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Response Inhibition, Response Execution, and Emotion Regulation Among Children with Attention-Deficit/Hyperactivity Disorder

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Abstract

Attention-deficit/hyperactivity disorder (ADHD) is associated with deficits in response inhibition, response execution, and emotion regulation. However, the nature of the associations among these deficits remains unclear. Thus, this study examines these associations using a multi-method design. One hundred sixty-six children (aged 5-13 years; 66.3% male; 75 with ADHD) completed two conditions (i.e., neutral and fear) of an emotional go/no-go task. Parasympathetic-based regulation was indexed via respiratory sinus arrhythmia (RSA), and sympathetic-based reactivity was indexed via cardiac pre-ejection period (PEP). Overall, children exhibited more difficulty with response execution (i.e., more omission errors, fewer correct go responses) and less difficulty with response inhibition (i.e., fewer commission errors, more correct no-go responses) during the fear condition than the neutral condition. Children with ADHD displayed more difficulty with response execution during the fear condition compared to typically developing youth. Additionally, children with ADHD displayed parasympathetic-based dysregulation (i.e., RSA increase from baseline) and reduced sympathetic-based reactivity (i.e., PEP lengthening) compared to typically developing youth across task conditions. In sum, children with ADHD demonstrate greater difficulty with response execution during emotionally salient contexts, as well as parasympathetic-based emotion dysregulation. Future work should examine these associations longitudinally with the aim of predicting impairment and treatment response in youth with ADHD.

Keywords

attention-deficit/hyperactivity disorder; autonomic nervous system; emotion regulation; response inhibition; response execution

Attention-deficit/hyperactivity disorder (ADHD) is the most common mental disorder of childhood, with a 7.2% prevalence rate among children and adolescents worldwide (Thomas, Sanders, Doust, Beller, & Glasziou, 2015). ADHD is characterized by inattention and/or hyperactivity/impulsivity, as well as functional impairment across multiple contexts (American Psychiatric Association, 2013). Several theories have been proposed regarding

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the nature of ADHD, such as theories proposing underlying deficits in attention, executive function, reward processing, self-regulation, and temporal processing (Nigg, 2001; Nigg & Casey, 2005; Sonuga-Barke, 2005; Sonuga-Barke & Halperin, 2010; Toplack, Dockstader, & Tannock, 2006). With respect to self-regulation, one domain that has received attention in the ADHD literature is response inhibition, or the ability to inhibit a pre-potent response to a stimulus or to deliberately suppress an action to achieve a goal (Barkley, 2004; Nigg, 2001; Seymour, Motofsky, & Rosch, 2016; Walcott & Landau, 2004). Additionally, a related sub-domain of response inhibition, response execution, or the ability to initiate a cognitive and motor response to a stimulus has been examined in children with ADHD (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006; Tillman, Thorell, Brocki, & Bohlin, 2008). A second domain of self-regulation that has received recent attention in the ADHD literature is emotion regulation, or the ability to effectively respond to emotional stimuli and modulate emotional reactivity in a flexible manner that facilitates adaptive functioning (Bunford, Evans, & Langberg, 2014; Bunford, Evans, & Wymbs, 2015; Graziano & Garcia, 2016; Shaw, Stringaris, Nigg, & Leibenluft, 2014). However, to date, these components of self-regulation have been examined relatively separately among children with ADHD. Thus, it is unclear whether response inhibition, response execution, and emotion regulation represent a single deficit manifest in different contexts, or whether there is an additive or synergistic effect when these domains of self-regulation are required to function together. Furthermore, elucidation of these processes and their potential interactive relation in children with ADHD, may increase our understanding of difficulties associated with behavioral and emotional control present in children with ADHD, as well as inform potential treatment targets to improve behavioral and social functioning among children with ADHD. To address this gap, this study examines response inhibition and execution, as well as the added impact of responding to emotionally salient stimuli in children with and without ADHD.

ADHD, Response Inhibition, and Response Execution

Response inhibition and response execution have frequently been investigated in children with ADHD using paradigms, including stop-signal and go/no-go tasks. These tasks require participants to respond to pre-specified stimuli and to inhibit responses to other pre-specified stimuli (Castellanos et al., 2006; Gomez, 2003; Iaboni, Douglas, & Baker, 1995; Oosterlaan, Logan, & Sergeant, 1998; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Meta-analytic work and systematic reviews reveal deficits in both response inhibition and response execution among children with ADHD in comparison to typically developing youth (Metin, Roeyers, Wiersma, van der Meere, & Sonuga-Barke, 2012; Oosterlaan et al., 1998). Children with ADHD tend to respond with slower reaction times and more errors of both commission (an index of response inhibition) and omission (an index of response execution) (Desman, Petermann, & Hampel, 2008; Gomez, 2003; Iaboni et al., 1995; Metin et al., 2012; Oosterlaan et al., 1998; Tillman et al., 2008). With respect to go/no-go tasks specifically, children with ADHD have been shown to exhibit more commission errors during no-go trials (i.e., inhibit trials; Rubia, Smith, & Taylor, 2007) and/or more omission errors during go trials (i.e., execution trials; Desman et al., 2008; Wodka et al., 2007).

ADHD and Emotion Regulation

It is now well-established via meta-analytic work and systematic review that children with ADHD have difficulty with emotion regulation (Bunford et al., 2015; Graziano & Garcia, 2016; Petrovic & Castellanos, 2016; Shaw et al., 2014). A recent systematic review indicated that problems with emotion regulation are present in about 25-45% of children with ADHD and are associated with increased impairment and poor prognosis (Shaw et al., 2014). Difficulties with emotion regulation may originate in the deficient ability to attend to and process emotional stimuli (Shaw et al., 2014). Furthermore, multiple domains of emotion regulation have been associated with impairment in children with ADHD (Graziano & Garcia, 2016; Shaw et al., 2014). Specifically, ADHD has been associated with impairment in emotion regulation broadly (weighted ES $d=.80$), as well as impairment with deficits in emotion reactivity/negativity/lability (weighted ES $d=.95$; Graziano & Garcia, 2016).

