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Beyond the ACE score: Examining relationships between timing of developmental adversity, relational health and developmental outcomes in children

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ABSTRACT

Background: The association between developmental adversity and children's functioning is complex, particularly given the multifaceted nature of adverse experiences. The association between the timing of experience and outcomes is underresearched and clinically under-appreciated. We examine how the timing of both adverse (including potentially traumatic) events and relational poverty are associated with developmental outcomes.
Method: Clinicians using the Neurosequential Model of Therapeutics (NMT), an approach to clinical problem solving, reported on the timing of children's developmental experiences, their degree of current relational health, and current functioning in key brain-mediated domains ($N = 3523$ 6- to 13-year-old children). A regularized hierarchical model produced stable and generalizable estimates regarding associations between the timing of experiences across four developmental periods: Perinatal (0–2 mos), Infancy (2–12 mos), Early Childhood (13 mos to 4 years), and Childhood (4 to 11 years) and current functioning.
Results: Perinatal developmental experiences were more strongly associated with compromised current functioning than such experiences occurring during other periods. Perinatal relational poverty was a stronger predictor than perinatal adversity. During subsequent developmental periods, the influence of relational poverty diminished, while the influence of adversity remained strong throughout early childhood. Current relational health, however, was the strongest predictor of functioning.
Conclusion: Findings expand the understanding of the association between the timing of adversity and relationally impoverished experiences and children's functioning. Although early life experiences are significantly impactful, relationally enriched environments may buffer these effects.

Introduction

In 1998, a landmark epidemiological study, the Adverse Childhood Experiences (ACEs) Study, was published (Felitti et al., 1998). While associations between maltreatment in childhood and a range of detrimental outcomes were well known in clinical and academic communities, the ACE study helped to catalyze a broader public and systemic awareness of the detrimental impact of 'adversity' on physical health, mental health, social functioning, health risk behaviors, and life expectancy. Awareness of "ACEs" has been a central component of 'trauma-informed' policy, program development and practice changes. Screening for childhood adversity, often using the 10–12 question ACE inventory, is more prevalent now than a decade ago, across a wide range of human service providers (Burke Harris, Silvério Marques, Oh, Bucci, & Cloutier, 2017). One of the features of the ACE study that makes public engagement effective is the simplicity and clarity of the dose-dependent correlations seen between the number of adversities in childhood and risk for negative outcomes in adult life (Anda et al., 2006). This simplicity, however, can lead to misunderstanding. Correlation and causality become conflated as ACE 'awareness' spreads into

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non-academic and lay audiences, including those making practice, program and policy decisions in child-serving systems (e.g., medical, education, social services, mental health). Public awareness about the potential impact of adversity and trauma on development is important, yet knowing that these matter is only the first step in the informed creation of programs, practice and policy to address the physical, social and emotional morbidity associated with developmental adversity.

A primary challenge is that human development is not simple; the current emotional, social, cognitive and physiological functioning of each individual is influenced by myriad factors ranging from genetics to developmental experiences and context. Clinically relevant questions persist regarding the ways in which developmental experience shapes functional outcomes. Going beyond the ACE score is essential to inform practice, programs and incorporate what is known about: 1) the timing of adversity; 2) the pattern of developmental stress and distress; and 3) the presence of attenuating and resilience-related factors. Further, it is imperative to continue more granular examinations of the complex effects of development on experience.

Babies are born experience-dependent. They require developmental experience to express underlying genetic potentials in all brain-mediated domains of functioning. Decades of research indicate that disruptions in typical development are associated with negative experiences such as chronic (Felitti et al., 1998) or severe (Jackson, Gabrielli, Fleming, Tunno, & Makanui, 2014) trauma and adversity (henceforth adversity), and with a range of negative outcomes, including behavioral, emotional, social, and cognitive (Bos, Fox, Zeanah, & Nelson, 2009; McDermott et al., 2013; Schatz, Smith, Borkowski, Whitman, & Keogh, 2008). In contrast, attentive attuned and responsive caregiving paired with cognitive and social enrichment is associated with positive outcomes in these domains (Masten & Coatsworth, 1998). Similarly, positive relationships, or social support, appear to buffer the effects of developmental adversity (Dai et al., 2016; Ludy-Dobson & Perry, 2010). Yet, the complexities of development, the timing, nature and pattern of adversity, the relational context in which adversity is experienced, and the heterogeneity of responses to adversity create theoretical and methodological challenges to understanding the myriad effects of developmental adversity.

