Title:	Intervening Early with Neglected Children
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SIGNIFICANCE

Caregivers serve as co-regulators for infants, helping children regulate behaviors, emotions, and physiology. Neglecting parents fail to provide this critical co-regulating function. It is not surprising, then, that neglected infants are at risk for problems developing adequate self-regulatory capabilities. The Attachment and Biobehavioral Catch-up (ABC) Intervention was designed to help neglecting parents learn to behave in synchronous, nurturing, and non-frightening ways with their young children, thus providing children the necessary input for the development of regulatory capabilities. In early childhood, we have found that the ABC intervention is effective in enhancing children's ability to regulate behaviors, emotions, and physiology. The proposed study would assess whether change is sustained as demands for regulating behaviors, emotions, and physiology are placed squarely on the child in middle childhood.

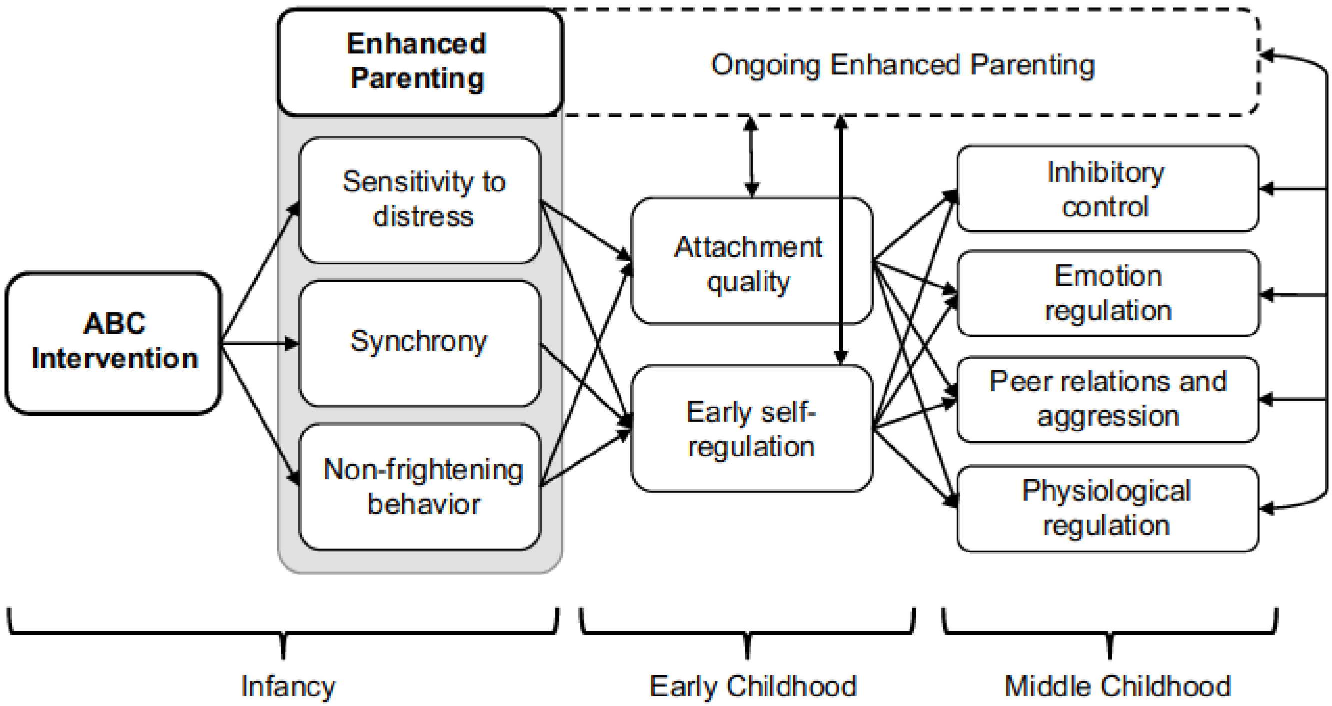
In infancy and early childhood, children are almost fully dependent on their parents for help regulating behavior, emotions, and physiology. Parents are most effective as co-regulators if they behave in soothing ways when children are distressed and in responsive, synchronous ways when infants are not distressed. Neglecting parents fail with respect to providing nurturing and/or synchronous care. Some fail to soothe their distressed child, and indeed are the source of distress. Other parents do not interact in smooth, responsive ways, and may instead behave in ways that are intrusive. In the absence of an effective co-regulator, neglected infants do not have repeated successful experiences of managing challenging conditions, and therefore may fail to develop adequate strategies for regulating emotions, behavior, and physiology. Problems are seen in infancy and early childhood in the form of disorganized attachments, lack of behavioral control, and disrupted patterns of cortisol production (e.g., Bernard et al., 2010; Calkins et al., 1998; Fearon et al., 2010). As neglected children become older, effects are seen in difficulties with inhibitory control, emotion regulation, and peer relations (e.g., Bruce et al., 2009; Doan et al., 2012; Dodge et al., 1995; Fox & Calkins, 2003), and atypical patterns of physiological regulation (Bernard et al., 2010).