ADHD and Autonomic Regulation

In addition to indexing emotion regulation behaviorally, cardiac-based psychophysiological indices of autonomic nervous system functioning are routinely employed to index emotion regulatory abilities (Beauchaine 2015; Bunford et al., 2016; Holtzman & Bridgett, 2017; Karalunas et al., 2014; Musser et al., 2011; Petrovic & Castellanos, 2016). Specifically, parasympathetic control of the heart by the vagus nerve has been indexed via respiratory sinus arrhythmia (RSA), as demonstrated by pharmacological blockade (Berntson et al., 1994, 1997; Hayano et al., 1991). Greater RSA withdrawal from rest has been associated with adaptive emotional regulation abilities in specific contexts (Beauchaine, 2001; Calkins, Graziano, & Keane, 2007; Graziano & Derefinko, 2013; Porges, 2003, 2007). Additionally, sympathetic-linked beta-adrenal influence over the heart has been indexed via cardiac pre-ejection period (PEP), or the systolic time interval from left ventricular polarization to the onset of ejection of blood into the aorta (Berntson et al., 1994; Cacioppo et al., 1994; Sherwood, Allen, Orbist, & Langer, 1986; Sherwood et al., 1990). Shortened PEP has been associated with sympathetic activation and linked to emotional reactivity/arousal, and approach behaviors (Beauchaine, Katkin, Strassberg, & Snarr, 2001; Brenner, Beauchaine, & Sylvers, 2005; Brenner & Beauchaine, 2011; Cacioppo, Uchino, & Berntson, 1994; Richter & Gendolla, 2009; Sherwood et al., 1986). Of note, PEP tends to be associated with reward systems and is typically examined during paradigms involving reward/punishment, thus it is not expected that the particular go/no-go tasks utilized in this study will have an effect on PEP (Beauchaine et al., 2013; Brenner & Beauchaine, 2011; Richter & Gendolla, 2009). However, PEP should be included as an index of the sympathetic nervous system (SNS) branch of autonomic functioning in order to interpret parasympathetic-based regulation in context (Bauer, Quas, & Boyce, 2002; El-Sheikh et al., 2009).

With respect to ADHD, a systematic review showed that ADHD is associated with deficient parasympathetic-based regulation, indexed via tonic RSA and context-dependent RSA reactivity (Rash & Aguirre-Camacho, 2012). Additionally, children with ADHD have been shown to demonstrate disruptions in RSA reactivity (depending on the nature of the challenge) during emotional and cognitive challenges compared to healthy controls

(Beauchaine et al., 2001; Karalunas et al., 2014; Musser et al., 2011). However, parasympathetic-based regulation has yet to be examined during a response inhibition task among youth with ADHD. Thus, it remains unclear the role the interaction of these deficits will play in response inhibition difficulties demonstrated by children with ADHD.

Emotion Regulation and Response Inhibition in Typically Developing Samples

Emotionally salient stimuli are believed to automatically capture attention, and thus such stimuli may interrupt ongoing inhibitory activities and/or require additional effort to inhibit or execute responses (Schimmack & Derryberry, 2005). For example, prior studies conducted with healthy adults demonstrate that the experience of emotions impaired the ability to both engage in response inhibition and execution, as demonstrated by the comparison of performance and reaction times on emotional and non-emotional response inhibition tasks (Goldstein et al., 2007; Hare, Tottenham, Davidson, Glover, & Casey, 2005; Herbert & Sutterlin, 2012; Schulz et al., 2007; Verbruggen & De Houwer, 2007). Furthermore, neuroimaging studies demonstrate similar patterns of neural activation among prefrontal cortex circuits during tasks that require emotion regulation (Goldin, McRae, Ramel, & Gross, 2008; Lewis & Stieben, 2004; Ochsner & Gross, 2005), and separately, response inhibition and execution tasks (Casey et al., 1997; de Zubicaray et al., 2000; Goldstein et al., 2007). Additionally, studies conducted with healthy adults and adolescents demonstrate that selective attention to emotionally salient stimuli is associated with increased amygdala activation, while inhibiting responses to emotionally salient stimuli results in activation of inferior frontal/insular cortex regions, supporting the notion that additional brain regions are activated during tasks that require emotion regulation and suggesting there is likely an increase in cognitive load that requires extra effort to respond to emotionally salient stimuli (Goldstein et al., 2007; Hare et al., 2005; Monk et al., 2003; Shafritz, Collins, & Blumberg, 2006). One type of emotional stimuli frequently utilized in tasks examining emotion regulation and response inhibition/execution is emotion-based facial expressions. In such tasks, responses to fearful expressions tend to be associated with slowed reaction time and amygdala activation, while responses to happy faces have been associated with more commission errors and caudate nucleus activity compared to responses to neutral expressions (Hare et al., 2005; Schulz et al., 2007). In summary, responding to emotionally salient stimuli is associated with impaired performance and differential neural activation than responding to neutral stimuli. This may suggest an increase in cognitive load, which may require additional effort, in order to engage in both response execution and inhibition when an emotional component is included within a task.

ADHD, Emotion Regulation, and Response Inhibition and Execution

Few studies have examined response inhibition and execution in youth with and without ADHD using both emotionally salient and neutral stimuli in order to address the question of the interactive effects of deficits of emotion regulation and response inhibition and execution. One such study examined response inhibition during an emotional go/no-go task, with three conditions (fear, happy, and neutral), and examined event-related potentials in

adolescents with and without ADHD. This study determined that adolescents with ADHD demonstrated fewer correct trials and differential patterns of neural responding, including larger N170 responses indicating greater emotional processing between neutral and emotional faces compared to healthy adolescents (Alperin, Gustafsson, Smith, & Karalunas, 2017). Among children with ADHD, one study examined event-related potentials and utilized letters as stimuli during a go/no-go task presented in three different emotional contexts: neutral, negative and positive (induced via emotional pictures in the background during trials; Lopez-Martin, Albert, Fernandez-Jaen & Carretie, 2015). While no performance differences were reported, children with ADHD demonstrated greater activation of inhibition-related neural mechanisms (i.e., no-go P3 amplitudes and orbitofrontal cortex activity), but only during emotionally salient contexts (i.e., emotional pictures in the background). Thus, to achieve similar levels of performance, children with ADHD appear to utilize more cognitive resources during emotional contexts (Lopez-Martin et al., 2015). However, this study included a relatively small sample ($N < 50$) and did not include emotionally salient stimuli as the response targets of the task, but rather included emotional pictures being viewed in the background. It may be that utilizing emotional images as response targets rather than passively viewing emotional pictures in the background, would be more likely to engage both emotion regulation and response inhibition and execution mechanisms given the requirements of the task to process emotionally salient stimuli while simultaneously inhibiting and executing responses (Rebetez, Rochat, Billieux, Gay, & Van der Linden, 2015).