Developmental psychopathology suggests that multiple dimensions of adversity, including type, timing, severity, frequency, chronicity, and the child's developmental status when the adversity occurs, are interrelated and uniquely meaningful for developmental outcomes (Cicchetti & Toth, 1995; Claessens et al., 2011). An infant whose caregivers are not attuned and attentive, but instead unpredictable or even threatening in their response to their child's cries during the first year after birth may have significantly different outcomes than an adolescent who is sexually abused by a stranger, but otherwise lives (and has lived) in a relationally-enriched environment. Though there are multiple dimensions of adverse experiences, timing appears to be a key – and under-researched – dimension that may influence the types of adverse experiences most likely to disrupt typical developmental trajectories, and the types of positive experiences most likely to promote optimal development.

Organizational theories of development suggest that children's current functioning is highly influenced by experiences during early developmental periods (Perry, 2001; Sroufe & Rutter, 1984). Developmental trajectories negatively impacted by adversity in early life jeopardize functions emerging later in life that will be constructed on these poorly organized developmental systems (Dunn, Nishimi, Powers, & Bradley, 2017). Consequently, experiences occurring early in life, particularly during the first year, can be devastating or protective (Schore, 2001). Evidence for this is seen in both animal and human research. Studies examining grooming behaviors of mouse and rat dams toward their pups suggest that maternal behaviors (licking/grooming and arched-back nursing) in the first weeks of a pup's life can alter pup DNA expression (Bedrosian, Quayle, Novaresi, & Gage, 2018; McGowan et al., 2009). Studies of institutionalized children are perhaps the most recognizable examples of the idea that early adversity, characterized by a profound lack of developmentally stimulating experience in the first year(s) of life, can have a lasting impact in cognitive, affective, and social/emotional domains (McDermott et al., 2013; Zeanah, Smyke, Koga, Carlson, & The Bucharest Early Intervention Project Core Group, 2005).

The notion that the timing of developmental experience matters is not new. Studies show that child maltreatment occurring during the first few years of life is associated with the severity of internalizing and externalizing problems during middle childhood (Manly, Kim, Rogosch, & Cicchetti, 2001). Adversity during the first five years of life is more predictive of maladaptive outcomes during adulthood, including risk for depressive or posttraumatic stress disorders (Dunn et al., 2017) and the severity of posttraumatic stress disorders (Ogle, Rubin, & Siegler, 2013), than is adversity occurring later in life.

There are, however, limitations to the available research on the timing of adversity. On one hand, the examination of timing has not been fine-grained, especially with regard to experiences very early in life. This is problematic because the rate of development is greatest during the first few months of life, sharply declining as a child ages in a logarithmic fashion (Johnson, 2001). Research collapsing trauma occurring during the first five or even three years of life still yields imprecise results regarding exactly when exposure to adversity or lack of developmentally positive experiences is most detrimental. Clearly, adversity during any developmental period can be detrimental, including adolescence (Crane & Clements, 2005), another time of rapid organizational change in the brain (Paus, 2005). Little research has been conducted on the relative impact of adversity or relational poverty during the first months of life compared to adversity occurring during later developmental periods. As such, it is unclear, for example, how the outcomes of children whose adversity occurs later in childhood, but not during infancy, compares to children whose adversity occurs during infancy, but not later in childhood.

The timing of relationally healthy experiences may also have implications for children's functioning due to the relative importance of certain types of positive caregiving experiences during infancy as opposed to childhood. The first few years of life are sensitive periods for children's acquisition of healthy attachment relationships (Zeanah, Smyke, Koga, & Carlson, 2005). Children require consistent, patterned, nurturing experiences with caregivers to form relationships that serve as templates for psychosocial functioning throughout development. Moreover, attuned caregiving during infancy provides the context in which affiliative, self-regulatory and ultimately higher-order cognitive capacities, such as the ability to plan, reason, and judge, form.

Not only can a lack of relational health, (i.e., 'connectedness'; essentially the presence of attuned caregivers, family members, mentors, teachers, and community members), itself be considered adversity, but when trauma occurs in the context of relational poverty, or an overall lack of attachment or otherwise meaningfully supportive relationships, the negative consequences for children can be amplified. Conversely, the effects of adversity are likely attenuated in relationally-rich environments. One study linking the severity of childhood maltreatment to the severity of posttraumatic stress symptoms (PTSS) in adulthood (Evans, Steel, & DiLillo, 2013) found that high levels of perceived familial social support buffered the development of PTSS among those whose maltreatment severity was low or moderate. A study examining social support among inner-city adult victims of interpersonal trauma found that high levels of social support buffered the "cumulative impact" of interpersonal victimization occurring in both childhood and adulthood (Schumm, Briggs-Phillips, & Hobfoll, 2006). The association between exposure to adversity and mental and physical health problems in adulthood is attenuated when individuals report having at least one consistently available adult throughout childhood (Bellis et al., 2017).