Inhibitory control. Inhibitory control refers to the ability to inhibit a prepotent response. Being able to inhibit a prepotent response (e.g., not jumping up to look out the window when sitting in a classroom) is critical to success in the classroom and with peers. Neglect has been associated with deficits in inhibitory control, with these deficits seen in behavioral, ERP, and fMRI assessments (e.g., Lewis et al., 2007; Loman et al., 2013; Mueller et al., 2010). Deficits in inhibitory control are associated with a range of behavioral problems, including substance abuse and conduct disorder, as well as internalizing problems (e.g., Doan et al., 2012).

Emotion regulation. Emotion regulation refers to the ability to regulate the expression of experienced affect. Maltreatment is associated with problems regulating emotion (Shields & Cicchetti, 2001). Children who have poor emotion regulation are at increased risk for both internalizing and externalizing behaviors, and for problems in peer relations (Blandon et al., 2010; Calkins & Keane, 2009; Shields & Cicchetti, 2001).

Peer relations and aggression. Positive relationships with peers are central to children's healthy development, and predict outcomes as diverse as academic success and behavior problems (Prinstein et al., 2009; Wentzel, 2009). Children who are maltreated are especially at risk for developing negative attributional biases, reacting aggressively toward peers, and being rejected by peers (Dodge et al., 1995; Shields & Cicchetti, 2001).

Physiological regulation. Neglect has effects on neurobiological as well as behavioral systems. The HPA (hypothalamus pituitary adrenal) axis is highly dependent upon environmental input, and thus susceptible to effects of neglect (Gunnar & Quevedo, 2007). Two primary functions of this axis involve the maintenance of a diurnal pattern (which helps ensure that adequate energy is available early in the day, for example), and the mounting of a stress response (which helps ensure that energy is diverted to critical functions under emergency conditions). We (Bernard et al., 2010) have found, as have others (Bruce et al., 2009; Gunnar & Vazquez, 2001), that neglect is most often associated with a flat pattern of cortisol production across the day. Although causal claims cannot be made, flat patterns are also associated with a number of problematic behavioral outcomes, in particular, problems with inhibitory control (McBurnett et al., 2000; Pajer et al., 2001).



Summary. Attachment and Biobehavioral Catch-up (ABC) was developed to help neglecting parents provide nurturing, synchronous, non-frightening/non-intrusive care to their young children. Thus, ABC sought to help parents behave in synchronous ways (e.g., following the child's lead) when the child was not distressed, to behave in nurturing ways when the child was distressed, and to behave in non-frightening/non-intrusive ways at all times. The intervention was expected to result in children developing more secure, organized attachments, and in developing better regulation of emotions and physiology. As described in the Progress Report, this intervention has important effects on young children's attachment, emotion expression, and physiological regulation, outcomes that are associated with later self-regulatory capabilities. The goal of this Competing Continuation Award is to examine the effects of this early intervention on children's inhibitory control, emotion regulation, peer relations, and regulation of physiology in middle childhood when the demands for self-regulation of behavior, emotions, and physiology are placed squarely on the child. We focus specifically on children between the ages of 8 and 10 for our assessment of middle childhood functioning because this represents a period in which self-regulatory functions are consolidated (Doan et al., 2012).

This project is highly significant in several ways. At this point, effects of the ABC intervention have been demonstrated among children and parents three years after the intervention. The aims of the proposed project would extend these findings into school-aged years when children are operating largely out of their parents' direct influence. Support for a brief early intervention that affects children's ability to regulate behaviors, emotions, and physiology in middle childhood would have high public health significance. Second, whereas most developmental studies relating early experience to later outcomes have relied on correlational designs (e.g., Doan et al., 2012), the random assignment to condition allows an experimental assessment of the effects of early experience on developmental outcomes. What is particularly exciting here is that parents have been randomly assigned to condition, allowing causal statements about the effects of parental synchrony, for example, on later outcomes. Third, children's behavioral and neurobiological functioning is studied in ways that are theoretically and empirically compelling.

INNOVATION

Although other studies have examined predictors of self-regulatory capabilities in middle childhood, this study is unique in examining experimentally whether a brief (10-session) intervention in infancy affects self-regulatory capabilities 6-8 years later in middle childhood.

- The intervention itself is innovative.
- The measurement of outcome variables is innovative, bringing biologic variables into a psychosocial intervention study.
- The experimental test of a process model of development, through an intervention experiment, is innovative.
- The long-term follow-up is unusual, if not innovative.
- The translation of basic developmental theory into a practical intervention to address a major social problem is innovative.
- The integration of intervention with high-risk children and longitudinal investigation of low-risk children is innovative, cross-informing basic developmental science and prevention.

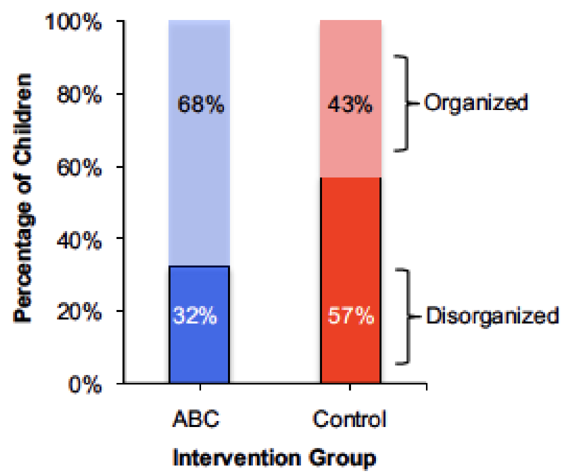
PROGRESS REPORT

In this randomized clinical trial, we studied the efficacy of an intervention for neglecting parents of young children. Our primary interest was in assessing whether the ABC intervention was effective in enhancing children's attachment organization, normalizing neuroendocrine functioning, and promoting better regulation of emotions and behaviors. We also examined changes in parental behavior and brain activity, and examined issues related to intervention fidelity. Because of space constraints, only the results considered most relevant are presented.