The Present Study

This study attempts to fill gaps in the prior literature by examining the interplay of cognition and emotion by including emotionally salient stimuli (e.g., fear and neutral faces) as response targets during an emotion and neutral go/no-go task conditions in a sample of 166 youth (75 with ADHD). Further, this study utilizes an index of parasympathetic-based regulation (i.e., RSA), in order to examine the interaction of response inhibition, response execution, and emotion regulation, among youth with and without ADHD. Additionally, an index of sympathetic-based reactivity (i.e., PEP) was included, given that physiological systems do not operate in isolation. No specific hypotheses were made regarding sympathetic-based reactivity given that the task used in this study is not proposed to primarily engage this system. However, an index of sympathetic reactivity was included as a counterpart to parasympathetic-based functioning in order to rule out alternative interpretations of effects. (Bauer et al., 2002; El-Sheikh et al., 2009).

It was hypothesized that both groups of children (i.e., children with ADHD and typically developing children) would exhibit poorer response inhibition and response execution (indexed by more errors of commission and omission, respectively) during the emotional go/no-go task condition compared to the neutral task condition, suggesting that the inclusion of emotionally salient stimuli results in added regulatory demand for all children. Next, it was hypothesized that ADHD would be associated with greater response inhibition and execution deficits across both task conditions (indexed by more errors of commission and omission, respectively) compared to typically developing children, and ADHD would be associated with parasympathetic-based dysregulation across both task conditions (indexed

by RSA augmentation) compared to typically developing children. Finally, it was hypothesized that children with ADHD would exhibit even greater response inhibition and execution deficits (indexed by more errors of commission and omission, respectively) during the emotion condition compared to typically developing youth, and exhibit even greater parasympathetic-based dysregulation during the emotional condition compared to typically developing children. That is, overall it was hypothesized that children with ADHD will demonstrate even greater difficulty during the emotional condition than typically developing youth, given the added cognitive load and biological resources required for emotion regulation in the context of the emotional go/no-go task condition (Graziano & Garcia, 2016; Shaw et al., 2014).

Method

Participants

Participants were 166 children aged 5 to 13 years ($M=8.32$, $SD=1.86$ years; 66.3% male); 75 met DSM 5 (American Psychiatric Association, 2013) criteria for ADHD (11 inattentive, eight hyperactive/impulsive, and 56 combined presentation) and 91 were typically developing comparison youth. The Florida International University review board approved all study procedures. Parents provided written consent, while children provided written assent.

Procedures

Recruitment and identification.—Recruitment and identification procedures were identical to those described in Tenenbaum et al., (2018) and are described here in brief. Children with ADHD were a sub-sample from a Summer Treatment Program (STP) recruited from a double-masked, cross-over study examining tolerance to stimulant medication. Participants were recruited from several sources, including a university treatment center, referrals from school personnel and physicians, and advertising. All STP participants were required to meet DSM 5 diagnostic criteria for ADHD, have an estimated Full Scale IQ score >80 , and have no documented contraindication, intolerance, or failed trial of methylphenidate. Children were excluded if they: met full DSM-5 criteria for Autism, currently or in the past 6 months, received psychotropic medication for conditions other than ADHD, or had active medical or psychiatric conditions that could be worsened by stimulants (seizures, arrhythmias, hypertension, Tourette's Disorder, etc.).

Typically developing youth were recruited from the community through advertisements and flyers, and pre-screened for the following exclusion criteria: use of psychoactive medication, pervasive developmental or neurological disorder, estimated IQ <80 , and the presence of four or more ADHD symptoms.

All children completed an intake assessment. All parents completed a questionnaire to obtain basic demographic information (e.g., age, ethnicity, race, sex, etc.). Additionally, a parent/guardian completed the Diagnostic Interview Schedule-Child Version (DISC-IV; Shaffer et al., 2000) with a trained master's level clinician. Parent-report was obtained for all children on the Disruptive Behavior Disorders Rating Scale (Pelham, Gnagy, Greenslade, &

Milich, 1992) and Pittsburgh Modified Conner's Rating Scale (Pelham et al., 2005). Teacher-report on the Disruptive Behavior Disorders Rating Scale (Pelham et al., 1992), Pittsburgh Modified Conner's Rating Scale (Pelham et al., 2005), and Impairment Rating Scale (Fabiano et al., 2006) were also obtained for children with ADHD. To obtain an estimated full-scale IQ, all children completed the Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II; Wechsler, 2011).

Diagnostic procedure.—Diagnoses of ADHD for children enrolled in the STP were identical to procedures described in Tenenbaum et al., (2018) and described here in brief. Diagnoses were made in accordance with best-practice recommendations (Pelham, Fabiano, & Massetti, 2005). Two Ph.D. level clinicians completed a review of all available data from the initial intake (i.e., DISC-IV, parent and teacher questionnaires) to confer diagnoses of ADHD, Conduct Disorder (CD), and Oppositional Defiant Disorder (ODD), and to ensure inclusion criteria for the STP were met. A third clinician conducted a file review to mitigate any disagreements (less than 1% of cases) and the majority decision was adopted.

For the purposes of this study, all other comorbid diagnoses (excluding CD and ODD) were determined solely based on endorsements of parent report on the Diagnostic Interview Schedule for Children IV (DISC IV; Shaffer et al., 2000). For all analyses, comorbid diagnoses were collapsed into the following categories: 1) "anxiety disorder" (including generalized anxiety, separation anxiety, and/or social anxiety disorders); 2) ODD; and 3) CD. No child met criteria for current or lifetime mood disorders.

Measures

Children with ADHD completed a wash out period for stimulant medications (equivalent to seven half-lives) prior to participation in all study tasks.

Go/no-go task.—Participants completed two conditions of a go/no-go task (described in Alperin et al., 2017; Cservenka, Fair, & Nagel, 2014) using E-Prime software. Each task condition consisted of the presentation of grey-scaled photos of facial stimuli (i.e., NimStim Face Stimulus Set including six females and six males). Participants viewed the facial stimuli on a computer monitor and indicated responses via a keyboard. For both task conditions, 60 stimuli were presented with a ratio of go to no-go stimuli of 70/30 (i.e., 42 go : 26 no-go). Each photo stimulus was presented for 500 ms, followed by a 200-to-1200 milli-second inter-trial interval consisting of a fixation cross on a blank screen (Cservenka et al., 2014; Hare et al., 2005). Neutral and emotional go/no-go task conditions were counterbalanced randomly, and order of task completion was accounted for statistically.

