regulation strategies and cognitive restructuring during treatments for paediatric anxiety. In this brief report, we present findings suggesting that anxious, but not typically developing, youth select avoidant goals via non-threatening resolution of ambiguity during a stressor, and that this resolution of ambiguity is accompanied by physiological reactivity (heart rate, heart rate variability, and respiratory sinus arrhythmia). We propose future empirical research on the interplay between interpretation bias, psychophysiology, and child anxiety, as well as clinical implications.

Keywords

Child; adolescent; anxiety; physiological arousal; interpretation; appraisal

Anxiety disorders are distressing and impairing, with onset during the developmental period affecting between 20% and 30% of children and adolescents (Merikangas et al., 2010).

Theoretical models have proposed that underlying cognitive processing biases and physiological reactivity may interact and lead to the development of avoidance behaviour, subsequently maintaining anxiety over time (e.g. Britton, Lissek, Grillon, Norcross, & Pine, 2011; Daleiden & Vasey, 1997; Field & Lester, 2010; Lang, Davis, & Öhman, 2000). In regards to cognition, empirical investigations have demonstrated that anxious youth are vigilant to environmental threat cues (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van Ijzendoorn, 2007) and make associations between threat and ambiguity when the two

CONTACT Michelle Rozenman, mrozenman@mednet.ucla.edu.

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are presented together during performance-based tasks (Rozenman, Amir, & Weersing, 2014); these interpretive biases may then lead anxious youth to select avoidant responses (Waite, Codd, & Creswell, 2015). In regards to autonomic arousal, anxious youth exhibit increased heart rate (HR), and decreased heart rate variability (HRV) and respiratory sinus arrhythmia (RSA), during stress (Blom, Olsson, Serlachius, Ericson, & Ingvar, 2010; Boyce, 2001; Krämer, Seefeldt, & Heinrichs, 2012; Monk, Kovenko, & Ellman, 2001; Schmitz, Blechert, Krämer, Asbrand, & Tuschen-Caffier, 2012). Despite our theories of the development and maintenance of anxiety, and findings that link each cognitive bias and physiological arousal to anxiety symptoms and diagnoses in youth, little work has been done to examine the links *between* cognitive and psychophysiological factors, particularly during acute stress when these factors might be most salient to youth.

Only a few extant studies have examined relationships between physiological arousal and cognition in youth. In one such investigation, typically developing youth who were told that a sound they were listening to was their own heart beat subsequently provided higher threat ratings for ambiguous events than youth who were told that the sound was a drum (Muris, Mayer, & Bervoets, 2010). In another study, typically developing youth who read ambiguous vignettes about another child rated the vignettes as more dangerous and made more interpretations that the child must be anxious when they were provided with information about the child's physical sensations than if they were not provided such information (Muris, Vermeer, & Horselenberg, 2008). These two experiments suggest that non-anxious children and adolescents may use internal physical cues as information regarding the safety or dangerousness of external events. Moreover, studies in which interpretation bias was induced in typically developing youth by providing information about the dangerousness of novel animals resulted in increases in objective measures of physiological arousal (Reynolds, Field, & Askew, 2015), as well as behavioural avoidance during an approach task (Askew, Hagel, & Morgan, 2015; Reynolds, Field, & Askew, 2014), implicating cognitive bias as a possible mechanism underlying anxious arousal. Together, these data suggest that cognition, interpretation bias specifically, and psychophysiology may be related in anxiety symptom presentation.

While these findings provide initial support for relationships between cognition and autonomic arousal in anxiety, they do not provide information about how these two features of the disorder might be linked during acute stress experiences, and whether these processes operate similarly in anxious and typically developing youth. Further, it is unclear whether these findings might extend to resolution of ambiguity, which involves information processing stages (Daleiden & Vasey, 1997; Field & Lester, 2010) of interpretation (is the outcome threatening or not?), goal clarification (how to transition from the current ambiguity to an outcome), and response selection (the means through which the outcome is achieved). In this brief report, we present findings from a preliminary investigation in which we examined how anxious and typically developing youth resolved an ambiguous story during a stressor task, and whether physiological reactivity accompanied their story resolutions. Specifically, youth completed the story portion of the Trier Social Stress Test for Children (TSST-C; Buske-Kirschbaum, Jobst, & Wustmans, 1997), during which time HR, HRV, and RSA data were acquired. Stories were subsequently coded for threat-relevant words and time to story resolution. Because a growing literature consistently finds that

anxious youth demonstrate interpretation biases for threat when presented with ambiguity, we hypothesised that anxious youth would use more threat words during their story resolutions than their healthy counterparts. We also hypothesised that anxious youth would exhibit greater physiological arousal, particularly during their story resolutions (as we anticipated that they would use more threat words to resolve their stories).