Parents were assigned to receive the Attachment and Biobehavioral Catch-up intervention (ABC: Experimental intervention) or Developmental Education for Families (DEF: Control intervention). The two interventions were of the same frequency (weekly), duration (about hourly for 10 sessions), and structure (in homes with parents and children present).

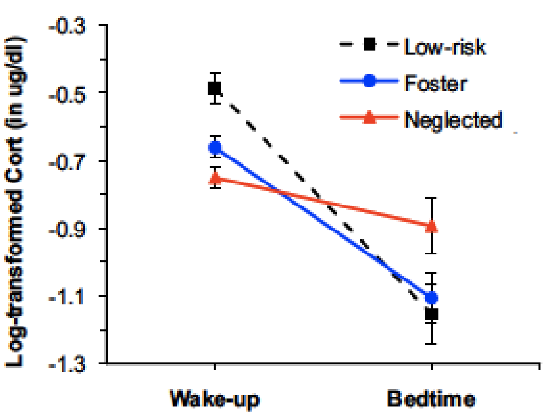
Summary of Intervention Effects

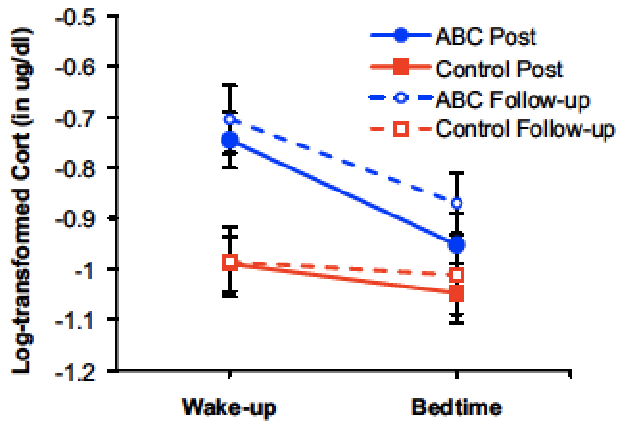
Attachment quality. Fewer children in the ABC group developed disorganized attachments than children in the treatment control group (Bernard et al., 2012). Children in the ABC intervention showed significantly lower rates of disorganized attachment (32%) and higher rates of secure attachment (52%), relative to children in the control intervention condition (57% and 33%, respectively). Disorganized attachment has been linked with a host of problematic outcomes, especially externalizing symptoms, as found in a meta-analysis by Fearon et al. (2010).



Cortisol regulation. Before presenting intervention outcomes for cortisol, we emphasize that we found that children living with neglecting birth parents showed flatter lower morning values and blunter slope across the day than children living with low-risk birth parents (Bernard et al., 2010). Thus, consistent with the findings of others (Bruce et al., 2009), we found that adversity is associated with a blunted, flat diurnal pattern of cortisol production. (See figure on the left below.)

Children whose parents received the ABC intervention showed higher wake-up values and steeper slopes than children in the control intervention group (see figure on right). The dashed lines show very similar results from when children were 5 years old (one year following the end of planned data collection for the original R01 and at least 3 years after intervention) (Bernard et al., 2013).





Emotion regulation. Children's emotion regulation was assessed in a frustrating task (Tool Task) when children were 2 and 3 years old. Children in the ABC group showed lower levels of negative affect, and less anger toward their caregivers than children in the control intervention group.

Parents' sensitivity. Parents receiving the two interventions were similar at the beginning of the intervention in synchrony, positive affect, and intrusive behavior. Three years after the intervention was completed (when children were 5), ABC parents continued to show greater synchrony, more positive affect, and less intrusiveness than control intervention parents (Bernard, Dozier, et al. 2013).

APPROACH

Research Design and Methods

A total of 280 families completed all enrollment procedures. Of these, 210 were neglecting parents and their children and 70 were low-risk parents and children, with gender, age, ethnicity, and race comparable for the groups. The neglecting parents were referred to the study by the child welfare system of a large mid-Atlantic city. These parents were involved with the city's diversion from foster care program and were considered by the city's child welfare system to be at high risk for neglect as the result of previous or current allegations, and/or very high risk conditions, such as homelessness or reports of domestic violence. Of the 280, 29 (10%) were lost before post-intervention data collection, 17 (6%) before the second year data collection, and 20 (7%) subsequently. We have begun work with a talented Participatory Action Researcher (Darryl Chambers) who has found a number of the previously lost participants. We expect that we will be able to enroll at least 220 participants and retain 210 through 10 year old assessments. (This is the most eager and involved sample we have ever worked with, with many contacting us to see when next assessments are. Although our retention estimates may seem ambitious, we think they are feasible because most drop-out occurs early in this and other studies, and we have been very successful in finding participants beyond the initial 5 year grant period.) Most (68%) of the children and families are African-American, and 18% are Hispanic.