Outcomes typically explored when examining how and when adversity may pose risk include DSM diagnoses, or derivatives of common

diagnoses, such as "internalizing and externalizing problems" (Dunn et al., 2017; Ogle et al., 2013). While there is nothing inherently wrong with either approach, adversity notably leads to heterogeneous outcomes (Toth & Cicchetti, 2013). Reliance on any one diagnostic category or symptom subset may restrict identification of the various ways that trauma, adversity, and relational poverty influence development. Study of these complexities in human populations requires very large samples.

To explore these issues, a large dataset collected for clinical purposes by clinicians using the Neurosequential Model of Therapeutics (NMT) was utilized (Perry, 2009; Perry & Dobson, 2013; Perry & Hambrick, 2008). The NMT examines the nature, timing and severity of both adverse experiences (AE) and relational health (RH), as well as a child's current functioning in multiple central nervous system-mediated developmental domains (e.g., clinician-rated sleep, arousal, concrete cognition) and the current degree of "connectedness" (Section 0 contains description about the NMT & NMT Metrics). Given the specifications of AE and RH clinicians provide across several developmental stages, and the number of metrics available (approximately 30,000), this dataset provided a unique opportunity to evaluate associations between the timing of developmental experience and current functioning.

We hypothesized that profound AE occurring perinatally (0 to 2 months) and during infancy (2 to 12 months) would account for more variance in the current functioning of 6- to 13-year-olds than profound AE occurring during early childhood (13 months to 4 years) or childhood (4 to 11 years). Further, we predicted that a profound lack of RH would be most detrimental during the perinatal period than during any other period, a time when a child's optimal growth and development are heavily reliant on external regulation and touch (Beeghly, Perry, & Tronick, 2016). On the other hand, we expected profound AE to be highly detrimental during infancy and early childhood - a time when children become more capable of discerning stressors in their environment, yet are still forming the foundations for emerging developmental capacities.

Method

Study design

Data collected by clinicians using the Clinical Practice Tools (NMT Metrics, see Measures section) associated with the NMT (Perry, 2009), were used. De-identified NMT Metric data were downloaded from the web-based repository of data tracked by the ChildTrauma Academy (NMT developers) as part of their quality improvement initiatives. The Institutional Review Board at the (blinded for review) deemed this study "Not Human Subjects Research." Below is a brief description of the NMT to contextualize the data.

The NMT is an approach to clinical problem solving that allows clinicians to catalogue the child's developmental history and current functioning using the web-based Clinical Practice Tools (NMT Metrics). The output report provides clinicians with information for intervention planning including: 1) historical and current Adverse Experiences, Relational Health and Developmental Risk; 2) current central nervous system functioning; and, 3) five functional domains of sensory integration, self-regulation, relational, cognitive, and cortical modulation ratio. The NMT has been named an "emerging practice" by the National Quality Improvement Center for Adoption/Guardianship Support and Preservation (QIC-AG.org). More information on the NMT and the use of the Metrics has been detailed in previous publications (Perry, 2014; Perry & Hambrick, 2008).

To complete the metrics, clinicians must report on the timing, severity, and type of a child's AE across several developmental periods, from the prenatal period through the current age of the index client being assessed. The developmental periods relevant to this study are: Perinatal (birth to two months), Infancy (2 to 12 months), Early Childhood (13 months to 4 years), Childhood (4 to 11 years). Clinicians then report on the quality of RH in like manner. These developmental periods are not exhaustive, but were selected by NMT developers to balance two objectives: 1) ease of clinician Metric use (if clinicians cannot complete Metrics efficiently, the metrics will likely go unused), and 2) age groups that allow for the most specificity during very early development (i.e., the first three years of life), when child development proceeds almost logrithmically (Johnson, 2001).

Next, clinicians report on a child's current functioning in 32 brain- or CNS-mediated domains, spanning self-regulatory, cognitive, relational, and sensorimotor functioning. These domains are subsumed under the broad category "CNS Functioning". Clinicians are provided with extensive training in metric use throughout the certification process (Phase I certification is approximately 150 h). NMT Trainers from the ChildTrauma Academy conduct biannual Fidelity Exercises, where Metric users are given hypothetical case-based data with which to complete the metrics. Clinician performance in the Fidelity Exercise yields a fidelity rating of None, Low, Acceptable, or High. This fidelity rating is a reflection of the degree of interrater reliability between the clinician and NMT developers. Clinicians whose metrics were included in this study were NMT Phase I Certified or in advanced stages of completing this certification process, and had achieved a rating of "acceptable" or "high" in the Fidelity exercises during the period of time from which study metrics were completed and included.

