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Parasympathetic Regulation and Inhibitory Control Predict the Development of Externalizing Problems in Early Childhood

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Abstract The current report examined the longitudinal relations between cognitive self-regulation, physiological self-regulation, and externalizing problems. At age 4 (n = 98; 49 girls) and 6 (n = 87; 42 girls), children completed the Day-Night task, which taps the inhibitory control dimension of executive function. During the task, cardiac activity was measured and respiratory sinus arrhythmia (RSA) was derived as an index of parasympathetic activity. Mothers reported on externalizing problems. A cross-lagged path model was used to estimate longitudinal predictions while controlling for stability in all constructs over time. Earlier inhibitory control negatively predicted later externalizing problems, but not vice versa. However, RSA reactivity moderated this link; better inhibitory control predicted fewer externalizing problems only when reactivity to the Day-Night task ranged from mild RSA suppression to RSA augmentation. Externalizing problems at 6 years were highest among preschoolers who augmented RSA but showed poor inhibitory control performance, suggesting that risk for psychopathology may be better delineated by viewing self-regulation from an integrated, multi-system perspective.

Keywords Externalizing problems · Executive function · Inhibitory control · Parasympathetic nervous system · Respiratory sinus arrhythmia (RSA) · Self-regulation

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Externalizing problems are characterized by weak control of emotions and behavior particularly with regard to anger or aggression (Campbell et al. 2000; Eisenberg et al. 2001). Given this, externalizing problems are often considered as stemming from broad difficulties with self-regulation (Barrett 2013; Eisenberg et al. 2001). Self-regulation is a multi-faceted construct, including multiple aspects of both cognitive and neurophysiological regulation (Barrett et al. 2013), but such an integrative perspective has infrequently been applied to the regulatory difficulties that may underlie externalizing problems. For example, externalizing problems have been consistently linked with deficits in executive function (Hughes et al. 1998), and specifically with poor inhibitory control (Schoemaker et al. 2013). Other examinations have shown that children with externalizing problems also show atypical patterns of parasympathetic activity (Calkins and Keane 2004; Graziano and Derefinko 2013; Obradović et al. 2010; see Beauchaine 2012 for a review), an aspect of physiology that is thought to be critical for the regulation of emotions and behavior (Porges 2007). However, little is known about how executive function and parasympathetic activity, together, contribute to the development of externalizing problems.

This gap in our understanding has been highlighted by recent calls for greater attention to the ways in which cognitive and physiological aspects of regulation may work together to support or undermine healthy, well-regulated functioning (Obradović 2016). In order to better capture the complexity of self-regulation processes as they relate to the development of maladaptive behavior, this study examined how inhibitory control and parasympathetic activity contributed, independently and interactively, to the development of externalizing problems across the transition from the preschool to primary school years in a sample of children at high risk for externalizing problems.

Inhibitory Control and Externalizing Behaviors

Inhibitory control is a component of executive function, a set of skills involving higher-order cognitive control of thought and behavior (Diamond 2013). Inhibitory control involves inhibiting a dominant or impulsive response, typically while also remembering and acting in accord with an alternate rule, and develops dramatically between 3 and 6 years (Best and Miller 2010). In the current study, we utilized the Day-Night task to index inhibitory control. In this task, children are shown pictures of a sun or a moon and must give an opposite label in response (e.g., "Say 'day' when you see a moon;" Gerstadt et al. 1994). Much like in the classic Stroop task, children must inhibit the dominant tendency to label the picture as depicted. Inhibiting inappropriate behaviors is clearly relevant to self-regulation, and, indeed, an inverse relation between inhibitory control and externalizing-type problems has been documented in studies of preschoolers (Floyd and Kirby 2001; Hughes and Ensor 2008; Olson et al. 2011; Utendale et al. 2011) and older children (Nigg et al. 1999; Oosterlaan and Sergeant 1996). Deficits in inhibitory control are also a central feature of attention deficit/hyperactivity disorder (ADHD; Barkley 1997; Willcutt et al. 2005), and the inattention and aggression aspects of externalizing problems share similar magnitudes of relations with poor inhibitory control (Utendale et al. 2011). In fact, a recent meta-analysis identified inhibitory control as being more strongly related to externalizing problems in preschoolers than any other aspect of executive function (Schoemaker et al. 2013).

Despite this consistent link, it has been unclear whether weak inhibitory control precedes or follows elevated externalizing problems across the transition from preschool to kindergarten, because very few studies have included measures of both constructs at multiple times. This is a developmental period of dynamic change in self-regulatory abilities, and, while externalizing problems are somewhat common in the preschool years and typically decrease after that (Barrett 2013), some children show stable or worsening externalizing problems, putting them at risk for psychopathologies such as conduct disorder and oppositional defiant disorder (Campbell et al. 2000). Although several studies have reported that earlier inhibitory control deficits predict later externalizing problems (Buss et al. 2014; Hardaway et al. 2012), these have not accounted for the potential stability of concurrent associations between inhibitory control and externalizing problems. Despite this, a predominant perspective is that early deficits in prefrontally mediated cognitive control may inhibit either the acquisition or implementation (or both) of appropriate regulatory skills, and thereby increase the likelihood of externalizing behavior problems (Hughes and Ensor 2008).