Neutral Go/No-Go. To index response inhibition and execution, a neutral go/no-go task condition was used. Participants were exposed to photos of male and female faces displaying calm facial affect and participants were instructed to respond to female faces (i.e., go trials) by pressing a button as quickly as possible and not to respond to male faces (i.e., no-go trials). This task was designed to serve as a control condition, as children were instructed to respond to gender and all facial expressions displayed were calm, therefore, not requiring emotion regulation. Calm faces have been previously validated for use as a control condition

especially for use with children (Lobaugh et al., 2006; Thomas et al., 2001; Tottenham et al., 2009).

Emotional Go/No-Go. To index response inhibition and execution during emotionally salient contexts, requiring emotion regulation, an emotional go/no-go task was employed. In the emotional go/no-go task participants were instructed to respond to fearful faces (i.e., go trials) by pressing a button as quickly as possible and not to respond to any other type of emotional face (i.e., calm; no-go trials).

Psychophysiological recording overview.—Procedures were identical to those described in Tenenbaum et al., (2018). In brief, disposable silver/silver-chloride electrodes were placed in an electrocardiogram (ECG) and impedance cardiography (ICG) configuration, and were both recorded throughout a two-minute resting baseline period and the go/no-go tasks.

Cardiac pre-ejection period (PEP; SNS-based responding).—To index SNS-based arousal during tasks, PEP was derived in 60-second epochs using ECG and ICG. PEP was indexed in milliseconds as the interval from the onset of the Q-wave to the B-point of the dZ/dt wave. MindWare Impedance Cardiography V.3.1 software was used to remove artifacts (MindWare, 2008). To establish inter-rater reliability, two raters processed 20% of cases for artifact removal ($k > 0.85$). There were no between-group differences in the rate of artifacts (all $p > .50$). PEP reactivity was calculated by creating a change score from the two-minute resting baseline period to the go/no-go tasks for each task condition separately, with shortened PEP indicating increased sympathetic-reactivity.

Respiratory sinus arrhythmia (RSA; Parasympathetic nervous system (PNS)-based regulation).—To index PNS-based regulation, RSA was derived in 60-second epochs derived from the ECG via spectral analysis of the R-R time series. The time series was detrended and submitted to a Fourier transformation. The high frequency band ($\ln(\text{ms}^2)$) was set over the respiratory frequency band of 0.24 to 1.040 Hz derived from impedance signal (Z0). MindWare Heart Rate Variability V.3.1 software was used to remove artifacts in the R-R waves. To ensure inter-rater reliability, 20% of cases were processed for artifacts by two raters ($k > .93$). There were no between-group differences in artifacts (all $p > .50$). RSA reactivity was calculated by creating a change score from the two-minute resting baseline period to the go/no-go tasks for each task condition separately, with adaptive functioning typically represented by RSA withdrawal to all for engagement with the task.

Data Analysis Plan

Data Analyses.—Group comparisons were conducted using repeated-measures analysis of covariance (RM-ANCOVA) to examine group differences in task performance, PEP reactivity, and RSA reactivity across task conditions (in separate analyses). Simple effects were probed with analysis of covariance (ANCOVA) to examine both main effects of task condition and group, as well as interactive effects of group and task condition, when statistically appropriate.

Results

Preliminary Analyses

Demographic and diagnostic overview of the sample.—Descriptive statistics are reported by group in Table 1. Groups did not differ with respect to age, ethnicity, and FSIQ (all $p > .08$; Table 1). Inclusion of these variables did not affect the results of the primary analyses, and results are reported without these variables included. Children with ADHD were more likely to be male and to be previously prescribed medication for behavior, emotional or psychiatric problems ($p < .001$; Table 1); as such, biological sex and previous medication use were treated as covariates in all results, and results are reported with these variables included.

Clinical characteristics and group comparisons for the sample are also provided in Table 1. As expected, CD and ODD diagnoses were more common among children with ADHD (all $p < .003$; Table 1), and CD and ODD diagnoses were treated as covariates in all analyses. In contrast, group differences were not observed for anxiety diagnoses ($p = .10$; Table 1). However, anxiety disorder diagnosis was included as a covariate in all analyses due to the well-established influence of anxiety on the autonomic nervous system (Beauchaine, 2001; Boyce et al., 2001; El-Sheikh, Arsiwalla, Hinnant, & Erath, 2011; Supplemental Table 1 includes all group-level analyses without anxiety disorders treated as a covariate). Importantly, the inclusion of anxiety diagnosis as a covariate did not affect the overall patterns of results. Medication order randomization assignment (either placebo first or medication first) was included as a covariate in all analyses to control for medication randomization required of the larger study from which participants with ADHD were recruited.

Primary Analyses: Task Performance, PEP, and RSA by ADHD Diagnosis

Go/no-go task performance, PEP raw scores and reactivity scores, and RSA raw scores and reactivity scores are presented in Table 2 according to ADHD diagnostic group status. All primary analyses are reported with covariates included. All analyses were first conducted without covariates included. Overall results did not differ with the inclusion of covariates, and thus, all results are reported with covariates to account for subtleties associated with the covariate variables. Results without covariates are available upon request from the first author. Effect sizes (Cohen's d s) were calculated from *partial eta squared* (η_p^2) and classified according to Cohen's principles: 0.2 for a small effect size, 0.5 for a medium effect size and 0.8 for a large effect size (Cohen, 1988).

Go/no-go task performance according to ADHD diagnosis.