Participants

For this study, NMT Metric data from 3523 children ages 6 to 13 years old seeking behavioral health services with histories of developmental adversity were analyzed. Descriptive data regarding gender and race/ethnicity are in Table 1. Data were collected from clinicians across 190 diverse clinical "sites" across the US, Canada, Europe, and Australia. Because both sites and individuals can be certified in the NMT, the majority of the "sites" (approximately 100) were a single clinician, while other sites contained ratings from many clinicians. Each site provides their estimated ratio of client settings to the NMT developers. Most sites are primarily outpatient, while some are a mixture of outpatient and residential/inpatient. One site was comprised of metrics completed by the NMT developers. At all sites, a percentage

Table 1
Descriptives.

	Typical sample
CNS Functioning (M, SD)	297.09 (41.19)
N	425
	Clinical sample
CNS Functioning (M, SD)	231.53 (39.63)
Female (%)	33.6
White (%)	42.1
Asian (%)	1.2
Black (%)	15.7
Hispanic (%)	7.6
Native American (%)	1.6
Other (%)	16.0
N	3834

Note. CNS = central nervous system. Typical CNS Functioning scores were obtained from metrics completed on children and youth well known to the clinician who have no obvious or known cognitive, mental, social or motor problem requiring 'clinical' intervention. As part of the NMT certification process, clinicians are asked to complete metrics on "typical" individuals to learn how to navigate the web-based app, and learn more about the items and anchors of the metrics. "Typical" children, youth and adults may have had some developmental adversity.

of patients were child welfare involved, ranging from 10 to 100%. Exact clinician characteristics are unknown. However, all NMT-certificated clinicians must have a masters degree in a relevant clinical discipline (e.g., nursing, social work, educational psychology, psychology) and have an active license. Approximately 80% of NMT clinicians have masters degrees, while the remainder have more advanced (e.g, Ph.D., Psy.D., DNP, M.D.) degrees. The NMT certification process is 150 h long and includes specific training on how to understand the Part C (CNS functioning) descriptors and anchors used to score various CNS-mediated functions.

Measures

NMT Metrics

The NMT Metrics are divided into four parts: Part A (Developmental Adversity; AE), Part B (Developmental Relational Health; RH), Part C (Central Nervous System (CNS) Functioning: Current), and Part D (Current Relational Health). Although the metrics are only completed by clinicians, clinicians are instructed to use information from clinical interviews, child welfare case files, observations of child/family, medical records, psychosocial assessments, etc. while completing them.

In Part A (AE), clinicians report whether a child experienced a range of potentially traumatic and/or adverse experiences during the following periods: Perinatal (0 to 2 months), Infancy (2 to 12 months), Early Childhood (13 months to four years), and Childhood (4 to 11 years). The six experiences assessed per developmental period are quality of primary caregiving, caregiver drug/alcohol use, neglect, domestic violence, transitions/chaos and "other trauma (e.g., natural disaster, gun violence)." Clinicians rate the severity of each experience from 1 to 12, ranging from None/Minimal (1–3), Mild (4–6), Moderate (7–9), to Severe (10 − 12). When clinicians are uncertain about a child's experience, they are instructed to provide a "neutral" score (6 or 7), use clinical reconstruction to estimate if the score should be marked up (more severe) or down (less severe) by a few points given what is known about the overall nature of the child's early experiences, and ultimately to underestimate the potential risk. Given these scoring instructions, scores falling in the range of 10 to 12 are highly likely to reflect documented, profoundly severe adversities.

In Part B (RH), clinicians report on the quality of a child's relationships across the same developmental periods. The six experiences assessed per period are primary caregiver safety, primary caregiver attunement, consistency in primary caregiving, paternal (or partner) support, kinship support, and community support on a scale of 1–12 from Poor (1–3), Episodic (4–6), Adequate (7–9), to Positive (10–12). These items are meant to assess quality of caregiving and overall "social support" but also, particularly in early developmental periods, risk for attachment disruption. The same scoring instructions are used to complete Parts A (AE) and Part B (RH). Part B scores ranging from 1 to 3 are likely to indicate profound absence of RH. Although some items in the Part A and Part B scales are similar, clinicians use a different lens when completing each section. In Part A, they are indicating adversities, where in Part B, they are indicating poverty or strength in a child's relational health. Moreover, Part A is scored with a "deficits-based" view, and Part B with a "strengths-" or "lack of strengths"-based view.