Approximately 1/3 of the children have birthdates in each of the years from 2006-2008, such that data collection for the full sample will be distributed over the 5 years of funding (with about 1/3 of the sample completing 8 year old assessments in year 1, 1/3 in year 2, and 1/3 in year 3). Parents of children who do not become 8 until years 2 or 3 will be contacted during the first year(s) of the study for parent-report measures to ensure continued contact and investment. We are currently following children in this interim period through donor support to ensure participant retention.

Primary available data. Data are available and coded for child attachment quality (Strange Situation: Ainsworth et al., 1978), child diurnal cortisol production (Bernard et al., 2010), and child emotion expression (Tool Task: Matas et al., 1978), as well as for parent attachment state of mind (Adult Attachment Interviews: Main et al., 2005) and parent synchrony, sensitivity to distress, and intrusiveness (from interactional tasks: NICHD, 1992), among other things. <u>(Most coding of parent behavior was not funded by original grant, and is now being completed with donor funding.)</u>

Data to be collected. Data for all constructs except cortisol will be collected in individually administered laboratory tasks, parent-child interaction tasks, and through parent-, teacher-, and child-report. Cortisol will be collected through diurnal sampling. Two of the four primary constructs, inhibitory control and HPA-axis activity, are identified in the NIMH Research Domain Criteria (RDoC), and we are using recommended assessments (NIMH, 2012).

Table 1. Proposed Data Collection Schedule

Construct	Assessment	Age		
		8	9	10
Inhibitory control	Simon	X		X
	Stop Signal	X		X
	Parent-, teacher-report	X	X	X
Emotion regulation	Impossible circle, maze	X		X
	Disappointing gift	X		X
	Parent-, teacher-report	X	X	X
Peer relations	Simulated peer interaction			X
	Child vignettes	X	X	X
	Parent-, teacher-report	X	X	X
	Child report	X	X	X
Cortisol production	Diurnal	X	X	X
Parenting	Parent-child interaction	X	X	X

Inhibitory control. The tasks have been chosen because they are well validated, have clear ERP signatures, and are associated with children's behavior in other contexts.

<u>*Simon Task:*</u> The Simon Task targets interference control, or the ability to resist the interference created by competing response tendencies. Children will complete a computer-administered Simon task (Hajcak et al., 2008; Simon, 1969). The task (or similar interference tasks) has been used successfully to differentiate children from low- and high-risk environments (Bruce et al., 2009; Loman et al., 2013).

At both ages, children will perform an 'arrows' variation of the classic Simon task (Simon, 1969). On each trial, children are asked to make a speeded response based on the color of an arrow presented on a computer monitor while ignoring the direction in which the arrow is pointing. The task is composed of 384 trials arranged into 6 blocks of 64 trials each. Stimuli will be arrows that point left or right and are either red or green. Arrows will be presented one at a time for 200ms and will be followed by a blank screen for an additional 800ms. Children are instructed to press the leftmost button on a response box on trials when the arrow is red and the rightmost button when the arrow is green. In congruent trials, the red arrow points left and the green arrow points right; in "incongruent" trials, the red arrow points right and the green arrow points left, resulting in conflict, or interference. Behavioral data for this task are accuracy and reaction times; the ERP data of primary interest are the ERN and Pe. Practice effects are not expected to be problematic because the tasks will be separated by 2 years, and will be slightly different.

Stop-Signal Task: The Stop Signal Reaction Time Task assesses children's ability to stop a response once it has been initiated (Barch et al., 2009). This task has two different trial types. The stop trials are identical to the go trials, but when the go stimulus is on the screen a red circle appears superimposed on the arrow at varying delay intervals. Subjects are instructed to inhibit their response to the go stimulus as soon as the stop signal is presented. The Stop-Signal task will consist of four blocks of 100 trials each. Stop trials will occur randomly during each of the four blocks and will make up about 1/3 of all of the trials. A tracking procedure that varies the delay between go and stop signals will be used to maintain accuracy at 50%. Behavioral data for this task are both stop and go reaction times, and ERP data of primary interest are frontal N200 and P300, as described below.

Event Related Potential (ERP) data acquisition: Electrophysiological data will be acquired during the Simon Task and the Stop-Signal Task using 32 Ag/AgCl electrodes. Placement of electrodes in the cap will be consistent with the International 10–20 System (Cooper et al., 1969). Advanced Neuro Technology Acquisition hardware (ANT, Enschede, the Netherlands) will be used for EEG data collection with an average electrode reference and forehead ground. The continuous EEG will be digitized at 512 samples per second and processed using advanced source analysis, a software package designed for ANT ERP systems. Re-referencing to the averaged mastoid will be performed off-line. The EEG will be corrected for artifacts such as eye blinks and EKG (electrocardiogram artifacts), and bandpass filtered from 0.1 Hz to 30 Hz. EEG data that exceed -75 uV or +75 uV will be rejected. Average ERP waveforms, locked to picture onset, will be computed for each condition at each electrode. Averages will be baseline corrected by subtracting the average voltage occurring during the 200ms before the presentation of the stimulus from the entire average.

