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Effects of an Attachment-Based Intervention on Autonomic Regulation Among Opioid-Exposed Infants

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Abstract

Little is known about whether postnatal intervention enhances autonomic regulation among infants at risk for dysregulation due to prenatal opioid exposure. The present study evaluated effects of modified Attachment Behavioral Catch-up (mABC) on autonomic regulation for opioid-exposed infants in a pilot randomized clinical trial. We hypothesized that, compared to a control intervention (mDEF), mABC would be associated with higher resting respiratory sinus arrhythmia (RSA) and pre-ejection period (PEP) as well as greater reactivity to and recovery from a social stressor (Still-Face Paradigm). Pregnant or peripartum women receiving opioid agonist therapy (61 mothers of 64 infants; final $N = 36$ infants) were randomly assigned to mABC or mDEF, 12-session home visiting programs beginning in the third trimester; mABC targets sensitive parenting and mDEF targets cognitive and motor development. mABC was associated with significantly greater RSA reactivity and marginally greater PEP reactivity. In models accommodating missing data, mABC was additionally associated with significantly greater RSA recovery. In sensitivity analyses removing siblings, mABC predicted significantly enhanced PEP reactivity. Overall, in these preliminary analyses, mABC was associated with healthier autonomic regulation during a social stressor than mDEF. Thus, mABC may be a promising strategy to promote autonomic regulation among opioid-exposed infants through parenting intervention.

Keywords: autonomic nervous system, attachment, substance exposure

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Prenatal opioid exposure is associated with negative developmental outcomes (Yeoh et al., 2019). Opioid exposure may impact the development of autonomic physiology because opioid withdrawal at birth primarily affects the central and autonomic nervous systems (Kocherlakota, 2014). Although postnatal caregiving experiences may mitigate negative effects of opioid exposure, few studies examine interventions with parents of opioid-exposed infants. The present study aims to test preliminary effects of a parenting intervention on autonomic regulation among opioid-exposed infants.

Prenatal Opioid Exposure and the Autonomic Nervous System

Exposure to early adversity, including prenatal substance exposure, is associated with altered autonomic nervous system (ANS) functioning among infants and children (Propper & Holochwost, 2013; Quigley & Moore, 2018). Autonomic dysregulation has important implications for physical and mental health. Respiratory sinus arrhythmia (RSA), an index of the parasympathetic nervous system influence over the heart, has emerged as a biomarker for emotion regulation (Beauchaine, 2015). Low resting RSA and atypical RSA reactivity (i.e., blunted or excessive RSA responding) have been associated with psychopathology (Beauchaine, 2015). Less is known about the implications of dysregulated cardiac pre-ejection period (PEP) activity, an indicator of sympathetic influence of the heart. However, an imbalance of the parasympathetic and sympathetic branches of the ANS (e.g., sympathetic dominance) is associated with poor mental and physical health (Berntson, 2019; Quigley & Moore, 2018; Thayer & Sternberg, 2006). Substance exposure is commonly associated with low resting RSA and blunted RSA reactivity to stressors in infancy and early childhood (Propper & Holochwost, 2013).

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In several studies, researchers have demonstrated the acute effects of maternal opioid agonist therapy (OAT) administration on fetal cardiac functioning. Both methadone and buprenorphine administration have been linked to acute reductions in fetal heart rate and heart rate variability throughout pregnancy (Jansson et al., 2005, 2017; Salisbury et al., 2012). Emerging evidence indicates that prenatal opioid exposure may be associated with sustained autonomic dysregulation after birth. Among neonates, opioid exposure has been associated with altered cardiac functioning at rest (Parikh et al., 2011) and during nutritive and non-nutritive sucking (Hambleton et al., 2013). Further, elevated neonatal opioid withdrawal syndrome (NOWS) symptomatology has been inversely related to neonatal parasympathetic tone at rest (Jansson et al., 2010). At one month, prenatal exposure to both opioids and cocaine was associated with lower RSA during visual orientation than exposure to only opioids or other substances (e.g., alcohol, tobacco; Conradt et al., 2013). However, research regarding ANS functioning after the neonatal period is limited.