Omission errors. 2×2 RM-ANOVA examined the main and interaction effects of task condition (i.e., fear vs. neutral go/no-go) and group (i.e., ADHD vs. typically developing) on errors of omission with relevant covariates. There was a significant main effect of task condition; such that, overall (i.e., averaging across children with ADHD and typically developing youth), children demonstrated more errors of omission during the fear condition ($M = 50.97$, $S.E. = .76$) than during the neutral condition ($M = 12.71$, $S.E. = .39$; $F(1,158) = 188.07$, $p < .001$, $\eta_p^2 = .54$, $d = 2.11$). Additionally, there was a significant main

effect of group; such that, overall (i.e., averaging across fear and neutral go/no-go task conditions) children with ADHD had more errors of omission ($M=34.61$, $S.E.=.48$) across the two conditions compared to typically developing youth ($M=29.08$, $S.E.=1.25$; $F(1,158)=4.59$, $p=.03$, $\eta_p^2=.03$, $d=.35$). The interaction of task condition by group was not significant ($F(1,158)=2.99$, $p=.09$, $\eta_p^2=.02$, $d=.29$).

Commission errors. 2×2 RM-ANOVA examined the main and interaction effects of task condition (i.e., fear vs. neutral go/no-go) and group (i.e., ADHD vs. typically developing) on errors of commission with covariates. There was a significant main effect of task condition; such that, overall children demonstrated fewer errors of commission during the fear condition ($M=3.13$, $S.E.=.29$) than during the neutral condition ($M=6.66$, $S.E.=.19$; $F(1,158)=17.06$, $p<.001$, $\eta_p^2=.10$, $d=.61$). The main effect of group was not significant ($F(1,158)=2.30$, $p=.13$, $\eta_p^2=.01$, $d=.20$). However, there was a significant interaction of task condition by group ($F(1,158)=7.10$, $p=.009$, $\eta_p^2=.04$, $d=.41$). Specifically, children with ADHD demonstrated fewer errors of commission during the fear condition ($M=1.12$, $S.E.=.94$) compared to typically developing youth ($M=5.14$, $S.E.=.79$; $F(1,158)=6.09$, $p=.02$, $\eta_p^2=.04$, $d=.41$), while groups did not differ during the neutral condition ($F(1,158)=.66$, $p=.42$, $\eta_p^2=.004$, $d=.13$).

Correct go responses. 2×2 RM-ANOVA was also used to examine the main and interaction effects of task condition (i.e., fear vs. neutral go/no-go) and group (i.e., ADHD vs. typically developing) on correct go responses with covariates. There was a significant main effect of task condition; such that, overall children demonstrated fewer correct go responses during the fear condition ($M=8.09$, $S.E.=.60$) compared to the neutral condition ($M=17.22$, $S.E.=.39$; $F(1,158)=20.18$, $p<.001$, $\eta_p^2=.11$, $d=.70$). Additionally, there was a significant main effect of group; such that, overall (i.e., averaging across go/no-go task conditions) children with ADHD demonstrated significantly fewer correct go responses ($M=9.81$, $S.E.=1.31$) than typically developing youth ($M=15.50$, $S.E.=1.11$; $F(1,158)=6.19$, $p=.01$, $\eta_p^2=.04$, $d=.41$). The interaction of task condition by group was also significant (Figure 1a; $F(1,158)=4.40$, $p=.04$, $\eta_p^2=.03$, $d=.35$). Specifically, children with ADHD demonstrated significantly fewer correct go responses during the fear condition ($M=3.47$, $S.E.=1.94$) compared to typically developing youth ($M=12.70$, $S.E.=1.63$; $F(1,158)=7.50$, $p=.007$, $\eta_p^2=.05$, $d=.46$), while no group-based differences were observed during the neutral condition ($F(1,158)=.95$, $p=.33$, $\eta_p^2=.006$, $d=.16$).

Correct no-go non-responses. 2×2 RM-ANOVA was also used to examine the main and interaction effects of task condition (i.e., fear vs. neutral go/no-go) and group (i.e., ADHD vs. typically developing) on correct no-go non-responses with covariates. There was a significant main effect of task condition; such that, overall children demonstrated more correct no-go responses during the fear condition ($M=22.42$, $S.E.=.37$) compared to the neutral condition ($M=6.30$, $S.E.=.19$, $F(1,158)=140.11$, $p<.001$, $\eta_p^2=.47$, $d=1.88$). The main effect of group was not significant ($F(1,158)=1.70$, $p=.19$, $\eta_p^2=.01$, $d=.20$). However, the interaction of task condition by group was significant (Figure 1b; $F(1,158)=5.50$, $p=.02$, $\eta_p^2=.03$, $d=.35$). Children with ADHD demonstrated significantly more correct no-go responses during the fear condition ($M=24.54$, $S.E.=1.19$) compared to typically developing

youth ($M=20.30$, $S.E.=1.00$; $F(1,158)=4.21$, $p=.04$, $\eta_p^2=.03$, $d=.35$), while no significant group differences were observed during the neutral condition ($F(1,158)=1.14$, $p=.29$, $\eta_p^2=.007$, $d=.17$).

PEP reactivity according to ADHD diagnosis.— 2×2 RM-ANOVA examined the main and interactive effects of task condition (i.e., fear vs. neutral go/no-go) and group (i.e., ADHD vs. typically developing youth) on PEP change scores from baseline with covariates. The main effect of task condition on PEP reactivity was not significant ($F(1,158)=1.70$, $p=.20$, $\eta_p^2=.01$, $d=.20$). However, there was a significant main effect of group ($F(1,158)=10.37$, $p=.002$, $\eta_p^2=.06$, $d=.51$). Specifically, when averaging across the two conditions, children with ADHD exhibited reductions in SNS-based activity (i.e., PEP lengthening; $M=8.10$, $S.E.=1.82$), while typically developing youth displayed increases in SNS-based activity (i.e., PEP shortening; $M=-2.10$, $S.E.=1.53$). The interaction of condition by group was non-significant (Figure 2b; $F(1,158)=.28$, $p=.56$, $\eta_p^2=.002$, $d=.09$).