On the Simon Task, the primary dependent measure is the ERN/Pe complex, observed over frontal brain regions beginning approximately 50ms after children execute an incorrect motor response. Both components have been associated with performance monitoring, with the ERN, in particular, sensitive to conflict and interference. For analyses, segments of EEG data surrounding each response will be extracted from the continuous EEG file. The ERN will be quantified as the average activity from 0-100ms post response and the Pe as the average activity from 250-450ms. On the Stop-Signal Task, the primary dependent measures are the N200 and P300. The N200 and P300 components are believed to reflect sequential subprocesses involved in inhibitory control (Barch et al., 2009). Specifically, the N200 component is conceptualized as a "flag" that signals the need to inhibit a response, and the P300 is the "brake" that puts response inhibition processes into effect (Pliszka et al., 2000). The N200 is lateralized to the right frontal recording sites; the stop P300 is more symmetrical but still frontal. Quantifying the N200 and P300 components is complex, given that stop signals closely follow the go stimuli, and the ERPs elicited by the two events overlap. In order to disentangle N200 and P300 associated with the stop signal from the go-stimulus induced brain activity, Simons and colleagues (Dr. Simons is an investigator on this award) have developed a set of reliable extraction algorithms (e.g., Krompinger et al., 2010).

Teacher- and parent-report: Teachers and parents will complete the Behavioral Assessment System for Children (BASC), as well as the Social Competence subscale from Harter's Teacher Rating Scale of Child's Actual Behavior. Both scales have good test-retest reliability and internal consistency (Cole et al., 1996; Harter, 1985). Subscale scores for attention problems and hyperactivity will be of particular relevance to the construct of inhibitory control. Research staff will use procedures developed by Dr. Hubbard and Dr. Dodge to ensure excellent teacher compliance, including most especially personal contact with teachers in the 30 minute period before children arrive at school.

Parents will complete the BASC and other questionnaires through an iPad system that reads questions to parents through headphones, while parents respond to a touch screen (thus eliminating problems with limited reading ability, and discouraging the tendency to rush through items).

Emotion regulation. Individually administered emotion regulation tasks will be completed when children are 8 and 10 years old. Emotion regulation will be coded in peer interaction tasks when children are 9 years old. Teachers and parents will complete the Emotion Regulation Checklist each year.

Impossibly Perfect Circle: The Impossibly Perfect Circle task was drawn from the Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith & Rothbart, 1996) to assess children's regulation of distress. The task has demonstrated validity in differentiating children who vary in emotion regulation, parenting experiences, and risk for behavior problems (e.g., Dennis, 2006; Dennis et al., 2011; Hayden, Klein, & Durbin, 2005).

In the Impossibly Perfect Circle task, the experimenter repeatedly asks the child to draw a "perfect" circle, critiquing each circle with specific statements that do not include suggestions for correcting the problem. After 3.5 minutes of critiques, the examiner leaves, after which a second examiner enters and praises the child's final circle, presenting the child with a certificate. At age 10, a maze will be used instead of perfect circles, and will be administered similarly (Cole et al., 2006).

Disappointing Gift: The Disappointing Gift task (also adapted from Lab-TAB, Goldsmith & Rothbart, 1996) has been used by a number of investigators to assess children's handling of disappointment (e.g., Dennis et al., 2011; Simonds et al., 2007). In this version of the Disappointing Gift, the child will be asked to rank prizes from favorite to least favorite at the beginning of the session by one experimenter. At the end of the session, a different examiner will give the child a wrapped package containing the least favorite gift (e.g., a broken toy). The child will then be with the experimenter for 30s, alone for 30s, interviewed about the experience by a second researcher, and reunited with his or her mother for 2 minutes. Finally, the experimenter will return with the desired gift while apologizing for making a mistake. An adapted version will be used when children are 10 years old.

The child's emotion regulation will be coded globally and second-by-second using an emotion regulation coding system (D.O.T.S. Emotion Coding System: Cole et al., 2006). (Dr. Cole is a consultant, and Dr. Roben is an investigator.) Second-by-second coding will be completed using video analysis software (NOLDUS Observer XT 11.0, Noldus Information Technology, Netherlands) to facilitate coding and provide sophisticated data management and analysis functionality. Microanalytic coding can be used for determining frequency, duration, and intensity of emotions and behaviors as well as examining contingencies between events.

Teacher- and parent-report: Teachers and parents will be asked to complete the Emotion Regulation Checklist (ERC: Shields & Cicchetti, 2001), an 8-item questionnaire. The ERC has good construct and discriminant validity.

Peer relations and aggression. Peer relations will be measured through simulated peer interactions in the lab when children are 10 years old, and through child interview measures, and teacher-, parent, and self-report when children are 8, 9, and 10 years old.

Simulated peer interactions: Simulated peer interactions have been used successfully to elicit aggressive responses in a number of studies (including those conducted by co-Investigator Hubbard and Consultant Dodge). An adapted version of Cherek's Point Subtraction Aggression Paradigm, used by Carre, Dodge and colleagues (2013), will be used here. This paradigm has been used extensively with children, adolescents, and adults (e.g. Casat et al., 1995; Cherek, 2006; Reijntnes et al., 2013), and provides a strong measure of reactive aggression. In this version of the task, children play a computer game against a fictitious peer. They are told that they will earn points that are exchangeable for money. Computer buttons represent different response options, with one earning points for the child, one protecting points, and a third subtracting points from the opponent. The children are told that the fictitious peers can take and keep points from them, and they see evidence of this at random times through their diminished point total. The number of points children take from the fictitious peer in each of three play periods serves as the measure of reactive aggression.