Parenting and the Postnatal Environment

Environmental risk factors account for significant variance in developmental outcomes among infants exposed to opioids prenatally (Konijnenberg & Melinder, 2011; Messinger et al., 2004). Parenting behaviors such as parental sensitivity and harshness may moderate or mediate the effects of prenatal substance exposure on developmental outcomes (Eiden et al., 2014; Flykt et al., 2021; Schuetze et al., 2019; Veira et al., 2014). Opioid-exposed infants often exhibit autonomic dysregulation and are difficult to soothe (Kocherlakota, 2014). Given this vulnerability, sensitive parenting may be particularly important to promote the development of healthy regulatory abilities. Although existing research is limited by small sample sizes and inadequate demographic controls, a recent review found that parents who misuse opioids tend to

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show lower sensitivity and warmth than parents who do not misuse opioids (Peisch et al., 2018). Taken together, parenting quality is a promising target of intervention for parents with opioid use disorder.

Parenting Interventions

Encouragingly, a small body of research has linked parenting interventions with reduced child maltreatment risk among women with opioid use disorder (Dawe & Harnett, 2007; Luthar et al., 2007; Luthar & Suchman, 2000; Peisch et al., 2018). However, existing interventions are not specifically designed for parents of *infants*. This is a substantial limitation, as infants are uniquely dependent on their parents for regulatory support (Kopp, 1982), including autonomic co-regulation (Quigley & Moore, 2018). Furthermore, the early infancy period is critical for infant development, poses unique challenges for parents, and is associated with heightened maltreatment risk (UDHHS, 2021). Thus, there is urgent need to evaluate parenting interventions for infants of women on OAT.

Attachment and Biobehavioral Catch-up (ABC) is a 10-week home-based parenting program designed for vulnerable parents and infants (Dozier & Bernard, 2019). ABC focuses on increasing parental sensitivity and nurturance and decreasing intrusive or frightening parent behaviors. Randomized clinical trials (RCTs) have been conducted with maltreating parents (Bernard et al., 2012), foster parents (Bick & Dozier, 2013), and parents of children adopted internationally (Yarger et al., 2019). The ABC intervention has demonstrated efficacy in increasing parental sensitivity (Bick & Dozier, 2013) as well as children's secure and organized attachment (Bernard et al., 2012), cortisol regulation (Bernard, Dozier, et al., 2015; Bernard, Hostinar, et al., 2015; Garnett et al., 2020), brain activity (Bick et al., 2019; Valadez et al., 2020), and inhibitory control (Korom et al., 2021; Lind et al., 2019). Receiving the ABC intervention in

infancy has also been associated with higher RSA and lower heart rate at rest and during a parent-child interaction in middle childhood than receiving a control intervention (Tabachnick et al., 2019). Although this effect suggests that ABC may impact autonomic regulation as early as infancy, autonomic regulation in infancy has not yet been assessed in studies of ABC.

The present study evaluates preliminary effects of modified ABC (mABC), which was adapted for women receiving OAT (Labella et al., 2021). ABC is particularly well-suited to adaptation for infants exposed to opioids because the parenting targets have significant continuity with non-pharmacological interventions currently being evaluated for NOWS symptoms in hospitals (Brogly, 2019; MacVicar & Kelly, 2019; e.g., staff providing nurturance to infants and persisting when infants are difficult to soothe). Intervening with parents directly may reduce acute symptoms and have sustained impact on infants' developmental trajectories by altering the long-term caregiving environment. Further, enhancing parent skills and confidence in providing nurturing care may reduce guilt and stigma.