Part C (CNS Functioning: Current) is clinician rating of a child's capabilities across several brain-mediated developmental functions spanning from basic autonomic regulation, such as cardiovascular regulation (heart rate), to sleep, feeding/appetite, fine motor skills, affect regulation, relational skills, arousal, ability to modulate reactivity/inhibit impulsivity, and abstract/reflective thinking skills. The rating clinicians are asked to review (when possible) medical records, and in gathering history from caregivers to ask about known medical conditions. In addition, many of the NMT-certified clinicians – particularly nurses and other medical professionals - obtain heart rate, heart rate variability and blood pressure data as part of their routine clinic visits. In addition, there are specific scoring "rules" that clinicians learn, such that clinicians should assume 'typical' cardiovascular regulation unless they obtain history or data that suggests otherwise. Clinicians rate whether a child's capabilities are "age typical" or whether they fall above or below age typical on the 32 items comprising the CNS Functioning checklist on a scale of 1–12, where 1–3 = Severe Dysfunction, 4–6 = Moderate Dysfunction, 7–9 = Mild Dysfunction, and 10–12 = Normal Range (for a fully-functioning adult).

The highest possible CNS Functioning score is 384, which represents the capacity of a "typical" adult. This score should not be interpreted like an IQ score. Instead, a score of 384 indicates a general lack of dysfunction in the measured brain-mediated capacities. As part of the NMT certification process, clinicians are asked to complete metrics on "typical" children and adults to learn how to navigate the web-based app, and to learn more about the items and anchors of the metrics. "Typical" children and adults may have had some developmental adversity; the selection of "typical" is based upon the clinician's impression that this individual's current functioning is within a non-clinical range. This set of typical metrics ($N = 1035$) provides a type of normative sample against which clinical scores can be compared.

Part D (Current RH) is clinician rating of the quality of a child's current relational context across nine different domains, including primary caregivers, siblings, extended family, school, peers, and community. Clinicians rate the quality of each of the child's current relational experiences from Poor (1–3), Episodic (4–6), Adequate (7–9) to Positive (10–12). Then, these nine items are summed to create a total Current RH score.

Evidence for the validity and reliability of the NMT metrics include the following. In a sample of children with fetal alcohol spectrum disorders, improvements in CNS Functioning following six months of NMT-guided intervention coincided with improvements in scores on the Battelle Developmental Inventory – 2nd Ed (BDI-2) and the Parenting Stress Inventory (PSI) (Zarnegar, Hambrick, Perry, Azen, & Peterson, 2016). The correlation between the BDI-2 and Part C (CNS Functioning) was 0.67 and the PSI and Part C was −0.38. Significant associations between Part C items and the Trauma Symptom Checklist for Young Children Posttraumatic Stress Total score include arousal ($r = -0.408$) and child ability to modulate reactivity/inhibit impulsivity ($r = -0.390$) (Jackson, Frederico, Hameed, Cox, & Kascamanidis, 2016). In an analysis using a subsample of the current dataset comprised of primarily child-welfare involved children, Cronbach's α was 0.95 for Part C, and was 0.84 for Part D (Hambrick, Brawner, & Perry, 2018).

In the current study, evidence of NMT Metric reliability include the following. Cronbach's α was 0.95 for Part C (CNS Functioning), and was 0.85 for Part D (Current RH). Cronbach's α was not computed for AE and RH scores, as this is an inappropriate statistic when an endorsement of one item does not necessarily increase the likelihood of an endorsement on other items (Bollen & Bauldry, 2011). In the statistical models, site bias of CNS Functioning ratings was roughly normally distributed around and statistically indistinguishable from the NMT developers' ratings (Fig. 1).

Data analysis

To create statistical indicators likely to represent documented occurrences of severe, profound adversity (AE) and relational poverty (RH), variables were created to indicate the number of experiences rated 10–12 (AE) or 1–3 (RH) per child, within each developmental period. Thus, ordinal variables were created for Perinatal – AE Severity (range 0–6, given that 6 possible adversities are assessed per developmental period), Perinatal – RH Severity (range 0–6), and so forth. These AE and RH severity scores, per developmental period, were independent variables. Part C scores were summed to create a broad indicator of a child's current developmental functioning, hereafter called CNS Functioning. The CNS Functioning score was our dependent variable. Part D scores were also summed to create a broad indicator of a