There is some evidence for the opposite direction of effect, however, and early instances of undercontrolled and aggressive behavior might limit children's opportunities for engaging in experiences that would build effective inhibitory control skills (Hughes and Ensor 2008). Indeed, young children who were hard-to-manage or highly negatively reactive have been shown to have inhibitory control deficits years later (Brophy et al. 2002; Ursache et al. 2013). In one of the few studies to examine both constructs as outcome variables, Hughes and Ensor (2008) found that executive function at age 3 predicted externalizing problems a year later more strongly than the reverse association; the link from problems to executive function was marginally significant. However, their regression analyses did not account for the potential stability of contemporaneous associations between executive function and externalizing problems over time.

To examine such temporal associations more informatively, both inhibitory control and externalizing problems should be measured at two or more time points while allowing both to be simultaneous dependent variables. This approach is important because inhibitory control and externalizing problems could show consistent concurrent relations at multiple time points, but failure to include both measures at the second time point could create a spurious longitudinal effect due to the stability in measures over time (Little et al. 2009). As far as we know, only one recent report of this kind of analysis has been published. Sulik et al. (2015) found that a general executive function composite predicted externalizing problems from 3 to 4 years and from 4 to 5 years, but the predictive path from externalizing to executive function was present only from 4 to 5 years. In the present study, we used a cross-lagged path analysis to probe the directionality of the relation between inhibitory control and externalizing problems. That is, we investigated whether earlier inhibitory control had a lagged effect on later externalizing problems, and whether earlier externalizing problems had a lagged effect on later inhibitory control. We focused on inhibitory control because it has been shown to be particularly relevant for early-emerging externalizing problems. We investigated the 2-year span from 4 to 6 years that captures both a time of important development in executive function and a dramatic shift in the way that self-regulation skills are put into play as children make the transition to primary school.

Parasympathetic Activity as a Component of Self-Regulation

There has been a call for further identification of the neurobiological mechanisms that may underlie persistent problems (Dougherty et al. 2015), and Obradović (2016) recently theorized that, specifically, the interplay between executive processes and physiological activity may be especially relevant for explaining adaptive outcomes. The activity of the parasympathetic nervous system has been theorized to be a physiological indicator of self-regulatory processes (Porges 2007), and shows associations with both executive function (Marcovitch et al. 2010) and externalizing problems in children (Beauchaine 2001). The *neurovisceral integration* hypothesis posits that cognitive control, and self-regulation more broadly, is partially supported by the brain areas that also control autonomic activity (Thayer and Lane 2000). For example, the anterior cingulate is implicated in aspects of executive function (Bush et al. 2000) and parasympathetic activity (Gianaros et al. 2004), as well as with externalizing problems (Woltering et al. 2011). It is not yet known whether this suggests a common neural origin for the observed associations among inhibitory control, externalizing problems, and parasympathetic activity, but further investigation of the developing links between cognitive, autonomic and behavioral regulation is clearly warranted.

The parasympathetic nervous system provides dynamic regulation of physiological arousal, allowing for adaptive responding to changing contexts. This activity can be indexed through cardiac measures, as the parasympathetic branch regulates the cardiac pacemaker via the vagus nerve. Respiratory sinus arrhythmia (RSA) is variability in heart rate that occurs at the frequency of respiration, and is an index of parasympathetic influence (Berntson et al. 1993). Greater parasympathetic influence (reflected in higher RSA values) results in lower arousal and allows for restorative processes and social engagement. Conversely, less parasympathetic influence allows for greater cardiac activation and rapid engagement with the environment (Porges 2007). Two measures of cardiac parasympathetic influence are often studied: baseline or resting levels of RSA, and measures of RSA reactivity to a task or stimulus.

Baseline RSA Higher baseline RSA has often been related to fewer externalizing problems (Beauchaine 2001; Beauchaine et al. 2007; Pine et al. 1998). However, there have also been failures to link baseline RSA with externalizing problems, particularly in young children (Beauchaine et al. 2007; Hastings et al. 2008). Higher baseline RSA is more consistently related to better performance on executive function tasks (Staton et al. 2009) as well as inhibitory control tasks specifically (Blankson et al. 2012; Mezzacappa et al. 1998; Skowron et al. 2014). Children with higher baseline RSA are thought to have a greater capacity for parasympathetic modulation in order to regulate attention and arousal in response to situational demands, but across studies, the magnitude of this association varies by child age and gender, task demands and other contextual factors (Eisenberg et al. 2012). Conceptualizing self-regulation as a multi-faceted and multi-component construct, in this study we examined whether low baseline RSA in conjunction with poor inhibitory control predicted the development of externalizing problems.

RSA Reactivity Several studies have shown that children with higher levels of externalizing problems show less reduction in RSA (less parasympathetic withdrawal) during challenging tasks (Boyce et al. 2001; Calkins and Dedmon 2000; Calkins and Keane 2004; Obradović et al. 2010), an association that was also found in a recent meta-analysis (Graziano and Derefinko 2013). This association has been less clear when examining ADHD specifically (Beauchaine et al. 2013; Musser et al. 2011), and some studies have failed to show a link between RSA reactivity and externalizing problems (Eisenberg et al. 2012; Gill and Calkins 2003). There has even been evidence of the opposite pattern, with RSA augmentation (increases in RSA) being associated with fewer externalizing problems and better self-regulation in both clinical (Beauchaine et al. 2007, 2013) and typical populations (Hastings et al. 2008; Morales et al. 2015). These studies have used a range of tasks to elicit RSA changes – from frustration inductions to peer interactions – and it is important to consider contextual factors when interpreting the meaning of autonomic changes (Beauchaine 2012; Obradović and Boyce 2012; Thompson et al. 2008). Given that these tasks are associated with a range of autonomic reactions even in typically-developing samples, it may be unlikely that a single pattern of RSA reactivity is uniformly characteristic of children with externalizing problems. Rather, externalizing problems might be characterized by showing deviations from physiological patterns that have been demonstrated to be effective for responding *to the task at hand* (Hastings et al. 2014).