Present Study

The aim of the present study was to examine preliminary effects of mABC on infant autonomic regulation in a pilot trial. It was hypothesized that receiving mABC would be associated with heathier autonomic regulation than receiving a control intervention (mDEF). Specifically, mABC was expected to be associated with higher resting RSA, longer resting PEP, and greater reactivity to and recovery from a stressor than a control intervention.

Method

Participants

Eighty-four pregnant and peripartum women receiving OAT were referred by treatment centers in Pennsylvania, Delaware, and Maryland or volunteered after seeing study materials.

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Sixty-one mothers of 64 infants completed informed consent and enrolled. A sample size of approximately 30 families in each group was determined for this pilot RCT based on feasibility. In the present sample, 32 infants (including one set of siblings) were randomized to mABC and 32 infants (including one set of twins and one set of siblings) were randomized to mDEF. Demographic data are presented in Table 1. This study was approved by the University of Delaware Institutional Review Board. The trial was registered on ClinicalTrials.gov (NCT03891628).

Intervention groups did not differ significantly in the number of infants whose mothers received methadone ($X^2(1, N = 64) = 0.00$, $p = .99$) or buprenorphine ($X^2(1, N = 64) = 0.39$, $p = .53$). There was no significant difference in the proportion of male and female infants ($X^2(1, N = 64) = 0.06$, $p = .80$) or White/non-Latino/a/x infants ($X^2(1, N = 64) = 0.20$, $p = .66$) across groups. Intervention groups did not significantly differ by maternal education ($t(60.22) = -0.51$, $p = .61$), family income ($t(53.97) = -0.01$, $p = .99$), infant birthweight ($t(52.03) = -.06$, $p = .95$), infant age at the time of outcome data collection for the present study ($t(34.64) = 0.50$, $p = .62$), or proportion of gestational days exposed to OAT ($t(60.55) = -0.11$, $p = .91$), non-OAT opioids ($t(59.58) = -0.62$, $p = .54$), or other substances measured with a polysubstance risk score ($t(56.61) = -1.10$, $p = .28$). Thus, random assignment was considered successful in balancing potentially important sociodemographic and substance exposure variables across intervention groups. On average, infants across both groups had completed six sessions at the time of the six-month data collection (mABC $M = 6.29$, $SD = 3.18$, range = 0-11; mDEF $M = 6.06$, $SD = 3.98$, range = 0-12), indicating that dyads were about halfway through the program in both conditions. This means that the average mABC dyad had completed primary sessions focused on nurturance and sensitivity.

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Procedure

During the third trimester of pregnancy or within one month postpartum, women completed a pre-intervention assessment and then were randomly assigned to receive mABC or mDEF using a random number generator with parallel assignment. When infants were approximately six months old (corrected for prematurity), infant autonomic nervous system data were collected at rest and during a social stressor. Women and infants completed additional tasks at this visit as part of the RCT. Parents were not aware of their intervention condition. Most research staff were also unaware of intervention condition; not all research staff could be kept unaware due to logistical limitations.

Recruitment and data collection took place from 2018-2021. Notably, the COVID-19 pandemic began in the middle of data collection for the RCT. Data collection continued with remote assessment only (e.g., interviews by Zoom) until mid-July 2020 when in-person data collection resumed on a limited basis, with some families electing remote-only or home assessments with virtual researcher support. Patterns of autonomic reactivity were similar across home and lab settings (Tabachnick et al., 2021), and community data suggest that intervention fidelity and effects on parenting were maintained in the transition to telehealth (Roben et al., 2021; Schein et al., 2022). Further information regarding RCT enrollment and attrition is provided in Supplement 1. Note that in certain circumstances (e.g., infant death), families completed research visits but not intervention sessions or dyadic assessments. Data collection for the full-scale RCT is ongoing as of 2022.