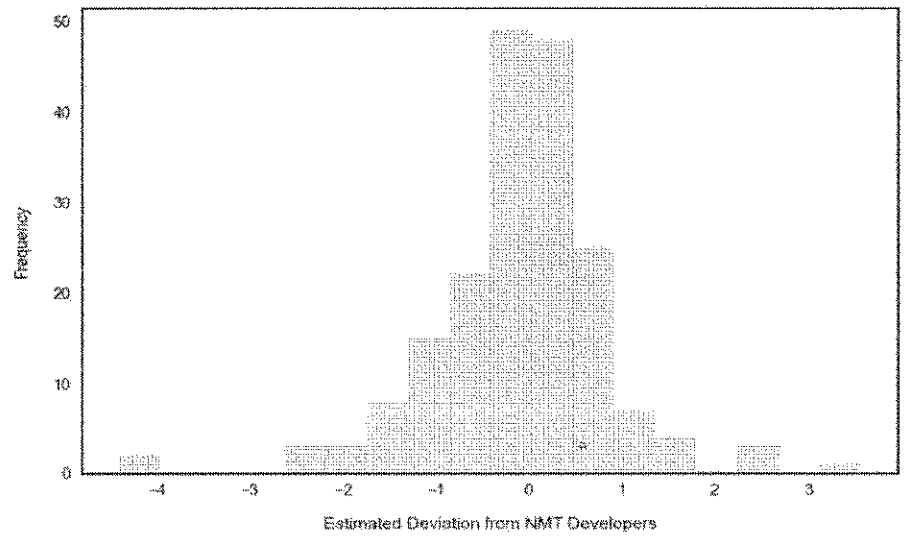

Fig. 1. Site bias in CNS Functioning scores.
Note. Distribution of the site intercepts in the regularized hierarchical model for the site indicators, where NMT developers are the reference category. Values represent deviations from the reference category in CNS Functioning scores.

child's current degree of RH. This score was also used as an independent variable.

We further controlled for degree of severity of intrauterine substance abuse (on a scale from 1 to 12, with 12 indicating the highest level of intrauterine substance use/abuse, and scores falling between 10 and 12 identified as "severe"). When completing Parts A (AE) and B (RH), clinicians are also asked to rate intrauterine experiences. Given the low degree of clinician-rated "confidence" in most intrauterine scores (other than the Part A item assessing degree of substance use/abuse), this was the only item that was included from the Part A intrauterine scale. Other controls included demographic attributes, including age (months), a binary indicator of gender (female = 1), binary indicators of race/ethnicity, and binary indicators for the 190 sites.

We also control for the "age category" a child was in (6 to 7 years, 8 to 10 years, and 11 to 13 years) at the time a Metric was completed. To promote ease of Metric use, clinicians are provided a different reference for what a "typical" score is expected to be on a given Part C (Current CNS Functioning) item per age category. Age category demarcations were roughly determined by considering the rate at which children's developmental functions are likely to change in a variety of CNS-mediated domains (e.g., most rapidly early in life, Johnson, 2001). Given this changing reference point per age category, we control for the scoring bias these reference points create. We restricted our analysis to children who were in these three age categories (6–7, 8–10, 11–13) at the time of Metric completion given that children in these three age categories all had the same developmental information (i.e., information regarding their experiences during the perinatal, infancy, early childhood, and childhood periods).

The analysis features a hierarchical linear model of CNS Functioning as a function of AE and RH severity scores for each of the developmental periods, and current RH. An important feature of the data is the correlation among the AE and RH scores, which produces a concern for collinearity. This collinearity is not surprising, because a child who lives in a chaotic, unpredictable, relationally depleted environment early in life is likely to live in a similar environment later in life. As evidence of this, the condition number, capturing the ratio of the largest and smallest eigenvalues in a matrix decomposition of the model inputs, was 22.69, indicative of unstable regression coefficients (Fox, 2008). To address this, we introduce a ridge penalty. Ridge regularization is commonly employed to reduce variance due to collinearity and improve the quality of inferences (Hastie, Tibshirani, & Friedman, 2016). In addition, in coordination with cross-validation, regularization helps prevent overfitting (Type I Errors). The value of the regularization parameter is chosen via generalized cross-validation.

The hierarchical component of the model is due to the nesting of individual observations within sites, among which we expect to observe variation. In the language of Gelman and Hill (2007), a linear model with no regularization and with estimated intercepts for each site is a hierarchical model with no pooling of the site intercepts. Such a model often inflates the estimated differences among sites, and Gelman and Hill instead suggest partial pooling of the intercepts, where site effects are assumed to follow a Normal distribution centered at zero. In our case, because linear regression with ridge regularization is equivalent to Bayesian regression with regularizing Gaussian priors, the model presented below is a hierarchical linear model with partial pooling of the site intercepts.