RSA reactivity according to ADHD diagnosis.— 2×2 RM-ANOVA examined main and interactive effects of task condition (i.e., fear vs. neutral go/no-go) and group (i.e., ADHD vs. typically developing youth) on RSA change scores from baseline with covariates. The main effect of task condition on RSA reactivity was not significant ($F(1,158)=2.97$, $p=.09$, $\eta_p^2=.02$, $d=.29$). However, there was a significant main effect of group ($F(1,158)=6.42$, $p=.01$, $\eta_p^2=.04$, $d=.41$). Specifically, when averaging across conditions, children with ADHD exhibited significantly reduced PNS-based regulation (i.e., RSA augmentation/reduced RSA withdrawal; $M=.57$, $S.E.=.19$) compared to typically developing youth (i.e., RSA withdrawal $M=-.26$, $S.E.=.16$). The interaction of condition by group was also significant (Figure 2a; $F(1,158)=4.46$, $p=.04$, $\eta_p^2=.03$, $d=.35$). Specifically, children with ADHD displayed reduced PNS-based regulation (i.e., RSA augmentation/reduced RSA withdrawal; $M=.76$, $S.E.=.21$) during the neutral condition compared to typically developing youth (i.e., RSA withdrawal $M=-.36$, $S.E.=.18$; $F(1,158)=9.47$, $p=.002$, $\eta_p^2=.06$, $d=.51$). No group-based differences were observed during the fear condition ($F(1,158)=2.31$, $p=.13$, $\eta_p^2=.01$, $d=.20$).

Discussion

This study examined the interaction of response inhibition, response execution, and emotion regulation among youth with and without ADHD. While it is well-established based on prior literature that youth with ADHD display impairments in response inhibition, response execution, and emotion regulation (Graziano & Garcia, 2016; Oosterlaan et al., 1998; Shaw et al., 2014), previous literature has examined these domains of self-regulation separately. Furthermore, while prior studies have demonstrated that the inclusion of emotional processing during self-regulation tasks requires additional cognitive load (Goldstein et al., 2007; Hare et al., 2005; Monk et al., 2003; Shafritz, Collins, & Blumberg, 2006), this is one of the first studies to use a multi-method approach to examine the nature of this interaction in youth with ADHD in attempts to better understand the nature of behavioral and emotional difficulties associated with ADHD. This study lays the groundwork for future research, and once replicated and extended, may be used to develop more targeted interventions for youth with ADHD by demonstrating the need to develop and improve emotion regulation

strategies among youth with ADHD, as the development of such strategies may improve not only behavior, but also cognitive functioning.

In support of our first hypothesis, children (i.e., both children with ADHD and typically developing children) were more likely to exhibit poorer performance on a response inhibition task in the presence of an emotion regulation demand as evidenced by greater errors of omission and fewer correct go responses during the emotional (i.e., fear) compared to the neutral (i.e., calm) go/no-go task. This finding supports our hypothesis that the addition of an emotion regulation demand resulted in greater challenge for youth, perhaps by requiring additional cognitive resources to regulate the emotional response generated by the emotionally salient stimuli prior to responding. This result is in line with prior literature in healthy samples, which has demonstrated poorer performance on response inhibition tasks that included an emotional component (Hare et al., 2005; Schulz et al., 2007). Interestingly, however, all children demonstrated fewer errors of commission and more correct no-go responses in the presence of an emotion regulation demand (i.e., during the emotional compared to neutral go/no-go task). Given that the emotional stimuli chosen for this study were fearful faces, it may be that children engaged in more avoidant behavior during the emotional condition than the neutral condition. This seems particularly likely in light of the increased number of omission errors during this condition. That is, when taken together the pattern of responding observed during the emotional condition is in line with under-responding, perhaps due to avoidance, during the emotional condition. This notion of increased avoidance behavior in response to fearful faces is supported by prior work showing that healthy participants displayed “freezing” behavior when viewing fearful faces as opposed to anger faces (Adams, Ambady, Macrae, & Kleck, 2006).

With respect to differences among youth with and without ADHD, in support of our hypothesis, children with ADHD differed from typically developing youth with respect to performance on the emotional response inhibition task. Specifically, in accordance with prior literature, children with ADHD displayed more errors of omission when averaging across task conditions, suggesting a deficit in the domain of correctly and quickly initiating responses during the task conditions (Alperin et al., 2017; Desman et al., 2008; Wodka et al., 2007). Additionally, children with ADHD demonstrated fewer correct go responses in the context of the emotional task condition compared to typically developing youth. Interestingly, children with ADHD also demonstrated fewer errors of commission and more correct no-go responses during the emotional task condition compared to typically developing children. These findings may suggest that children with ADHD had difficulty executing responses, particularly in the emotional condition, compared to typically developing youth. Thus, overall, children with ADHD exhibited greater difficulty executing correct responses in the presence of emotionally-salient stimuli, as evidenced by fewer “correct hits” or correct go-responses, as well as fewer “incorrect hits” or commission errors and a larger proportion of appropriate no-go responses, which may reflect an avoidant response style in the emotional condition (i.e., each of these response styles are representative of a reduced proportion of button presses either “correct” or “incorrect”). This notion is in line with prior work that demonstrated children with ADHD have difficulty attending to and processing tasks that involve facial emotion expressions (Yuill & Lyon, 2007).

Several explanations may account for this pattern of results. First, children with ADHD may have been more avoidant of the fear face stimuli utilized in the emotional condition. Specifically, prior work has demonstrated that children with ADHD demonstrated amygdala hyperactivity when viewing and rating fearful faces and perhaps were avoiding to engage with the fear faces in attempts to down regulate the emotional experience (Brotman et al., 2009). Second, children with ADHD may have been less engaged in the emotional task as evidenced by the pattern of fewer correct go trials and commission errors, or may have had difficulty attending to and processing the emotional stimuli, indicating that children with ADHD were less responsive throughout the task compared to healthy controls. This is in accordance with prior research examining children with ADHD's attention to emotional stimuli that revealed that youth with ADHD tend to have more difficulty sustaining attention to fear expressions (Corbett & Glidden, 2000), and tend to have more difficulty attending to appropriate cues of affect when attempting to recognize emotional facial expressions (Cadesky, Mota, & Schachar, 2000). Subsequently, children with ADHD may have had difficulty identifying the emotional faces appropriately, as prior work suggests that children with ADHD have difficulty recognizing emotions, particularly fear (Singh et al., 1998; Sinzig, Bruning, Morsch, & Lehmkuhl, 2008).