Method

Participants

In the current study, we selected a subsample of youth from a larger investigation of cognitive bias in paediatric anxiety (Rozenman, Vreeland, & Piacentini, 2017); youth were selected if they were video- or audio-recorded during completion of the stressor task.

The sample consisted of 44 youth aged 9–17 years (Mean age = 12.74, SD = 2.69) who either met diagnostic criteria for a primary anxiety disorder ($n = 22$) or were considered typically developing, with no history of mental health problems and no first degree relatives with history of mental health problems ($n = 20$). Anxious youth were 46% male, 54% racial/ethnic minority, and had a mean age of 13.57 (SD = 2.70). Their primary anxiety diagnoses included generalised anxiety ($n = 15$), social phobia ($n = 6$), and separation anxiety ($n = 3$), and 41% of the sample met diagnostic criteria for more than one anxiety disorder. Control youth were 60% male, 65% racial/ethnic minority and had a mean age of 11.96 (SD = 2.95). There were no significant group differences on gender, age, or ethnic minority status.

Materials and equipment

Anxiety disorders interview schedule for children, version IV (ADIS; Silverman & Albano, 1996) is a semi-structured diagnostic interview that assesses the major DSM-IV disorders. It is considered the gold-standard diagnostic tool in large-scale studies of paediatric anxiety (Walkup et al., 2008) and was used in this study to confirm primary anxiety diagnosis for youth in the anxious group, and ensure that youth in the control group did not meet for any current or past diagnoses. The first author, a Ph.D.-level clinical psychologist with expertise in assessment and treatment of paediatric anxiety, administered the ADIS to all youth.

Trier Social Stress Test for Children (TSST-C; Buske-Kirschbaum et al., 1997) is a well-validated, standardised stressor task that has been used in many studies to assess stress response in community and anxious samples (for review, see Allen, Kennedy, Cryan, Dinan, & Clarke, 2014). In this study, we used the story task phase of the TSST-C: the story prompt read by the experimenter describes the youth and their best friend going to visit a “crazy old man” who lives at the edge of town, arriving at his house to find the door open and noises coming from within, and slowly entering the house. Youth are instructed to prepare and deliver the ending of a story, with the expectation that their story ending will be evaluated by experts. If youth resolve the story prior to the 5-minute time limit, the experimenter indicates that they still have time left and asks the youth to continue telling the story.

TSST-C story transcriptions were transcribed and coded by a team of four undergraduate students, with each transcript coded by two different coders. Each youth’s story was transcribed and time stamped in 15-second increments by one coder, and then checked by

another coder twice, once for transcription content, and a second time for time stamp accuracy. Then, each transcription was coded separately by two coders for: (a) number of total words, (b) number of threat words, (c) length of time until first attempt to terminate the task, (d) total number of attempts to terminate the task, and (e) length of time to positive story resolution. Coding discrepancies (which only occurred in four instances for length of time to positive story resolution) were resolved by a third coder. Coders had reached criterion reliability on sample transcripts prior to coding the transcripts for this study, and were unaware of youth diagnostic status, inclusion criteria, and aims of the present study.

Physiological arousal measures included HR (measured by average beats per minute), HRV (measured by average inter-beat interval), and RSA (measured by difference between maximum and minimum change in HR during respiration). We used an MP150 Biopac Systems and Acknowledge III software, with wireless transmitters, a sample rate of 500 Hz from two Ag-AgCl electrodes filled with GEL 101 gel as a contact medium between the skin and electrode, and medical tape to ensure that electrodes did not shift. Electrodes were positioned on the right collarbone and lower left rib, with a respiration band placed around the ribcage. Youth were seated on a chair during the entirety of the data acquisition period. All recordings were screened for physiological artefacts (i.e. motion) and analysed offline using Mind-Ware software.