There are two consequences of regularization relevant for interpretation of regression estimates. First, analytical standard errors are not available, and therefore we evaluate uncertainty in the coefficient estimates using 95% accelerated bootstrap confidence intervals (Efron, 1987). Second, to penalize the terms in the model equally, all independent variables (IVs) are standardized to the same scale. Namely, unit changes in the standardized IVs correspond to one standard deviation, and estimates should be interpreted as the expected change in CNS Functioning due to a change of one standard deviation in the IV in question.

Results

Mean CNS Functioning was identified (Table 1). CNS Functioning scores in the clinical sample is presented alongside scores in age-matched typical peers, and indicate that clinical sample scores are approximately 2 SDs lower than typical scores. Descriptive statistics and bivariate correlations between predictors are in Table 2, and indicate correlations between most predictors.

Results from the Ridge Regression Model, assessing the association between severity of AE and RH per developmental period and CNS Functioning, indicated several significant associations (Table 3). A child's current degree of RH was the most significant indicator of a child's current CNS Functioning. The next strongest associations were RH and AE Severity scores, respectively, during the Perinatal period. AE Severity scores remained significant in Infancy and Early Childhood. RH Severity scores were only significant during the Perinatal period, and the AE score was no longer significant in Childhood.

Table 2
Bivariate Spearman correlations between predictor variables.

	M (SD)	CNS Functioning	Current relational health	Intrauterine drug abuse	AE Severity (Perinatal)	RH Severity (Perinatal)	AE Severity (Infancy)	RH Severity (Infancy)	RH Severity (Early childhood)	RH Severity (Early childhood)	AE Severity (Childhood)
CNS Functioning	231.53 (39.64)	–	–	–	–	–	–	–	–	–	–
Current relational health	59.14 (15.73)	0.338	–	–	–	–	–	–	–	–	–
Intrauterine drug abuse	0.216 (0.41)	−0.073	0.002	–	–	–	–	–	–	–	–
Perinatal - AE	0.944 (1.44)	−0.167	−0.013	0.446	–	–	–	–	–	–	–
Perinatal - RH	1.490 (1.70)	−0.196	−0.087	0.301	0.517	–	–	–	–	–	–
Infancy - AE	0.980 (1.54)	−0.171	−0.023	0.345	0.664	0.444	–	–	–	–	–
Infancy - RH	1.397 (1.63)	−0.175	−0.109	0.23	0.46	0.765	0.525	–	–	–	–
Early childhood - AE	1.181 (1.63)	−0.133	−0.111	0.197	0.372	0.252	0.5	0.341	–	–	–
Early childhood - RH	1.32 (1.6)	−0.136	−0.214	0.125	0.254	0.464	0.331	0.605	0.537	–	–
Childhood - AE	1.012 (1.50)	−0.01	−0.217	0.007	0.115	0.028	0.152	0.092	0.359	0.225	–
Childhood - RH	0.883 (1.23)	−0.117	−0.374	0.022	0.055	0.19	0.079	0.251	0.208	0.418	0.0382

Note. AE (adverse experiences) and RH (relational health) scores are ordinal indicators of the number of adversity or relational health indicators within the "severe" or "poor," respectively, range.

Table 3
Hierarchical Ridge Regression Model: Severity of adversity and relational poverty per developmental period and CNS Functioning.

	Estimate	Confidence interval
Intrauterine drug/alcohol	−0.204	[−1.232 0.823]
Current relational health	**13.149**	**[12.083 - 14.152]**
Perinatal – AE	**−2.314**	**[−3.735 −0.96]**
Perinatal – RH	**−3.455**	**[−4.77 −2.235]**
Infancy – AE	**−3.28**	**[−4.687 −1.873]**
Infancy – RH	0.24	[−1.099 1.544]
Early childhood – AE	**−2.116**	**[−3.28 −1.081]**
Early childhood – RH	0.3171	[−0.86 1.563]
Childhood – AE	0.943	[−0.063 1.937]
Childhood – RH	−0.435	[−1.476 0.636]
Age in months	6.747	[5.663 7.933]
Female	2.489	[1.556 3.514]
Asian	−0.287	[−1.468 0.906]
Black	−0.51	[−1.532 0.422]
Hispanic	−0.145	[−1.101 0.9]
Native American	−0.857	[−1.897 0.199]
Other	0.293	[−0.645 1.2749]
Age category 8 to 10	2.746	[1.787 3.814]
Age category 11 to 13	5.587	[4.427 6.722]

Note. CNS = central nervous system. AE (adverse experiences) and RH (relational health) scores are ordinal indicators of the number of adversity or relational health indicators within the "severe" or "poor," respectively, range. Site indicators are not represented here for brevity (190 site indicators), though their distribution is shown in Fig. 1. For ethnic/racial indicators, White is the reference category. For age category indicators, 6 to 7-year-olds are the reference category. Bolded are statistically significant findings.