The pattern of RSA reactivity to inhibitory control tasks that is likely to be most effective is showing some decrease in RSA, as RSA suppression has been associated with better performance (Becker et al. 2012; Blair and Peters 2003; Mathewson et al. 2010; Sulik et al. 2015), although extreme RSA suppression appears less adaptive (Marcovitch et al. 2010). A modest decrease in parasympathetic influence during a challenging task may reflect effective regulation in this context because it supports a moderate increase in arousal and orientation towards the task, allocating greater resources for coping without engaging the sympathetic branch (Porges 2007). Because children with externalizing problems struggle with inhibitory control, we might expect that they would show RSA changes that fail to support this kind of effective task engagement – either increases (RSA augmentation), or very strong decreases (extreme RSA suppression).

Integrating Cognitive and Physiological Self-Regulation

Children may be at particular risk for externalizing problems when they show a combination of deficits across multiple components of self-regulation, for example, both cognitive and physiological deficits as reflected by poor inhibitory control skills coupled with maladaptive autonomic responding, respectively. The interaction between inhibitory control and RSA might reveal greater specificity in regard to which children show the greatest difficulty with regulating behavior (Obradović 2016), and may clarify heterogeneity observed in past studies (e.g., failures to link RSA with externalizing problems, Eisenberg et al. 2012; Gill and Calkins 2003). Few studies have examined interactions between RSA reactivity to an executive function task and performance on the task. Recently, Ward et al. (2015) found that children's working memory performance (a component of executive function) only predicted the odds of an ADHD diagnosis if they showed decreases in RSA to the working memory task. In this task context, most children (ADHD and controls) showed RSA augmentation from baseline, and children who showed this typical pattern did not have a relation between task performance and odds of having an ADHD diagnosis. Thus, children with ADHD were characterized by a task-atypical pattern of RSA suppression in combination with poor working memory.

An interaction between task RSA reactivity and task performance was also found in a prior examination of the current sample at 4 years together with an additional group of 6-year-olds (Utendale et al. 2014). In that concurrent analysis, children with more externalizing problems showed stronger RSA suppression in response to inhibitory control tasks. Additionally, only children who showed RSA suppression to the tasks also showed a concurrent negative relation between inhibitory control and externalizing problems. Thus, it was specifically children with heightened reactivity in bottom-up, physiological aspects of regulation (strong RSA suppression) in combination with deficits in top-down, cognitive forms of regulation (weak inhibitory control) who showed the most externalizing problems. However, it is not known whether this same pattern would contribute to stability or increases in externalizing problems over time. Indeed, this pattern is just as likely to reflect children who are temporarily exhibiting behavior problems as they struggle to acquire cognitive control, but whose problems will eventually decrease. The current longitudinal examination aimed to address these developmental questions.

The Current Study

This prospective, longitudinal study examined inhibitory control, parasympathetic activity (indexed by RSA), and externalizing problems in a sample of children assessed at 4 and 6 years. This sample was over-recruited for externalizing problems, and thus represents a group in which we expect to have children who follow the normative course of decreasing problems as well as those evidencing potentially pathological stable or increasing problems over time. Regarding the developmental sequence between inhibitory control and externalizing problems, our first prediction was that earlier inhibitory control would more strongly predict later externalizing problems than the reverse association. This would suggest that prefrontal cognitive control lays the foundation for future patterns of behavior.

Second, in accord with a multi-faceted, neurobiological model of self-regulation, we expected that parasympathetic activity would contribute to the development of externalizing problems. Given past findings, we tentatively hypothesized that low baseline RSA at 4 years would predict more externalizing problems at 6 years. Prior work suggests that RSA reactivity must be understood in relation to task demands, and we speculated that RSA augmentation or extreme RSA suppression (e.g., hypo- or hyper-reactivity) during an inhibitory control task at 4 years would predict more externalizing problems at 6 years.

Third, we also hypothesized that parasympathetic activity would moderate the relation between inhibitory control and externalizing problems. Children with poor inhibitory control who also had low baseline RSA or atypical RSA reactivity (either augmentation or strong suppression) to the inhibitory control task at 4 years were expected to have the most externalizing problems at 6 years, reflecting the integrated multi-system nature of early self-regulation.

Method

Participants

At time one (T1), 49 girls and 49 boys (n = 98), aged 4.0–4.9 years at screening (age at lab visit M = 4.61 years, SD = 0.28), were recruited in a large city in Canada. At time two (T2), 42 girls and 45 boys (n = 87) returned to the lab when they were age 6.0–6.9 years (M = 6.57 years, SD = 0.30). Children who did not return for the second visit did not differ significantly from the retained sample with regard to sex, age, or income (all ts < 1.31, ps > 0.19) or on any T1 measures (inhibitory control, baseline RSA, task RSA, RSA change, or externalizing problems; all ts < 0.85, p-s > 0.40). Families were predominantly Caucasian (69.7%), English-speaking (81.6%) and from working to upper-middle SES (38% = $10–60,000 CND; 30% = $60–100,000; 24% = $100–200,000; 8% did not answer). Children with aggression and externalizing problems were over-recruited using targeted advertising; 37 children had aggression and/or externalizing T-scores ≥60 at screening. All children lived with their mothers and had no identified cognitive deficits or physical challenges. Mothers received $75 for participation, and children received a t-shirt.