Interventions

mABC is a 12-session home visiting parenting program that was adapted from ABC for women receiving OAT and their infants (Dozier & Bernard, 2019; Labella et al., 2021). mABC

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retains the same intervention targets as ABC, namely: enhancing parental nurturance to infant distress, increasing parental sensitivity to infant non-distress, and decreasing intrusive or frightening parent behaviors. Whereas ABC begins at six months, mABC was adapted to begin prenatally to help mitigate potential withdrawal symptoms at birth. Adaptations included the use of an infant simulator to practice parenting targets prenatally, the addition of a session conducted in the hospital in the infant's first days of life, and the development of relevant material for young infants (e.g., cues for engagement or overstimulation). mDEF, or modified Developmental Education for Families, is a 12-session home visiting program matched to mABC in timeline and format. mDEF content included education about developmental milestones and the ways in which parents can promote infant cognitive and motor development through play, rather than focusing on attachment-relevant behaviors (e.g., responding with nurturance to infant distress).

Both mABC and mDEF were delivered beginning in the third trimester of pregnancy or postpartum, depending on the timing of enrollment and completion of the pre-intervention assessment. For both interventions, sessions were ideally conducted every 2 to 3 weeks depending on the infant's age, and sessions included content delivery, interactive dyadic activities, and discussion of between-session skill practice. Interventionists were graduate students, postdoctoral fellows, post-baccalaureate research staff, and paraprofessionals. Fidelity was monitored for both interventions via group supervision and video review.

Measures

When infants were six months old (corrected for prematurity), ANS data were collected continuously during a baseline resting period and the Still-Face Paradigm (SFP; Tronick et al., 1978). First, the infant viewed a three-minute clip of a Baby Einstein video, either sitting in the parent's lap or in a highchair next to the parent. Next, the infant was moved to a highchair facing

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the parent and soothed until reasonably calm prior to beginning the SFP. The SFP consists of three two-minute episodes: gentle play (Play 1), maintaining a neutral face and avoiding interaction (Still-Face), and gentle play (Play 2).

Infant physiological data were collected and cleaned with MindWare hardware and software. Three disposable pediatric electrodes in a bipolar configuration were used to collect electrocardiogram (ECG) data and four disposable pediatric electrodes placed on the infant chest and back were used to collect cardiac impedance (IMP) data. Physiological data were divided into one-minute segments for cleaning.

Heart Rate Variability Analysis Software (version 3.2) was used to calculate RSA. Segments that required estimation of greater than 10% of total beats were excluded from analyses. RSA in each segment was estimated as the natural log of the infant's average high-frequency heart rate variability in that segment based on the frequency band recommended for use with infants (i.e., 0.20 to 1.04 Hz; Bar-Haim et al., 2000). Finally, average RSA was calculated for each task epoch, and RSA reactivity (Still-Face – Play 1) and recovery (Play 2 – Still-Face) change scores were calculated. Impedance Cardiography Analysis Software (version 3.2) was used to calculate PEP. Segments were excluded from analyses if fewer than 50% of beats could be retained. PEP reactivity and recovery values were calculated as described for RSA.

Missing Data

Descriptively, 27 infants were missing autonomic nervous system data, including 7 whose mothers lost custody, 8 who completed remote-only assessment during the COVID-19 pandemic, and the remainder who did not complete the SFP or did not complete ANS due to technical problems, time constraints, or the infant being nine months or older. Missingness was

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not statistically related to intervention condition or the following sociodemographic variables: caregiver educational attainment, family income, caregiver depressive symptoms, caregiver substance use during pregnancy, infant birthweight, infant gestational age, infant sex assigned at birth, or infant race/ethnicity (all p values > .05; t-tests for continuous variables and chi-squared tests for dichotomous variables). Autonomic nervous system data was determined to be missing at random or completely at random.