Moving on to physiological results, in accordance with our hypothesis, children with ADHD displayed greater parasympathetic-based dysregulation (indexed via RSA augmentation) across the task conditions, while typically developing children displayed RSA withdrawal. This is in line with prior research, which has shown children with ADHD display excessive and/or inflexible RSA reactivity during emotional challenges compared to healthy children (Karalunas et al., 2014; Musser et al., 2011). In contrast to our hypotheses, children with ADHD displayed significantly augmented RSA during the neutral task condition compared to typically developing youth with respect to RSA reactivity (i.e., parasympathetic-based dysregulation), while this pattern was not evident during the fear task condition. In conjunction with PNS-based functioning, when examining SNS-based reactivity across tasks, children with ADHD displayed reduced SNS-based reactivity (i.e., PEP lengthening) while typically developing children displayed increased SNS-based reactivity (i.e., PEP shortening). When taken together, this may suggest that children with ADHD were less motivated to engage in the task or found the task to be less stressful than typically developing children which is in accordance with research demonstrating reduced SNS-based reactivity (i.e. PEP lengthening) during challenging and rewarding tasks among children with externalizing behavior broadly (i.e., ADHD and/or disruptive behavior disorder diagnoses or symptomology; (Beauchaine et al., 2001, 2013; Boyce et al., 2001; Crowell et al., 2006). This pattern of reduced SNS-based activity and a lack of PNS-based dysregulation displayed during the fear condition is in accordance with theories proposing underarousal of the mesolimbic dopamine system in children with ADHD and/or disruptive behavior disorders (Beauchaine, 2012; Gatzke-Kopp et al., 2009). Furthermore, this theory of underarousal has been associated with reduced effort and motivation during response inhibition tasks in children with ADHD and may help explain our findings (Shaw, Grayson, & Lewis, 2005; Slusarek, Velling, Bunk, & Eggers, 2001).

In summary, children with ADHD displayed impaired response inhibition performance, parasympathetic-based dysregulation, and reduced SNS-based reactivity when averaging

across task conditions compared to healthy controls. With the addition of emotional challenge, children with ADHD demonstrated a specific deficit in executing responses as opposed to inhibition of responses. While it remains unclear the exact cause of this pattern, one promising explanation may be that children with ADHD had difficulty processing the emotionally salient stimuli due to either, problems of attention and attending to facial affect cues, and/or problems of emotion recognition causing additional difficulty when responding to emotionally salient stimuli. Future work should continue to examine this association to further elucidate the roles of response inhibition, execution and emotion regulation deficits in children with ADHD. Building upon these results may allow for a better understanding of the role inhibition, execution and emotion regulation play in the etiology and maintenance of ADHD. Additionally, once replicated and extended, further demonstration that youth with ADHD have difficulty inhibiting their behavior, particularly in the context of emotionally laden information, can inform potential treatment targets. For example, clinicians may focus on increasing emotion recognition and regulation abilities while practicing inhibition of behavior in emotionally provocative situations, such as with peers to improve social-emotional functioning.

While this study is a first step in understanding the relation between response inhibition, execution and emotion regulation in ADHD, key limitations should be noted. First, this study is cross-sectional, and longitudinal analyses of these domains may aid in understanding the temporal relation, differential trajectory, and predictions of prognosis in children with ADHD. Second, the inclusion of fear faces as the sole emotional target stimuli for the emotional task condition may have limited generalizability of findings, and inclusion of other emotional stimuli would allow for an added specificity of questions related to regulating both positive and negative affect. Third, the inclusion of a different go/no-go task that requires additional cognitive processing, but does not include emotionally salient stimuli, would help evaluate whether the effects were specific to emotion or that the effect results from an increased general cognitive demand. Fourth, the sample recruited for study did not include children with comorbid mood disorders, which may limit generalizability of results and future work should include such youth. Fifth, the magnitude of effects observed should be considered when interpreting results, given the effect sizes observed in this study were somewhat modest and require further replication. Finally, future investigations should attempt to examine these processes using additional methodology such as eye tracking, event related potentials or youth self-report in order to elucidate children's orienting and processing patterns to determine attention to the task and potential avoidance of emotionally salient stimuli as a regulatory mechanism.

In conclusion, this study included a multi-method assessment of response inhibition, execution and emotion regulation during an emotional and neutral go/no-go task and revealed distinct patterns for children with ADHD. Children with ADHD demonstrated greater difficulty executing responses to fearful faces and general parasympathetic-based dysregulation and sympathetic-based under-arousal across conditions, providing an initial step in attempting to elucidate deficits commonly associated with ADHD. Future work should continue to examine the relation between response inhibition, execution and emotion regulation including additional methods of measurement, across contexts in order to improve

our understanding of the functioning of these processes in children with ADHD and their contribution to behavior and impairment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1A and Fig. 1B.

Go/No-Go Performance (A: Correct Go Responses; B: Correct No-Go Responses) according to task (i.e., neutral vs. fear) and by group (i.e., typically developing vs. ADHD)

A. The interaction of task condition by group was significant ($F=4.40$, $p=.04$, $\eta_p^2=.03$); Children with ADHD demonstrated significantly fewer correct go responses during the fear condition ($M=3.47$, $S.E.=1.94$) compared to typically developing youth ($M=12.70$, $S.E.=1.63$; $F=7.50$, $p=.007$, $\eta_p^2=.05$), no group-based differences were observed during the neutral condition ($F=.95$, $p=.33$, $\eta_p^2=.006$).

B. The interaction of task condition by group was significant ($F=5.50$, $p=.02$, $\eta_p^2=.03$); Children with ADHD demonstrated significantly more correct no-go responses during the fear condition ($M=24.54$, $S.E.=1.19$) compared to typically developing youth ($M=20.30$, $S.E.=1.00$; $F=4.21$, $p=.04$, $\eta_p^2=.03$), while no significant group differences were observed during the neutral condition ($F=1.14$, $p=.29$, $\eta_p^2=.007$).

Fig. 2A and Fig. 2B.

Psychophysiological Reactivity (A: RSA reactivity; B: PEP reactivity) according to task (i.e., neutral vs. fear) and by group (i.e., typically developing vs. ADHD)

A. Mean change scores in respiratory sinus arrhythmia (RSA) from baseline to each of the task conditions by group. The interaction of condition by group was significant ($F=4.46$, $p=.04$, $\eta_p^2=.03$), children with ADHD displayed reduced PNS-based regulation (i.e., RSA augmentation; $M=.76$, $S.E.=.21$) during the neutral condition compared to typically developing youth (i.e., RSA withdrawal $M=-.36$, $S.E.=.18$; $F=9.47$, $p=.002$, $\eta_p^2=.06$), while

no significant group-based differences were demonstrated during the fear condition ($F=2.31$, $p=.13$, $\eta_p^2=.01$).