Procedure

Time 1 Families were contacted through direct mailing, letters distributed to daycares and preschools, and advertisements in local, free magazines. Interested parents contacted the lab and were preliminarily screened with items on the Child Behavior Checklist (CBCL) Preschool form (ages 1 ½- 5). Mothers completed consent forms and questionnaires, including the full version of the CBCL prior to the laboratory assessment. Children and their mothers attended an approximately 3-h visit to a university laboratory which was conducted in children's first language, either English or French. Cardiac monitors were attached approximately 1 h into the testing session, after which baseline cardiac data were recorded. Approximately 10 min later, children completed the Day-Night task.

Time 2 Families were invited back to the laboratory 2 years after their first visit. Procedures at T2 paralleled T1. At the visit, mothers completed the CBCL School Age form (ages 6–18). The cardiac monitor was attached to children 1 h after arrival, followed by the baseline recordings, and approximately 10 min later, the administration of the Day-Night task.

Measures

Cardiac Data Cardiac data were acquired using a MiniLogger Series 2000 (Mini-Mitter Company, Inc 1999) telemetric ambulatory monitor, which was attached to the child's chest. Two adhesive electrodes were used to record interbeat intervals. Baseline cardiac data were acquired during three phases. First, the child was asked to sit quietly with eyes closed while listening to 1 min of soft music. Then, the child was asked to sit quietly and watch a 3-min video of a gentle lullaby. Finally, the child was asked to sit quietly for 1 min with eyes closed. Correlations among the three measures were high, all rs > 0.82 at 4 and 6 years. An average was calculated for each child at each time and used as the measure of baseline RSA.

Cardiac data were edited and analyzed using Mxedit computer software (Porges 1988). The raw inter-beat interval (IBI) values were inspected to correct recording artifacts by trained, reliable IBI editors as outlined by Berntson et al. (1997). RSA was then computed using Porges' method (1988) in the Mxedit software package, which applies a 21-point moving polynomial filter to index variability in IBI within the respiratory frequency band. A band-pass filter was applied between 0.24 and 1.04 Hz, the frequency of young children's spontaneous respiration (Huffman et al. 1998; Stifter and Fox 1990), with sampling rate set at 250 ms. Mean duration of the Day-Night task was 62.25 s (SD = 23.71) at 4 years and 46.69 s (SD = 7.78) at 6 years. RSA was calculated from each child's full task duration to extract the most reliable estimates of RSA (Berntson et al. 1997).

To index RSA reactivity during the Day-Night task, change scores were calculated by subtracting baseline RSA from task RSA. More negative scores of mean RSA change reflect greater reductions in RSA from baseline to the task (i.e., decreases in parasympathetic influence). There are multiple ways to examine change in physiology (Burt and Obradović 2013), and we chose an arithmetic change score because it is straightforward to interpret and is not a relative metric as are residualized change scores. We included baseline RSA in the path model to account for the degree to which change in RSA is dependent on initial values of RSA.

Child Behavior Checklist (CBCL; Achenbach and Rescorla 2000). At T1, mothers completed the 1.5–5-year-old version of the CBCL. At T2, mothers completed the 6–18-year-old version. The broad-band externalizing problems scale was used in current analyses. This scale contains 24 items from the aggressive behavior and attention problem subscales on the 1.5–5 year-old version, and 35 items from the aggressive behavior and rule-breaking behavior on the 6–18-year-old version. The externalizing problem scale showed good internal consistency, with $\alpha = 0.94$ at T1 and $\alpha = 0.91$ at T2.

Day/Night Task (Gerstadt et al. 1994). This task assesses the inhibition of prepotent responding, and is also known as the Child Stroop test. Children were shown laminated cards (13.5 × 10 cm), half showing an image of the sun, to which children were instructed to say "night," and the other half showing an image of the moon and stars, to which children were instructed to say "day." Thus children had to inhibit the dominant response to match the picture to its label and say a semantically opposite word. Cards were presented in a fixed pseudo-random order by trained graduate students. Children were asked to repeat the rules after the experimenter had explained them. To ensure that children understood the rules, they were given training trials until the child passed both a "night" and "day" trial. During the training trials, children were given positive feedback for correct responses and were corrected on incorrect responses. Children were then given 16 test trials. No feedback was provided during test trials.

Trained coders who were blind to children's levels of externalizing problems scored accuracy from video recordings. The sum of correct responses for each task was recorded as the response accuracy score. Nine children were missing inhibitory control data at T1 due to child refusal, administration error, or video recording error. All children provided data at T2. Reliability between two coders was r = 1.00 at both time points.

Data Analyses

Due to experimenter error, audiovisual and physiology recording problems, child refusal or mother not completing a questionnaire, 19 children at T1 and 18 children at T2 had partially missing data (*n*s for all variables are listed in Table 1). Children with any missing data did not differ from the rest of sample on any study variable (all *t*s < 2.87; Bonferroni-corrected value for 12 tests). Outliers +/− 3 *SD* from the mean were identified in five variables. At T1, one child had very low baseline RSA and one child had a very low RSA change score. At T2, three children had very low performance on Day-Night, one child had very low baseline RSA and one child had an extremely high RSA change score. In each case, the individual score was replaced with a missing value, which allows it to be estimated in the model. This is preferable in this case because the RSA change score is a computation of another variable in the model. (We also examined models with winsorized scores to be less extreme, by replacing outliers with the next value present in the data (Wilcox 2012), and found that this approach did not change the main findings.) We retained the full sample for the path analysis by using full information maximum likelihood (FIML) estimation, which fits models directly to the raw data matrix, using all available data points for all individuals to account for missingness. FIML estimation has been shown to be the most efficient and least biased approach to estimation in the presence of missing data (Arbuckle 1996; Widaman 2006).