Analytic Plan

Intent-to-treat analyses were conducted in R (R Core Team, 2021). First, intervention effects were examined using t-tests to evaluate the impact of mABC without incorporating covariates or accommodating missing data. For primary analyses, regressions were used to estimate intervention effects while accommodating missing data and controlling for infant sex assigned at birth, due to sex differences observed in the literature. Regressions were modeled using the 'lavaan' package with robust standard errors and full information maximum likelihood (FIML) to accommodate missing data (Arbuckle, 1996; Rosseel, 2012). In addition, sensitivity analyses were conducted to determine if results changed when younger/non-target siblings were removed.

Results

Descriptive statistics with sample sizes are presented in Tables 1 and 2. Results of t-tests indicated that infants in the mABC group had significantly greater RSA reactivity (withdrawal) to the Still-Face episode ($t(28.65) = -2.45$, $p = .02$, 95% CI[-1.73, -0.15]), marginally greater PEP reactivity ($t(25.39) = -1.91$, $p = .07$, 95% CI[-4.81, 0.18] and marginally greater RSA recovery ($t(29.98) = 1.76$, $p = .09$, 95% CI[-0.09, 1.14]) than infants in the mDEF group. Figure 1 depicts group differences in RSA and PEP reactivity. In sensitivity analyses removing siblings,

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the mABC group had significantly greater RSA reactivity and PEP reactivity than the control group (PEP: $t(24.69) = -2.28$, $p = .03$, 95% CI[-5.07, -0.25]), but the groups did not significantly differ on RSA recovery ($t(27.99) = 1.45$, $p = .16$, 95% CI[-0.19, 1.11]).

For primary analyses, regressions were run controlling for infant sex assigned at birth using FIML to accommodate missing data (mABC $n = 32$; mDEF $n = 32$). mABC was again associated with significantly greater RSA reactivity than receiving mDEF ($\beta = -.33$, $p = .01$, 95% CI[-0.58, -0.08]). mABC was also associated with significantly greater RSA recovery ($\beta = .35$, $p = .02$, 95% CI[0.05, 0.64]) and marginally greater PEP reactivity ($\beta = -.30$, $p = .06$, 95% CI[-0.60, 0.01]) than mDEF. In sensitivity analyses removing siblings, intervention effects on RSA reactivity and recovery became marginal, whereas intervention effects on PEP reactivity became significant ($\beta = -.34$, $p = .01$, 95% CI[-0.61, -0.07]).

Discussion

The present study provides preliminary evidence that receiving mABC promotes healthy autonomic regulation among opioid-exposed infants. Compared to a control intervention, mABC was associated with significantly greater RSA reactivity and marginally greater PEP reactivity to the Still-Face Paradigm, as well as greater RSA recovery when accommodating missing data and controlling for infant sex assigned at birth. Further, effects on PEP reactivity became significant when removing siblings. Effects were in the expected directions.

Healthy autonomic regulation among infants in the mABC group may reflect a history of effective physiological co-regulation by their parents. Additionally, given the intervention's focus on increasing parental sensitivity and nurturance and decreasing frightening behaviors, infants in the mABC group may have experienced the Still-Face episode as more surprising - and more physiologically activating - than infants in the control group. If mABC effectively

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increases parents' engagement in play, the abrupt transition to the Still-Face episode may have been especially jarring for the mABC group. Similarly, if mABC enhances nurturance to infant distress, maternal non-responsiveness to distress cues during the Still-Face episode may have been more unfamiliar for the mABC group than the control group. Finally, ABC has been found to decrease maternal withdrawal, an atypical maternal behavior associated with disorganized attachment (Hesse & Main, 2006; Lyons-Ruth et al., 1999; Lyons-Ruth & Jacobvitz, 2016; Yarger et al., 2020), so perhaps infants in the mABC group were exposed to fewer dissociative-type frightening behaviors than infants in the control group.