Procedure

Approval was obtained from the university Institutional Review Board. All youth were recruited from the community with flyers and online advertisement. During initial phone screen, verbal consent was obtained from parents calling in response to flyers. Parents calling in response to the typically developing youth flyer were carefully queried to ensure that the target child, parents, and any other first-degree relatives (i.e. siblings) had never received mental health services or reported emotional or behavioural difficulties. Parents calling in response to the anxious youth flyer were queried regarding current symptoms and screened for exclusion (i.e. apparent primary mental health problem that was not anxiety, any health conditions that might interfere with acquisition of physiological data). In-person participation occurred during a one-time study visit. Written informed consent and assent were obtained from parents and youth, respectively, prior to commencement of any study activities. Both youth and parent participated in the diagnostic interview, and then youth completed the TSST-C with the first author and two research assistants. Following the completion of all study procedures, the first author debriefed each participant about the TSST-C.

Results

Story presentation and resolution

We used independent samples *t*-tests to compare anxious and control youth on the variables selected *a priori* from which to examine their responses and behaviour during the TSST-C story task. An experiment-wise $\alpha = .01$ was used (.05/5 comparisons). Youth did not differ on total words spoken during the task ($t(42) = 0.88, p = .382$) or on length of time until first attempt to terminate the task ($t(44) = 1.46, p = .153$). However, anxious youth attempted to

terminate the task significantly more times ($t(42) = -3.89, p = .001$) and resolved the story with a happy ending more quickly ($t(42) = 4.40, p < .001$) than their non-anxious counterparts. Conversely, the stories of youth in the control group contained a significantly greater proportion of threat words out of total words spoken than the stories told by anxious youth ($t(42) = 2.88, p = .008$). See Table 1 for means and SDs by group.

Physiological arousal during the TSST-C

Arousal indices were examined over the course of the story presentation to explore potential differences in reactivity during story resolution. Physiological data were divided into one-minute increments for the periods before, during, and after youths' initial story resolutions. As with other investigations of physiological arousal during a stressor (Krämer et al., 2012; Schmitz & Krämer, 2011), resting baseline arousal for each index was subtracted from each of the three story resolution time increments (before, during after) for each respective analysis (HR, HRV, RSA) in order to account for potential pre-existing differences between individual subjects in arousal. We conducted three mixed 2 (group) $\times$ 3 (time) ANOVAs with repeated measures on the second factor to examine potential group differences for HR, HRV, and RSA. Bonferroni correction was used for each analysis to reduce likelihood of Type I error. See Figure 1 for graphical representation of results.

There was a significant group $\times$ time interaction ($F(2,84) = 6.07, p = .004$) for HR. Examination of simple effects revealed that, while the control group did not exhibit significantly different HR at any of the three task phases ($F(2,41) = 1.36, p = .270$), the anxious group exhibited significantly higher HR during story resolution as compared to the minute before (Mean difference = 5.98, SE = 1.65, $p = .003$) and minute after (Mean difference = -5.25, SE = 1.20, $p < .001$) story resolution ($F(2,41) = 10.26, p < .001$). There were no significant differences between anxious and control groups on HR at any of the three task phases, although there was a trend towards group differences in HR during story resolution (Mean difference = 7.42, SE = 3.87, $F(1,42) = 3.68, p = .063$).

There was also a significant group $\times$ time interaction ($F(2,84) = 4.64, p = .013$) for HRV. Examination of simple effects revealed that, while the control group did not exhibit significantly different HRV at any of the three task phases ($F(2,41) = 0.70, p = .505$), the anxious group demonstrated higher HRV during story resolution as compared to the minute before (Mean difference = -45.78, SE = 12.262, $p = .002$) and minute after (Mean difference = -36.44, SE = 8.89, $p < .001$) story resolution ($F = 10.63, p < .001$). We did not find significant group differences on HRV at any of the three task phases.