We tested our three hypotheses using a path model fit in MPlus Version 7.3. The 4 year variables were mean-centered prior to analysis and prior to computing interactions. Because the 6 year measures were only endogenous variables, these were left uncentered. We fit a model that contained stability paths for all constructs over time as well as predictive paths from all T1 variables to T2 inhibitory control and externalizing problems. This model included two T1 interaction terms predicting age 6 externalizing problems – inhibitory control X baseline RSA and inhibitory control X RSA change. Follow-up analyses were conducted to probe significant interaction effects, and supplementary analyses were examined to rule out alternative explanations for findings.

Results

Descriptive Statistics

Descriptive statistics are presented in Table 1. Paired samples *t*-tests revealed significant decreases in RSA from baseline to the Day-Night Task at 4 years, $t(74) = 5.16$, $p < 0.001$, $d = 0.43$, and 6 years, $t(67) = 6.28$, $p < 0.001$, $d = 0.48$. At both ages, children on average showed reductions in RSA to the Day-Night task, with notable variability (at 4 years, $M = -0.42$, $SD = 0.78$; at 6 years, $M = -0.62$, $SD = 0.67$).

Paired samples *t*-tests revealed significant increases in all variables from 4 to 6 years, all $|t|$s > 2.14, all *p*s < 0.04, all *d*s > 0.26, except for RSA change scores, $t(51) = 1.24$, $p = 0.22$, $d = 0.22$. Thus, with age, children performed better on the Day-Night task, and showed higher RSA both at rest and during the Day-Night task. In contrast, maturational changes in RSA levels were not reflected in consistent increases or decreases in reactivity change scores. Across time, all measures were moderately to highly stable, with the exception of the RSA change scores, $r = 0.13$, $p = 0.34$, indicating that over time, different children showed RSA modulations to different degrees.

Table 1 Descriptive statistics and correlations for study variables

Measure	*N*	*M*	*SD*	1	2	3	4	5	6	7	8	9	10	11	12
1. Gender	98	--	--												
2. T1 Age	98	4.61	0.28	−0.03											
3. T1 DN Accuracy	89	10.76	5.14	0.01	0.15										
4. T1 Baseline RSA	85	6.71	1.20	−0.03	0.01	0.03									
5. T1 RSA during DN	79	6.12	1.11	−0.01	−0.06	0.14	0.74**								
6. T1 RSA reactivity	75	−0.42	0.78	0.08	0.12	0.27*	−0.44**	0.12							
7. T1 Externalizing	95	51.92	11.35	−0.13	−0.01	−0.18	−0.01	−0.23*	−0.31**						
8. T2 Age	87	6.57	0.30	−0.03	0.83**	0.18	−0.02	−0.08	0.13	−0.08					
9. T2 DN Accuracy	84	14.45	2.22	0.12	0.12	0.24*	0.04	0.09	0.03	−0.11	0.14				
10. T2 Baseline RSA	79	7.08	1.10	−0.13	0.01	0.04	0.49**	0.48**	−0.30*	0.00	0.09	−0.01			
11. T2 RSA during DN	69	6.49	1.33	−0.12	−0.05	0.00	0.53**	0.57**	−0.19	−0.10	0.03	−0.03	0.80**		
12. T2 RSA reactivity	68	−0.62	0.67	−0.01	0.08	−0.05	−0.08	0.03	0.13	−0.12	0.10	−0.08	−0.20	0.33**	
13. T2 Externalizing	87	54.16	10.31	−0.08	0.09	−0.26*	0.01	−0.12	−0.31*	0.67**	0.12	−0.05	0.11	−0.12	−0.21*

T1 = 4 year visit; T2 = 6 year visit; DN = Day-Night task; RSA = respiratory sinus arrhythmia.

* $p < 0.05$; ** $p < 0.01$.

Correlations are presented in Table 1. At 4 years, RSA during the task and RSA change scores were negatively associated with externalizing problems. Lower RSA during the Day-Night task, and more RSA suppression to the task was associated with higher levels of externalizing problems. RSA change was positively associated with inhibitory control. Thus, more RSA suppression to the Day-Night task was associated with poorer performance. These associations were no longer present at 6 years. Longitudinally, poorer inhibitory control and more RSA suppression at 4 years predicted higher levels of externalizing problems at 6 years. In contrast, earlier externalizing problems did not predict inhibitory control or any RSA measure 2 years later. Gender, age at T1, and age at T2 were not associated with any target variables.

Path Analysis

Results from the path analysis are shown in Fig. 1. Model fit to the data was good, χ^2 (12) = 11.68, $p = 0.47$; RMSEA = 0.00, $p = 0.68$; CFI = 1.00, TLI = 1.01. Regarding our first hypothesis, the path analysis confirmed what was seen in the correlations. Better inhibitory control at 4 years had a significant lagged effect, predicting fewer externalizing problems at 6 years, $\beta = -0.21$, $p = 0.02$. This lagged effect of inhibitory control was notable, given the rather strong stability path for externalizing problems, $\beta = 0.65$, $p < 0.001$. Importantly, externalizing problems at 4 years did not have a lagged effect on inhibitory control at 6 years.

Our second hypothesis was not supported, as there were no direct effects of either baseline RSA or RSA reactivity at 4 years on externalizing problems at 6 years. Stronger RSA suppression was associated with both poorer inhibitory control and more externalizing problems concurrently at 4 years, but physiology did not have a lagged direct effect on later externalizing problems.