B. Mean change scores in pre-ejection period from baseline to each of the task conditions by group. Interaction of task condition by group for PEP reactivity was not significant but is represented in order to evaluate RSA reactivity. The interaction of condition by group was non-significant ($F=.28$, $p=.56$, $\eta_p^2=.002$), the main effect of group was significant ($F=10.37$, $p=.002$, $\eta_p^2=.06$), children with ADHD exhibited reductions in SNS-based activity (i.e., PEP lengthening; $M=8.10$ $S.E=1.82$), while typically developing youth displayed increases in SNS-based activity (i.e., PEP shortening; $M=-2.10$, $S.E=1.53$).

Table 1.

Descriptive and diagnostic statistics for ADHD and control participants

Variable	Control (<i>n</i> =91)	ADHD (<i>n</i> =75)	<i>F</i> (1,164)/ χ^2 (1)	Partial η^2/η
Demographics				
Age, mean (<i>SD</i>)	8.56(1.91)	8.03 (1.76)	3.45	.02
Gender (% male)	55	80	11.55 *	.26
Ethnicity (%Hispanic or Latino)	87.9	89.3	.08	.02
WASI-II FSIQ, mean (<i>SD</i>)	100.53 (12.05)	98.04 (12.85)	1.65	.01
Previous medication use (%received) ^a	0	69.3	91.87 *	.74
Parent Rating Scales				
Impairment Rating	--	5.15 (.87)		
Inattention Symptoms	.59 (1.20)	6.25 (2.66)	331.67 *	.67
Hyperactivity/Impulsivity Symptoms	.44 (.92)	5.41 (2.83)	249.70 *	.60
ODD Symptoms	.20 (.63)	3.08 (2.56)	107.53 *	.40
CD Symptoms	.03 (.22)	.69 (1.05)	34.33 *	.17
IOWA Conners Inattention/Overactivity	1.82 (2.26)	9.83 (3.44)	323.34 *	.66
IOWA Conners Oppositional-Defiant	1.11 (1.64)	7.74 (3.84)	222.37 *	.58
Teacher Rating Scales				
Impairment Rating	--	5.13 (1.28)		
Inattention Symptoms	--	6.38 (2.85)		
Hyperactivity/Impulsivity Symptoms	--	5.42 (2.99)		
ODD Symptoms	--	2.99 (2.69)		
CD Symptoms	--	.93 (1.46)		
IOWA Conners Inattention/Overactivity	--	10.97 (3.98)		
IOWA Conners Oppositional-Defiant	--	7.74 (3.84)		
Comorbid Disorders (%Diagnosis)				
ODD ^b	0	69.3	91.87 *	.74
CD ^b	0	9.30	8.87 *	.23
Anxiety ^c	3.30	9.30	2.65	.13

Note=

* $p < .01$.

SD= Standard Deviation; WASI-II= Wechsler Abbreviated Scale of Intelligence-Second Edition; FSIQ=Full-Scale Intelligence Quotient (estimated); Parent Rating Scales=The Impairment Rating Scale Overall Severity (0=no problem to 6=extreme problem), Disruptive Behavior Disorders Parent Rating Scale indexed total symptoms and two subscales of the IOWA Conners Rating Scale comprising the Pittsburgh Modified Conners Parent Rating Scale (0-15 with higher scores indicating more symptoms); Teacher Rating Scales= The Impairment Rating Scale Overall Severity (0=no problem to 6=extreme problem), Disruptive Behavior Disorders Teacher Rating Scale indexed total symptoms and two subscales of the IOWA Conners Rating Scale comprising the Pittsburgh Modified Conners Teacher Rating Scale 0-15 with higher scores indicating more symptoms); ODD= Oppositional Defiant Disorder; CD= Conduct Disorder.

^aParent-report of children who previously received medication for behavior, emotional or psychiatric problems

^b Oppositional defiant disorder and conduct disorder for the ADHD group was diagnosed by the clinical diagnostic team and the Diagnostic Interview Schedule for Children-Parent Version (DISC-IV) was used for the control group.

^c Anxiety disorders; Generalized anxiety disorder, separation anxiety disorder and social anxiety disorder were diagnosed based off of endorsements of the DISC-IV parent report.

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Table 2.

Physiology and Go/No-Go task data for controls and ADHD participants

Variable Estimated Marginal Means (SE)	Control (n=91)	ADHD (n=75)	F(1,158)	Partial η^2
Resting Baseline				
RSA	6.97 (.24)	6.19 (.28)	2.53	.02
PEP	99.29 (2.57)	92.65 (3.05)	1.56	.01
Neutral Go/No-Go Task Physiology				
RSA	6.61 (.21)	6.95 (.25)	.62	.004
PEP	97.75 (2.62)	100.37 (3.11)	.23	.001
RSA Reactivity	-.36 (.18)	.76 (.21)	9.47 *	.06
PEP Reactivity	-1.54 (1.73)	7.72 (2.06)	6.67 *	.04
Fear Go/No-Go Task Physiology				
RSA	6.82 (.20)	6.57 (.23)	.40	.003
PEP	96.64 (2.75)	101.12(3.27)	.62	.004
RSA Reactivity	-.15 (.17)	.38 (.20)	2.31	.01
PEP Reactivity	-2.67 (1.77)	8.47 (2.10)	9.28 *	.06
Neutral Go/No-Go Task Data				
Omission errors	11.85 (1.06)	13.58 (1.26)	.62	.004
Commission errors	6.22 (.52)	7.10 (.62)	.66	.004
Correct go responses	18.29 (1.06)	16.15 (1.26)	.95	.006
Correct no-go/non-responses	6.88 (.52)	5.72 (.62)	1.14	.007
Fear Go/No-Go Task Data				
Omission errors	46.31 (2.06)	55.64 (2.45)	4.78 *	.03
Commission errors	5.14 (.79)	1.12 (.94)	6.09 *	.04
Correct go responses	12.70 (1.63)	3.47 (1.94)	7.50 *	.05
Correct no-go/non-responses	20.30 (1.00)	24.54 (1.19)	4.21 *	.03

Note=

*
 $p < .05$.

RSA= Respiratory Sinus Arrhythmia (ms^2); PEP= Pre-ejection period. All models include covariates (previous medication use, gender, ODD diagnosis, CD diagnosis, anxiety diagnosis and medication randomization order). Physiology reactivity scores are calculated by subtracting resting baseline physiology from the task physiology.