Finally, there was a significant group $\times$ time interaction ($F(2,84) = 9.209, p = .036$) for RSA. Examination of simple effects revealed that, while the control group did not exhibit significantly different RSA at any of the three task phases ($F(2,41) = 0.745, p = .482$), the anxious group exhibited significantly lower RSA after story resolution than before story resolution (Mean difference = -.910, SE = .351, $p = .040$; $F(2,41) = 4.034, p = .019$). We did not find significant differences between groups on RSA at any of the three task phases.

Discussion

Despite theories proposing an interplay between cognitive bias and physiological arousal in predicting anxious behaviour, and empirical studies supporting links between anxiety symptoms to verbal expressions of anxious avoidance and arousal during stress, few studies have directly linked behavioural indices of youths' cognitive processing with physiological arousal. The prior work in this area has either focused on typically developing youths' interpretations of their own (Muris et al., 2010) and other's (Muris et al., 2008) physical sensations, or experimentally induced an interpretation threat bias about physical danger, which in turn increased physiological arousal (Reynolds et al., 2015). These studies have almost exclusively been conducted with typically developing samples, and findings provide preliminary evidence that, for typically developing youth, information about internal sensations leads to evaluations of environmental threat and, conversely, that interpretation biases about threat lead to autonomic arousal. In this brief report, we sought to examine whether anxious and typically developing youth differ in their resolutions of ambiguity during a stressor task, and whether this was linked to their physiological reactivity.

Based on the prior interpretation bias literature, we had predicted that anxious youth would use more threat words than their typically developing counterparts. In contrast, our data provided behavioural evidence that anxious youth attempted to resolve ambiguity with proportionally fewer threat words than control youth. Anxious youth also attempted to terminate the task significantly more times, although youth did not differ on total words spoken during the task or on length of time until first attempt to terminate the task. It may be possible that anxious youth interpreted task instructions to make the story "as interesting and exciting as possible" to mean that their stories should include positive information, or that anxious youth may have felt that resolving the story with a happy ending would result in positive judgment from the "experts" they were told would review their stories. An alternate explanation might be that anxious youth used fewer threat words as a result of the cognitive processing likely involved during the TSST-C story task. While prior literature has utilised methodology to specifically assess interpretation bias, or rather what type (threat vs. benign/positive) of attributions anxious youth make about ambiguous situations in their daily lives (e.g. hearing a noise outside at night; Rozenman et al., 2014), the TSST-C story task combines three stages of information processing (Daleiden & Vasey, 1997; Field & Lester, 2010): interpretation (is the outcome threatening or benign?), goal clarification (how to get from the end of the story prompt to the end of the story in an exciting, interesting way), and response selection (the means through which the story ending is achieved). One explanation for the present results in the context of the extant literature is that anxious youth responded to ambiguity in the TSST-C story task by clarifying and selecting a "happy" or avoidant goal, even though they still have demonstrated interpretation bias for threat if these information processing stages were methodologically decoupled during the TSST-C. Future work might attempt to replicate and extend the current findings by comparing stages of information processing in anxious and control youth as related to physiological reactivity.

Affirming our second set of hypotheses, anxious youth experienced autonomic reactivity across psychophysiological indices, which was linked to their story resolutions, while typically developing youth exhibited a relatively stable pattern of reactivity during the task.

More specifically, control youth did not exhibit significant changes in HR, HRV, or RSA before, during, and after story resolution, despite telling stories with a relatively large proportion of threat words. In contrast, anxious youth demonstrated significantly higher HR and lower HRV during story resolution than in the minute before and after, and suppressed RSA after, story resolution. As HR reflects sympathetic nervous system functioning, and HRV and RSA reflect the interaction between sympathetic and parasympathetic influences, it can be assumed that these variations over the course of the task reflect youths' physiological reactivity and subsequent attempts to down-regulate arousal. Interestingly, the overall lack of group differences in arousal at each phase of the task demonstrates the importance of examining both between- and within-group differences when comparing clinical and non-clinical samples. These findings also have implications for the deconstruction of the TSST-C and other laboratory-based stressors into their components for more fine-grained examination of real-time physiological reactivity in response to internal and external processes that may occur even within a single phase (e.g. story presentation) of a task.