In line with our third hypothesis, the relation between earlier inhibitory control and later externalizing problems was moderated by RSA reactivity at 4 years, $\beta = -0.25$, $p = 0.02$. Following the recommendations of Aiken and West (1991), we probed the interaction by rerunning the full model re-centering values of RSA activity at high (+1 *SD* from the mean) and low (−1 *SD* from the mean) values so we could evaluate the significance of simple main effects. The resulting high and low values reflect RSA augmentation (difference score = +0.36) versus strong RSA suppression (difference score = −1.20), respectively (Fig. 2). The relation between earlier inhibitory control and later externalizing problems was not significant at low change scores that reflected strong RSA suppression, $\beta = 0.09$, $p = 0.51$. Conversely, earlier inhibitory control significantly predicted later externalizing problems at mean change scores reflecting mild RSA suppression, $\beta = -0.21$, $p = 0.02$, and at high change scores reflecting RSA augmentation, $\beta = -0.50$, $p = 0.01$. Thus, for a child who increased RSA to the inhibitory control task 1 *SD* (+0.36), each 1 *SD* increase in performance on the Day-Night task at T1 (~ 5 trials) was associated with a 0.5 *SD* decrease in externalizing problems at T2 (5.16 points). In other words, when children had RSA augmentation paired with good inhibitory control at 4 years, the lowest levels of externalizing problems were predicted at 6 years. However, when children responded to the inhibitory control task at 4 years with RSA augmentation and also had *poor* inhibitory control, the highest levels of externalizing problems were predicted at 6 years, in the sub-clinical range.

A regions of significance test was used to examine whether the slope for RSA augmentation can be interpreted as being associated with both greater and fewer externalizing

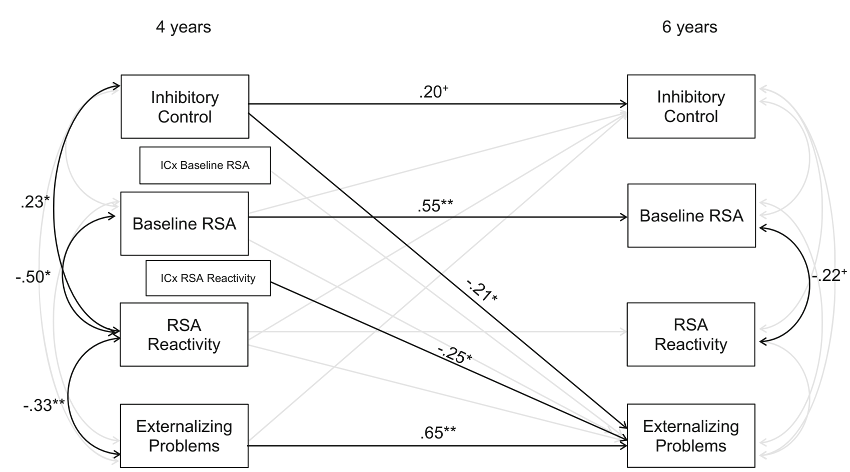

Fig. 1 Path model predicting age 6 externalizing problems. Note. $^{+}p < 0.10$; * $p < 0.05$; ** $p < 0.01$. IC = inhibitory control; RSA = respiratory sinus arrhythmia. Standardized estimates are shown. Grey lines indicate non-significant paths that were retained in the model. Interaction terms were allowed to covary with exogenous variables

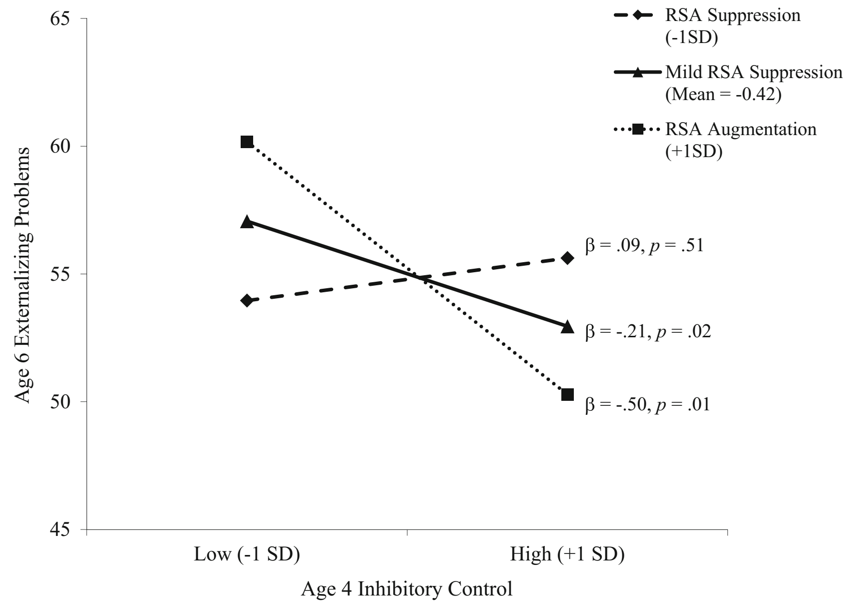

Fig. 2 Plot of the interaction between earlier inhibitory control and RSA reactivity in the prediction of later externalizing problems

problems. We examined whether the projected values for T2 externalizing problems were significantly different for the RSA suppression versus RSA augmentation slopes at +/− 2 *SD* of inhibitory control and RSA change (see Hastings et al. 2015). Projected values of externalizing problems were significantly different for children who showed augmentation versus suppression at both low, $z = -2.19$, $p = 0.03$, and high, $z = -2.16$, $p = 0.03$ values of inhibitory control. This confirmed that RSA augmentation was associated with both more and fewer externalizing problems than RSA suppression, depending on inhibitory control.