Previous work has demonstrated that, compared to a control intervention, receiving the ABC intervention in infancy was associated with higher resting RSA at age nine (Tabachnick et al., 2019). Although resting RSA and PEP are thought to stabilize in infancy, experiences of reactivity and recovery across infancy and early childhood may further calibrate or recalibrate parasympathetic and sympathetic tone (Quigley & Moore, 2018). For infants who consistently experience autonomic reactivity and recovery with regulatory support from their parents, it may be adaptive to increase their autonomic space (i.e., increases in resting RSA and PEP to enhance physiological capacity for dynamic reactivity). Although mABC was not associated with resting RSA or PEP in the current study, it is possible that effects on resting autonomic activity will emerge over time, following repeated experiences of naturally occurring physiological stress and subsequent regulation or recovery (or lack thereof) with their parents.

Strengths of the study include the intent-to-treat approach, and measurement of both branches of the autonomic nervous system at rest and in response to a theoretically meaningful social stressor, which is in line with current methodological recommendations and extends previous work. Further, evaluating physiological outcomes in the context of a randomized trial

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allows for causal interpretation and generates mechanistic questions for future research. The present study also complements randomized trials of other parenting programs with impacts on autonomic regulation like Family Nurture Intervention, Kangaroo Care, and others (Feldman et al., 2014; Hastings et al., 2018; Ludwig et al., 2021; Porges et al., 2019; Welch et al., 2020). Although these interventions were designed based on distinct and in some ways opposing theoretical models, evidence is mounting that early experiences with sensitive caregivers impact autonomic nervous system development.

The present study is limited in that it presents results of a pilot trial. Thus, the sample is relatively small and susceptible to noise, we could not analytically nest within families or control for factors such as treatment modality, and results cannot be interpreted as final outcomes of the intervention given that most families had not completed all intervention sessions by the time of data collection. The study is further limited by the impact of COVID-19 on the sample size and intervention modality. Thus, results should be taken as preliminary, but promising and timely.

Future research will aim to replicate these results in the full randomized clinical trial, both with a larger sample and following intervention completion. With a larger sample, it may be possible to examine the impact of factors such as treatment center, type of medication, timing of intervention initiation (pre- or post-partum), number of sessions completed, and modality (virtual vs. in person). Future studies may also examine dose effects and potential intervention effects on trajectories of autonomic development. Additional future directions include evaluating prenatal substance exposure and infant NOWS symptoms as predictors of autonomic outcomes and potential moderators of intervention effects. With this information, providers could prioritize mABC for infants most likely to benefit.

Conclusion

The present study examined the degree to which an attachment-based intervention affected autonomic nervous system activity for infants with prenatal opioid exposure. Analyses of this small pilot trial indicated that after receiving about six of twelve sessions, the mABC intervention was associated with healthier autonomic regulation during the Still-Face Paradigm than the control intervention, evidenced by significantly greater RSA reactivity and marginally greater PEP reactivity across models, in addition to significantly greater RSA recovery controlling for infant sex assigned at birth and significantly greater PEP reactivity when removing siblings. Overall, the present study provides preliminary evidence that an attachment-based intervention may improve autonomic regulation among opioid-exposed infants by empowering parents to serve as sensitive co-regulators.

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Table 1
Demographic Data and Descriptive Statistics of Study Variables

Characteristic	Overall, N = 64[1]	mABC, N = 32	mDEF, N = 32	Difference[2]	95% CI[23]	p-value[2]
Infant Race						
White	30 (48%)	18 (56%)	12 (39%)			
Multiracial	21 (33%)	8 (25%)	13 (42%)			
Black or African American	12 (19%)	6 (19%)	6 (19%)			
Infant Latino/a/x	12 (19%)	8 (25%)	4 (13%)			
Infant Sex						
Female	32 (50%)	17 (53%)	15 (47%)			
Male	32 (50%)	15 (47%)	17 (53%)			
Infant Corrected Age (Weeks)				0.76	-2.4, 3.9	0.6
N	37.00	20.00	17.00			
Mean (SD)	30.79 (4.65)	31.14 (4.84)	30.38 (4.53)			
Range	26.14, 43.29	26.14, 43.29	26.57, 39.86			
Prenatal OAT Exposure (Days)				0.81	-33, 35	>0.9
N	64.00	32.00	32.00			
Mean (SD)	221.31 (67.01)	221.72 (70.80)	220.91 (64.13)			
Range	58.00, 299.00	58.00, 299.00	64.00, 291.00			
Prenatal OAT Exposure (Proportion)				-0.01	-0.12, 0.11	>0.9