This study had several limitations. First, we examined how youths would respond to an ambiguous prompt naturalistically, and therefore did not experimentally manipulate the type (i.e. positive, threatening) of resolution to be provided and/or information about internal cues that would youth perceptions of dangerousness of external events. Along with the relatively small sample size, this precludes examination of potential interactions between autonomic arousal and type of story resolution provided within and between diagnostic groups. Use of larger samples and prospective longitudinal, rather than cross-sectional, design would strengthen the ability to draw inferences from this work. In addition, because HR and respiration take several seconds to respond to environmental stimuli (as compared to pure measures of sympathetic reactivity such as galvanic skin response), we were unable to test causality hypotheses; namely, whether arousal or story resolution occur first, and whether one process influences the other. Next, it is possible that some other process that underlies anxiety, but was not measured in this investigation, may be responsible for the ways in which anxious and typically developing youth resolve ambiguity and/or physiological differences in responding. Finally, as the TSST_C story task taps several stages of information processing (i.e. interpretation, goal clarification, goal selection), we are limited in our ability to identify specific aberrations in cognitive processing that might account for group differences in our dependent variables (i.e. proportion of threat words, length of time to happy ending). Nonetheless, these findings provide preliminary evidence for a relationship between verbal avoidance of threat and physiological arousal.

We view several avenues for possible replication and extension of this initial investigation, with the ultimate goal of examining the potential causal role of verbal self-regulation on autonomic reactivity, and the role of physiological arousal in aberrant cognitive processing. For example, future studies might compare anxious and control youth on autonomic arousal indices when youth have been randomly assigned to conditions in which they are specifically instructed to provide threatening vs. positive story endings. Such studies might attempt to methodological disentangle the specific roles of interpretation bias, goal clarification, and goal selection in anxious youth. Conversely, studies might attempt to experimentally manipulate youths' actual or perceptions of physiological reactivity, and

examine cognitive processing as the dependent variable. Such work might then draw links to our theoretical understanding of clinical interventions. For example, newer theories of behaviour therapy suggest that elevated levels of physiological arousal and distress during exposure facilitate learning new associations between previously feared stimuli and non-threat (Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014) and eventually leads to symptom reduction, whereas use of cognitive reappraisal does not (Kircanski, Lieberman, & Craske, 2012). If we view resolution of ambiguity with happy endings in this investigation as an attempt at cognitive restructuring, it is not surprising that physiological reactivity occurred for the anxious, but not the control, group. Of course, replication and extension of our preliminary work is necessarily to make inferences and causal claims about how anxious youth verbally self-regulate during stress, and the role of this putative interplay between cognitive and physiological processes on our theoretical and clinical understanding of paediatric anxiety.

Concluding remarks

Cognitive processing, particularly interpretation of ambiguity, and physiological arousal, have each been empirically associated with and proposed as mechanisms underlying anxiety disorder. However, few studies have been conducted to examine whether physiological reactivity during acute stress and resolution of ambiguity are linked, and whether these processes are comparable for anxious and non-anxious youth. In this brief report, we provide preliminary evidence that anxious youth engage in verbal avoidance of threat during resolution of ambiguity, as compared to their non-anxious counterparts, and that this is linked to physiological reactivity. We hope that these findings lead to future investigations of the relationship between physiological arousal and cognitive processes in youth; such information may have important clinical implications for use of cognitive and verbal self-regulation strategies during psychosocial interventions for paediatric anxiety.

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Figure 1.

Physiological reactivity measures: before, during, and after initial story resolution. (a) HR before, during, and after story resolution; (b) HRV before, during, and after story resolution; (c) RSA before, during, and after story resolution. *Physiological variable estimated marginal means based on difference scores from baseline at each time point.

Table 1

Differences in story presentation between anxious and typically developing youth.

	Anxious	Control	<i>T</i>	<i>P</i>
First attempt to terminate story (seconds)	125	166	1.457	.153
Total number of attempts to terminate story *	3.21	1.05	-3.89	< .001
Time to first story resolution (seconds) *	103	234	4.40	< .001
Total words spoken	492	551	0.88	.382
Proportion threat words spoken (%) *	18%	34%	2.88	.008

*
 $p < .01$