Child interview measures: Hostile attributional biases and positive outcome expectations for aggression will be assessed through children's responses to hypothetical vignettes developed by Dodge et al. (1986). The vignettes will be read aloud to children and accompanied by cartoon depictions. All vignettes assessing hostile attributional bias describe an interaction between a protagonist and a peer that results in a negative outcome for the protagonist, but in which the intention of the peer is ambiguous. Children will be asked an open-ended question about why the peer acted as he or she did, and responses will be coded as benign or hostile. All vignettes assessing positive outcome expectations for aggression describe the protagonist engaging in an aggressive act against a peer. Children will be asked open-ended questions about the instrumental and social outcomes of this aggressive behavior, and responses will be coded as positive or negative. Previous studies (Dodge et al., 1986; Dodge et al., 1995) have found high inter-rater reliability and internal consistency for these ratings. Children with histories of abuse report more hostile intent than children without such histories (Dodge et al., 1995), and children with stronger hostile attributional biases and more positive outcome expectations for aggression have higher levels of current aggressive behavior (Dodge et al., 1986).

Teacher- and parent-report: The Aggression and Social Skills of the BASC subscales of the teacher and parent BASC will be particularly relevant to the assessment of children's peer relations. (See psychometrics above.)

Child self-report measures: Children will also complete a self-report measure of peer rejection, the 6-item Social Competence subscale of the Self-Perception Profile for Children (SPPC; Harter, 1985). The subscale has demonstrated strong convergent, concurrent, and discriminant validity (Harter, 1985).

Assessment of salivary cortisol. Cortisol is an end product of the HPA axis. Early adversity is associated with perturbations to the diurnal pattern of cortisol production and perturbations in stress reactivity (Bernard et al., 2010).

Diurnal cortisol: Diurnal cortisol will be assessed when children are 8, 9, and 10 years old. Saliva samples will be taken from children two times daily over a 3-day period through passive drool. The two samples each day will include when the child first wakes up and at bedtime. The normative pattern is a high wake-up level, decreasing throughout the day, with the nadir in the evening (Larson et al., 1998).

The bottle containing the Salivabio device (used for collecting passive drool with a straw) will have an automated time/date stamp that records the time the container is opened. The use of the time-date stamping caps has been found to enhance compliance (Broderick et al., 2004; Kudielka et al., 2003). A sleep, feeding, heath, medication, and behavior diary will be completed by parents for the days that salivary cortisol is collected. These data will be available for assessment of confounding factors. If the child is sick or having other acute physical problems, assessments will be delayed for one week or until the child's health has recovered. Analyses will exclude children taking steroids (e.g., prednisone, inhalers) or other medications known to affect cortisol levels.

Saliva samples will be stored in a freezer at -20 °C until they are assayed in our laboratory. Assays will be performed using the Salimetrics, Inc. High Cortisol Salivary Cortisol Enzyme Immunoassay Kit (catalog No. 1-1102/1-1112). Assaying duplicate samples results in correlations of .98 for different batches of assays. All samples from a child from a single time-point will be run in duplicate on the same assay plate, along with a control. All samples will be within an acceptable pH range, as demonstrated by an absence of color change when indicator (as part of the assay dilutant) is added.

Parent-child interaction: To provide a current assessment of parenting, children and primary parent will participate in videotaped interactions annually. Adapted from Rubin and Burgess (2006), the tasks will include discussion of an issue that the child is concerned about (chosen by research staff from three possibilities suggested), an event that the child is excited about, and planning a night out (or other similar task). Parental synchrony, intrusiveness, and delight will be coded for all contexts, and sensitivity to distress will be coded in the concern condition only, using an adaptation of Rubin and Burgess' (2006) scoring scheme. Behavior will be coded in 30s intervals and on global scales. Inter-rater reliability and construct validity are well established (Rubin and Burgess, 2006).

Cumulative risk index: Early childhood and middle childhood risk indices will be computed, as specified by Appleyard et al. (2005), and adapted from a rich literature using risk indices (e.g., Sameroff et al., 1987). As defined by Appleyard et al., early childhood will include the period between birth and 64 months of age, and middle childhood will include the period between 64 months and 10 years (coinciding with the final data collection). The factors will include disruptions in care, maltreatment, parent jailed or hospitalized for more than 2 weeks, exposure to violence, high maternal stress, and poverty, and will be assessed through interviews with parents (Appleyard et al., 2005). Risk factors will be coded as present or absent, and summed to yield two summary scores, one for early childhood, and one for middle childhood. Cumulative risk indices have proven more robust than factors considered individually (Appleyard et al., 2005; Sameroff et al., 1987).

Secondary variables. We will collect data regarding child intelligence, and parents will complete background questionnaires that will ask about child's medications, use of mental health services, physical health, and school history.

Child IQ: The Vocabulary and Matrix Reasoning sections of the Wechsler Abbreviated Scale of Intelligence (WASI-II; Wechsler, 2011) will be completed with the child to provide an index of child intelligence. This brief measure has been found to have good test-retest reliability and to be highly predictive of Full Scale IQ on the Wechsler Intelligence Scale for Children (WISC-IV).