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Characteristic	Overall, N = 64[1]	mABC, N = 32	mDEF, N = 32	Difference[2]	95% CI[23]	p-value[2]
N	64.00	32.00	32.00			
Mean (SD)	0.83 (0.23)	0.83 (0.25)	0.83 (0.21)			
Range	0.21, 1.00	0.21, 1.00	0.25, 1.00			
OAT Type: Methadone	47 (73%)	24 (75%)	23 (72%)			
OAT Type: Buprenorphine	21 (33%)	12 (38%)	9 (28%)			
Mother Race						
White	49 (77%)	25 (78%)	24 (75%)			
Black or African American	10 (16%)	5 (16%)	5 (16%)			
Multiracial	5 (7.8%)	2 (6.2%)	3 (9.4%)			
Mother Latina						
No	60 (94%)	29 (91%)	31 (97%)			
Yes	3 (4.7%)	2 (6.2%)	1 (3.1%)			
Unknown	1 (1.6%)	1 (3.1%)	0 (0%)			
Mother Age (Years)				-0.18	-2.2, 1.9	0.9
N	63.00	31.00	32.00			
Mean (SD)	29.69 (4.06)	29.60 (4.23)	29.78 (3.95)			
Range	21.37, 38.30	21.37, 36.34	24.45, 38.30			
Mother Education						

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Characteristic	Overall, N = 64[1]	mABC, N = 32	mDEF, N = 32	Difference[2]	95% CI[23]	p-value[2]
High school degree or equivalent (e.g., GED)	27 (42%)	14 (44%)	13 (41%)			
Less than a high school diploma	21 (33%)	12 (38%)	9 (28%)			
Some college, no degree	10 (16%)	2 (6.2%)	8 (25%)			
Certificate from Technical School	5 (7.8%)	3 (9.4%)	2 (6.2%)			
Associate degree (e.g., AA, AS)	1 (1.6%)	1 (3.1%)	0 (0%)			
Family Income						
Less than $10,000	32 (53%)	13 (45%)	19 (61%)			
$20,000 to $34,999	12 (20%)	6 (21%)	6 (19%)			
$10,000 to $19,999	9 (15%)	7 (24%)	2 (6.5%)			
$35,000 to $49,999	5 (8.3%)	3 (10%)	2 (6.5%)			
$50,000 to $74,999	1 (1.7%)	0 (0%)	1 (3.2%)			
Over $100,000	1 (1.7%)	0 (0%)	1 (3.2%)			
Intervention Sessions Completed				0.24	-2.3, 2.8	0.9
N	34.00	17.00	17.00			
Mean (SD)	6.18 (3.55)	6.29 (3.18)	6.06 (3.98)			
Range	0.00, 12.00	0.00, 11.00	0.00, 12.00			
Intervention Modality						
In Person	22 (69%)	10 (62%)	12 (75%)			