To interpret effect sizes, we examined the R^2 for externalizing problems at 6 years. Compared to a model with only stability paths for each construct, $R^2 = 0.43$, $p < 0.001$, the addition of the lagged effects resulted in $R^2 = 0.45$, $p < 0.001$, representing a small effect size, $\Delta R^2 = 0.02$, $F = 0.92$, $p > 0.10$. The inclusion of interaction terms resulted in $R^2 = 0.53$, $p < 0.001$, a medium-sized effect, $\Delta R^2 = 0.08$, $F = 2.47$, $p < 0.05$, and a significant improvement over the model with only main effects.

Supplementary Analyses

Because an interaction effect can be present even in the absence of a main effect, we examined whether a relation between earlier externalizing problems and later inhibitory control might be present at different levels of baseline RSA or RSA reactivity. We tested a model which contained the linear-by-linear interaction terms for externalizing X baseline RSA and externalizing X RSA reactivity. These interactions did not predict Day-Night accuracy at 6 years. This means that, even at different levels of parasympathetic activity, earlier problems did not predict later inhibitory control.

Because non-linear associations between RSA reactivity and self-regulation have been observed (Marcovitch et al. 2010), models including the quadratic effect of RSA reactivity at each age was examined, but no significant effects were observed. Supplementary models were run to examine whether baseline RSA or RSA reactivity moderated the concurrent association between inhibitory control and externalizing problems at either time point. Neither model revealed significant interaction effects within T1 or T2. Finally, because performance on the Day-Night task approached ceiling at T2, we ran the final model again with specifications indicating that T2 Day-Night accuracy was censored above. This MPlus command accounts for the non-normality in this variable by estimating it as if scores >16 were possible and the resulting scores would follow a normal distribution. Parameter estimates were virtually unchanged, suggesting that restricted variability in T2 inhibitory control did not impact results.

Discussion

We found that preschoolers with better inhibitory control had fewer externalizing problems 2 years later, but earlier externalizing problems did not predict inhibitory control. This suggests that early executive function competencies may protect against the maintenance or exacerbation of externalizing problems in children at elevated risk. However, the significant moderation effect showed that this effect was stronger for children who showed particular parasympathetic responses to the inhibitory control task. Children who showed RSA augmentation had the strongest link between inhibitory control at 4 years and externalizing problems at 6 years, for better and for worse. Preschoolers with very good performance and RSA augmentation in the inhibitory control task were projected to have the fewest problems at 6 years, whereas those with very poor performance and RSA augmentation were projected to have the most externalizing problems two years later. Understanding the multi-system interactions between cognitive and physiological self-regulation may be critical for predicting children's developmental outcomes.

Examining the Interactions between Components of Self-Regulation

Preschoolers who had poor inhibitory control were projected to have moderate to high levels of externalizing problems, particularly if they also had shown RSA augmentation. Considerable research has shown that, when individuals are presented with a challenging task, some RSA suppression appears to facilitate orientation, engagement, and performance (Graziano and Derefinko 2013; Porges 2007). Because of this, we had hypothesized that both RSA augmentation and extreme suppression could represent risky profiles when paired with poor inhibitory control. Our results suggest that RSA suppression may be a bottom-up source of physiological regulation that provides effective engagement with the task demands. For preschoolers with less mature neuropsychological development, such that they are less capable of implementing top-down cognitive regulation, the demands of an inhibitory control task are quite challenging. If RSA augmentation to cognitive challenges results in these children being too underaroused to engage with such tasks, then they may fail to allocate the attentional resources necessary to practice or master these essential self-control skills. Over time, this would be reflected in the behavioral dysregulation characteristic of externalizing problems.

On the other hand, for preschoolers with more developed neuropsychological competencies, as reflected in better inhibitory control performance, RSA augmentation may have been appropriate. Because they had sufficient cognitive resources to bring to the demands of the task, reflecting top-down regulation, they did not need to engage bottom-up physiological regulatory resources. Strong RSA suppression would have been less advantageous for them, as it would have reflected approaching the task as a challenge requiring physiological arousal (Friedman 2007), potentially interfering with the application of their cognitive regulatory competency. It is worth noting, though, that children with good inhibitory control at 4 years were not projected to have high levels of externalizing problems at 6 years, regardless of their earlier RSA reactivity. Rather, their externalizing problem scores ranged from moderate when they showed strong RSA suppression to low when they also showed RSA augmentation.

As observed previously (see Utendale et al. 2014), overall children tended to do more poorly on the Day-Night task at 4 years if they had stronger RSA suppression. Thus, for some children, a physiological response that is commonly thought of as normative or adaptive may interfere with their ability to utilize other regulatory resources. These findings are similar to those of Healy et al. (2011) where young adults who self-reported good attentional control also reported better behavioral self-regulation if they showed less RSA suppression during a Stroop task. In a recent study on sleep, RSA, and externalizing problems in preschoolers, Cho et al. (2017) also found that RSA augmentation, or less suppression, to an inhibitory control challenge was associated with preschool externalizing problems, for better and worse. Among children who showed augmentation or less suppression, high sleep duration at 2 years predicted fewer externalizing problems at 3 years, whereas less sleep duration predicted more problems; these effects were not seen for children who showed more RSA suppression. Thus, the meaning or appropriateness of physiological changes should be evaluated in context with children's other regulatory abilities (Obradović 2016), as well as in consideration of appropriate or typical task-specific patterns of physiological responding (Beauchaine 2012; Hastings et al. 2014). Our findings suggest that risk for psychopathology may be better delineated by viewing self-regulation from an integrated, multi-system perspective.