Data Analyses

The conceptual model presented earlier guides the plan for analyses. The focus of this study is to follow neglected children from a randomized clinical trial begun in children's infancy into middle childhood. Intervention effects on inhibitory control, emotion regulation, peer relations, and cortisol production are of primary interest, and we expect that these effects will be mediated by parental behavior. We will assess whether parenting during early or middle childhood best predicts outcomes for children during middle childhood, accounting for across-time stability in both child and parent behaviors. We will first examine whether there are main effects of risk status or interactions of risk status with intervention group in predicting middle childhood parenting or child outcomes. Although risk status has emerged as a powerful predictor in other studies, we have not found that to be the case in this sample, perhaps because the sample represents a relatively homogeneous group with regard to risk (i.e., high-risk). We will also consider the effects of variables such as gender, ethnicity, and child intelligence in preliminary analyses. Such variables will be included in primary analyses as moderators or covariates when indicated in preliminary analyses. Pre-intervention measures of child behaviors can also be considered for inclusion in analyses where appropriate. These pre-intervention data will not always provide direct assessments of constructs of interest (e.g., there will be no pre-intervention measure of peer relations), but will provide checks on the equivalence of groups at baseline. Also, post-intervention outcomes from early childhood will be evaluated as possible predictors, mediators, or moderators of later outcomes, as appropriate. A low-risk comparison group is included to ensure that differences that we consider preferable are consistent with findings from a low-risk comparison group.

For most constructs, data at 8, 9, and 10 years of age will be available from multiple informants and/or multiple measures. Reduction of multiple indicators to a few composites or latent variables will result in more valid and reliable measures of constructs than if we were to use individual measures. To achieve this, composites (where this is the standard measurement practice) and latent factors (where there are multiple measures of the same constructs with the advantage of separating error variance from common variance) will be formed and evaluated for further substantive modeling.

Analyses will be conducted to examine development over time in inhibitory control, emotion regulation, peer relations, and cortisol production as a function of intervention. Multilevel or hierarchical linear models (HLM; Raudenbush & Bryk, 2002) will be the primary method for analyzing intervention effectiveness. We will also extend the multilevel analyses into a structural equation modeling (SEM) framework in order to accommodate latent variables with multiple indicators and to conduct mediation analyses (Bollen & Curran, 2006). This data analytic framework can accommodate time-varying covariates, data that are missing at random (or ignorable missing data), and unequal time intervals between repeated measurements.

Missing data considerations. Restricting analyses to complete cases can substantially bias statistical findings (e.g., Graham & Donaldson, 1993). Assuming data are missing at random or missing completely at random, multiple imputation and full information maximum likelihood estimation are two principled and recommended techniques for dealing with missingness (e.g., Allison, 2001; Howell, 2007; Schafer & Graham, 2002). We will be using statistical packages (i.e., HLM, Mplus) that can accommodate missing data on the outcome variables, assuming data are missing at random (MAR; Rubin, 1987; Schafer & Graham, 2002), via full information maximum likelihood estimation (FIML). (We note that the term "missing at random" is misleading because data are considered missing at random when they are ignorable by virtue of systematic association with a third variable or variables that can be covaried, even though the data are not actually missing at random.) Although the approach is not failsafe, we will assess whether data are missing at random by examining whether participants with missing data are distinguishable from those without missing data in terms of important variables (e.g., risk status, ethnicity, intervention group, etc., as well as outcomes from early childhood). If, however, data are not missing at random (MNAR), we will use approaches recommended such as modeling missingness (Dunning & Freedman, 2008; Enders, 2010). Even in cases where data are not missing at random (MNAR), multiple imputation can be used (Verbeke & Molenberghs, 2000). To this point, we have not found evidence of systematically different attrition, or different levels of attrition, from the two intervention groups.

Data analytic plan. A description of primary analyses follows. Because of space constraints, analyses will be described briefly, referring to previous examples when possible.

Hypothesis 1: Neglected children whose parents received the ABC intervention and low-risk comparison children will show better inhibitory control than neglected children whose parents received the DEF intervention.

ERP data will be analyzed as analyses of variance, with group as the independent variable, age (8 vs. 10) as the repeated measures variable, and the relevant ERP component (ERN and Pe for Simon task; N200 and P300 for Stop-Signal task) as the dependent variable. Of primary interest will be group differences related to intervention status. A main effect for intervention group is expected, with planned comparisons of the relevant ERP component yielding differences between the ABC and DEF group, and between the DEF and comparison (low-risk) group. Risk indices (and other variables as indicated in preliminary analyses) will also be considered as moderators or as covariates in this and other analyses. We will include the low-risk comparison group in all analyses, but because of space constraints, we do not discuss this group with regard to all hypotheses.

Behavioral data from the Simon and Stop-Signal tasks and teacher- and parent-report will also be examined as dependent variables. Correlations among behavioral data will be examined for the creation of a latent construct. The resulting latent construct of inhibitory control will be examined as a dependent variable and intervention group status will be examined as a predictor. We expect children in the ABC group will show stronger inhibitory control than children in the DEF group. Additional higher order latent constructs that include both behavioral and informant report data will be considered.