Characteristic	Overall, N = 64[1]	mABC, N = 32	mDEF, N = 32	Difference[2]	95% CI[23]	p-value[2]
Mixed/Hybrid	7 (22%)	5 (31%)	2 (12%)			
Telehealth	3 (9.4%)	1 (6.2%)	2 (12%)			
Baseline RSA				0.13	-0.66, 0.92	0.7
N	36.00	19.00	17.00			
Mean (SD)	3.30 (1.18)	3.36 (1.42)	3.23 (0.87)			
Range	0.58, 5.65	0.58, 5.65	1.18, 4.61			
RSA Reactivity				-0.94	-1.7, -0.15	0.021
N	34.00	18.00	16.00			
Mean (SD)	-0.44 (1.23)	-0.88 (1.37)	0.06 (0.84)			
Range	-3.61, 1.37	-3.61, 0.98	-1.56, 1.37			
RSA Recovery				0.53	-0.09, 1.1	0.089
N	32.00	17.00	15.00			
Mean (SD)	0.21 (0.88)	0.45 (0.91)	-0.07 (0.78)			
Range	-2.05, 2.09	-1.48, 2.09	-2.05, 1.20			
Baseline PEP				2.5	-4.4, 9.3	0.5
N	30.00	14.00	16.00			
Mean (SD)	57.98 (9.09)	59.29 (8.58)	56.83 (9.65)			
Range	42.67, 77.33	50.67, 77.33	42.67, 76.00			

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Characteristic	Overall, N = 64[1]	mABC, N = 32	mDEF, N = 32	Difference[2]	95% CI[23]	p-value[2]
PEP Reactivity				-2.3	-4.8, 0.18	0.068
N	29.00	14.00	15.00			
Mean (SD)	-2.52 (3.40)	-3.71 (3.54)	-1.40 (2.95)			
Range	-12.00, 3.00	-12.00, 3.00	-7.00, 2.00			
PEP Recovery				-0.15	-2.9, 2.6	>0.9
N	26.00	13.00	13.00			
Mean (SD)	0.92 (3.35)	0.85 (3.83)	1.00 (2.94)			
Range	-4.00, 12.00	-3.00, 12.00	-4.00, 6.00			

[1]n (%);

[2]Welch Two Sample t-test

[3]CI = Confidence Interval

Note: P-values are provided for continuous variables, reflecting results of *t*-tests by intervention group. For categorical variables, no statistical differences were found by intervention group for infant sex ($p = .80$), infant race/ethnicity ($p = .66$), maternal education ($p = .61$), or family income ($p = .99$). More information regarding group matching can be found in the text. RSA = Respiratory sinus arrhythmia. PEP = Pre-ejection period. mABC = Modified Attachment and Biobehavioral Catch-up. mDEF = Modified Developmental Education for Families. OAT = Opioid agonist therapy.

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Table 2

Correlations of primary study variables with confidence intervals

Variable	1	2	3	4	5	6
1. Intervention						
2. Baseline RSA	.06 [-.28, .38]					
3. RSA Reactivity	-.39* [-.64, -.06]	-.15 [-.47, .20]				
4. RSA Recovery	.30 [-.05, .59]	-.13 [-.46, .23]	-.56** [-.76, -.26]			
5. Baseline PEP	.14 [-.24, .47]	.17 [-.20, .50]	-.11 [-.47, .27]	.20 [-.19, .54]		
6. PEP Reactivity	-.35 [-.63, .02]	-.08 [-.43, .30]	.30 [-.08, .60]	.05 [-.33, .41]	-.42* [-.68, -.05]	
7. PEP Recovery	-.02 [-.41, .37]	-.35 [-.65, .05]	-.03 [-.42, .36]	.10 [-.30, .47]	.02 [-.38, .41]	-.53** [-.76, -.18]

Note. M and *SD* are used to represent mean and standard deviation, respectively. Values in square brackets indicate the 95% confidence interval for each correlation. The confidence interval is a plausible range of population correlations that could have caused the sample correlation (Cumming, 2014). * indicates $p < .05$. ** indicates $p < .01$.RSA = Respiratory sinus arrhythmia. PEP = Pre-ejection period. mABC was coded as "1", and mDEF was coded as "0."

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Figure 1
Intervention effects on ANS reactivity

Note: ANS = Autonomic nervous system. RSA = Respiratory sinus arrhythmia. PEP = Pre-ejection period. mABC = Modified Attachment and Biobehavioral Catch-up. mDEF = Modified Developmental Education for Families.