Developmental Effects

We highlighted the importance of considering the complementary nature of the components of self-regulation, but our results also suggest that the consequences of the interaction between physiology and cognitive control play out over time. At 4 years, an interaction between RSA reactivity and inhibitory control was not present. Instead, it was strong RSA suppression that was associated with more externalizing problems and poorer inhibitory control. This is in line with past work that suggests that children with problems may show hyperarousal to challenging tasks (Beauchaine 2001), but the lack of a longitudinal association also suggests that these children may not necessarily continue to have higher-than-average problems. Apparent changes in the links between physiology and behavior over time may reflect the rapid changes in self-regulation that are typical of early childhood.

Children's inhibitory control skills are just beginning to develop during the preschool years (Best and Miller 2010), and we documented wide variability in performance. Thus, children who perform poorly at this age will appear typical or developmentally normative to observers, perhaps especially if they appear quite calm and relaxed in such situations. Young children who show high physiological arousal in response to inhibitory demands may stand out as more demonstrative or worked-up by the tasks. This may explain why stronger RSA suppression was initially associated with mothers' ratings of more externalizing problems within time at 4 years. However, if children continue to approach impulse-control challenges with moderate RSA suppression, which supports orientation to the task and engagement, their burgeoning inhibitory control skills may develop more rapidly, leading to an eventual decrease in their angry and undercontrolled behaviors.

This interpretation helps to synthesize the findings from our prior analysis using this sample at 4 years combined with another sample of 6 year olds. Using composite inhibitory control and RSA variables across two tasks, Utendale et al. (2014) showed that children who showed strong RSA suppression had the strongest concurrent association between the inhibitory control and externalizing problems. In other words, when children had poor inhibitory control and high physiological arousal their mothers reported high levels of externalizing problems. The present analysis suggests that these associations may not be predictive of stability or escalation of problems over time, however. In this longitudinal analysis, we see that RSA suppression appeared to protect 4 year olds with poor inhibitory control from stable or increasing problems, possibly by allowing these children to continue to effectively engage with challenges, and therefore build their skillset. Although Utendale et al. (2014) originally interpreted their findings as suggesting that RSA suppression could be a maladaptive response to the challenge of completing inhibitory control tasks that were beyond the capabilities of children with many externalizing problems, it may have been an adaptive bottom-up aspect of regulation that contributed to a "late bloomer" profile of children who were likely to change from appearing dysregulated at 4 years to better behavioral outcomes at 6 years. As others have noted, relations within time do not necessarily speak to predictive patterns (Hastings et al. 2011; Kraemer et al. 2000). RSA reactivity during the preschool years may act as a catalyst for developmental change that predicts school-age behavior, even if the link between RSA reactivity and behavior is not observable at either age alone.

Order of Effect between Inhibitory Control and Externalizing Problems

The fully autoregressive design of our path model revealed a potential developmental inconsistency, wherein inhibitory control was more robustly related to externalizing problems over time than within time. It should be noted, however, that the concurrent relation between inhibitory control and externalizing problems at 4 years ($|r| = 0.18$) is similar in size to the effect found in a recent meta-analysis for Stroop-like tasks ($ESzr = 0.16$; Schoemaker et al. 2013). Thus, the small concurrent effects observed in the present study may have reached the 95% confidence level or been more clearly detected in a larger sample or multi-method design. Even given these limitations, it is interesting to consider that in the current study, the early acquisition of cognitive control predicted fewer problems over time at least as strongly as within time. This kind of lagged effect has been theorized to be common in executive function abilities (Best et al. 2009). For example, Riggs et al. (2003) reported that executive functions at 1st and 2nd grade were only related to changes in behavior problems over 2 years, not to concurrent measures. This may suggest that executive function skills become imbedded in children's repertoire of self-regulation skills over time, and the consequences of poor inhibitory control become more visible at later ages as children's regulatory challenges increase (Thompson 2011). This presents a challenge in terms of identifying children at need for interventions if the consequences of poor executive function become more evident later in time. It also suggests that the skills acquired in the preschool years have significant and potentially long-term effects, highlighting the need for interventions and curricula that support self-regulation skills (Blair 2016).

Limitations and Conclusions

One limitation of this study was the use of single measures to index each construct. However, this allowed us to look at changes in RSA that were associated with a single task (Day-Night), as opposed to aggregating physiological change across several tasks, which can be difficult to interpret. The modest sample size may have prohibited the detection of small effects, although we had sufficient power for detecting the robust interaction effect. Our sample was also low in ethnic diversity and moderately high in SES, and thus future work is needed to document the extent to which the current findings extend to other samples.

These findings indicate that preschoolers with better inhibitory control had fewer externalizing problems two years later, but the converse association was not present. However, this protective effect was strongest for preschoolers who exhibited RSA augmentation, or increases in parasympathetic influence, in response to the inhibitory control task. When children had good inhibitory control, showing increases in parasympathetic activity appeared to be especially advantageous. However, this parasympathetic augmentation was related to the development of externalizing problems in preschoolers who had poor inhibitory control. Thus, the appropriate level of physiological adaptation to the task may depend on the child's cognitive ability to complete it. If preschoolers with poor inhibitory control also failed to show some physiological arousal that would support task engagement, they showed increases in externalizing problems two years later. This consideration of the multiple, interacting components of self-regulation led to a more nuanced identification of the longitudinal antecedents of externalizing problems.

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Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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