We will test whether these effects are mediated by parental behavior. In particular, synchronous behavior (i.e., following the child's lead) has been associated with children developing better regulatory capabilities. We will test this mediation hypotheses using a path analysis to estimate indirect and direct effects, examining whether parental synchronous behavior mediates the impact of intervention (ABC or DEF) on child inhibitory control in middle childhood using recommended approaches (i.e., MacKinnon et al., 2007; Preacher et al., 2010; Kraemer et al., 2002). We will account for child behaviors in infancy, and test competing models with early and concurrent measures of parent synchrony.

Hypothesis 2: Children in the ABC intervention condition and low-risk comparison children will show better emotion regulation than children in the DEF condition.

Analogous to inhibitory control analyses described above, differences related to intervention status are of particular interest. We expect that children in the ABC group and the comparison (low-risk) group will show more mature levels (higher levels of control) of emotion regulation than children in the DEF group.

The dependent variable, emotion regulation, will be measured through multiple informants and multiple measures, including global coding of observational tasks, second-by-second coding of observational tasks, parent-report, and teacher-report. First, correlations among global coding of emotion expression, global coding of regulation strategies, and parent- and teacher-reports on the Emotion Regulation Checklist will be examined for the creation of a latent construct, and then examined as the dependent variable in the intervention group comparison.

In addition to examining globally indicated differences in emotion regulation, microanalytic coding of emotion expression and purported regulatory strategy will allow us to examine dynamic and contingent measures of emotions and strategies. We will create the following variables: average intensity of bouts of emotions, latency to the first bout of both emotions and strategies, and average bout duration of both emotions and strategies (Cole et al., 2011). We will test whether intervention groups differ in these variables, expecting that children in the ABC intervention and low-risk children will have lower average intensity of sadness and anger, longer latency to the first bout of anger, and shorter duration of sadness and anger, relative to children in the DEF intervention. Children in the ABC group are also expected to use regulatory strategies more quickly and for longer than children in the DEF group. Parental sensitivity to distress and synchrony will be assessed as possible mediators of treatment effects.

Hypothesis 3: Children in the ABC intervention condition and low-risk children are expected to show less negative attributional bias through vignettes, to show less reactive aggression in the peer simulation, and to be assessed as less aggressive and more prosocial by parents and teachers, than children in the DEF condition.

The analyses will be analogous to those described for hypothesis 1. As in hypothesis 2, both sensitivity to distress and synchrony are expected to predict attributional bias, aggression, and ratings of aggression and prosocial behaviors, and will be examined as possible mediators of outcomes.

Hypothesis 4: Children in the ABC intervention group and low-risk children will show more normative cortisol production, as assessed through salivary cortisol measured diurnally, than children in the DEF intervention group. More specifically, a steeper slope from morning to evening is expected for children in the ABC and low-risk groups relative to children in the DEF group.

Salivary cortisol will be collected at every age (8, 9, and 10 years, as well as from earlier assessments at pre-intervention, 2, 3, and 4 years). Changes in cortisol as the result of the intervention will be analyzed using Hierarchical Linear Modeling (HLM: Raudenbush et al., 2004; Snijders & Bosker, 1993). HLM allows separate estimates of level 1 (as a function of within person) and level 2 (as a function of between subjects) variation.

Initial cortisol values and changes in cortisol values from wake-up to bedtime will be analyzed. The dependent variable will be the log-transformed cortisol wake-up (or bedtime) values measured across each assessment, measured in µg/dl. Parental synchrony is expected to be associated with cortisol production, and will be examined as a mediator of treatment effects.

Power analyses. Analyses were conducted to estimate the power needed to detect differences between experimental and control groups for outcomes most central to proposed hypotheses. For most analyses, appropriate pilot data were available to allow estimates of group means and standard deviations. Power to detect differences in inhibitory control were based on Dr. Simons' work and represent large effects (e.g., Hajcak et al., 2008); power to detect differences in emotion regulation were based on our findings, as well as our Consultant Cole/Investigator Roben, and range from medium to large effect sizes (e.g., Cole et al., 2011; Dozier et al., 2013); for peer relations, estimates were based on Dr. Hubbard and Dr. Dodge's work (co-investigator and consultant, respectively) and represent medium to large effects (e.g., Carre et al., 2013; Hane et al., 2008; Smith et al., 2011); and for cortisol, estimates were based on our work and represent medium to large effects (e.g., Bernard et al., 2013).

Power to detect medium or large effect sizes for the full sample of 210 would be .99, and would range from .84 to .99 for the reduced sample of 140 (Cohen, 1988). In a "worst case scenario" of very high attrition, power to detect medium and large effects would range from .78 to .99 for a full sample of 150, and .70 to .98 for the reduced sample of 100 neglected children. Although effects might be expected to be smaller as children become older, that is in fact not what we have found. Intervention effects for cortisol production were at least as large at the age of 5, at least 3 years post-intervention (d = .85), as they were immediately following the intervention (d = .53).

Statistical power considerations for multilevel models. Estimates of statistical power for multilevel models are substantially more complex than power analyses presented here. This is because statistical power is based not only on the hypothesized effect size, overall sample size, and alpha level, but also on additional factors such as the level-1 sample size, the level-2 sample size, and the intraclass correlation (i.e., the amount of dependency in the data). Raudenbush and Liu (2001) have extended statistical power for group differences in multilevel models by incorporating these factors, resulting in a software package to this end. Based on estimates for these factors from observed effect sizes for intervention effects, we estimate that power will range from .80 to .99, even when considering the most pessimistic attrition estimates.