To visually represent the potential functional impact of the major findings regarding the timing of negative developmental experiences, Fig. 2 shows a nonparametric local regression of the predicted developmental trajectory in CNS Functioning over time (0 to 18 years) across three groups: children with scores ranging from four to six on the AE Severity Perinatal variable but not the RH Severity Perinatal variable and vice-versa, and then children in the typical sample. Fig. 2 shows a widening gap over time in CNS scores for the typical and clinical samples, or evidence of a "developmental lag" that continues to widen over time in children with early life adversity – be it nodal adversities or lack of relational health.

Discussion

Previous research indicates that the timing of adversity likely matters for children's mental health, developmental, and psychosocial outcomes (Dunn et al., 2017). Yet, the association between timing and child outcomes has yet to be examined in a fine-grained manner. This study sought to promote a deeper appreciation of the complex association between the timing of adverse and relationally impoverished experiences and children's current functioning in 32 brain-mediated domains. Adversity and relationally healthy experiences throughout four developmental stages spanning from perinatal (birth to two months) to childhood (4 to 11 years) and children's current functioning were reported by clinicians using the NMT Metrics. We sought to determine the relative impact of adverse (AE) and relationally impoverished (RH) experiences on current functioning across these four developmental periods.

We found that children in our clinical sample had CNS Functioning scores significantly below the scores seen in age-matched samples of typically developing children (Table 1). This is not surprising, but perhaps a sobering realization of just how far from typical functioning significantly trauma-exposed children can, collectively, appear. Bivariate correlations showed correlations across predictors (Table 2). This was also unsurprising, given that children who live in chaotic, unpredictable, and relationally impoverished environments during the first months or year of life are likely to remain in such settings unless caregivers change significantly and/or the child is removed from their home and placed in a setting with quality caregivers. Therefore, these correlations across predictors identified a need to use regularized regression models to help determine which predictors, when considered together, were most influential for outcomes.

Results from the regularized regression indicated that a child's degree of current RH was the strongest predictor of outcomes (Table 3). This finding is consistent with a previous study conducted with a subset of the NMT Metric data comprised of child-welfare involved youth. This may be because many children entering therapy have been removed

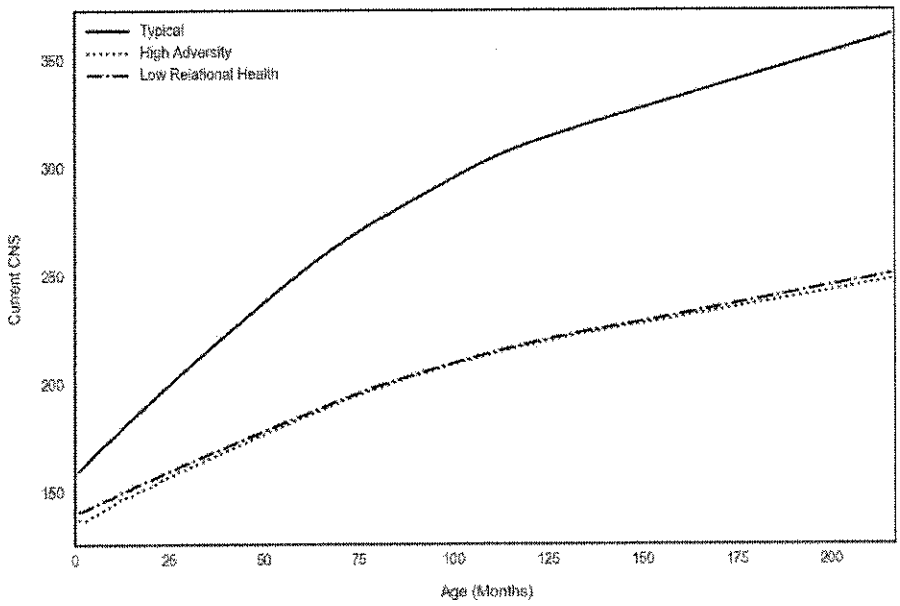

Fig. 2. Nonparametric Local Regression: Predicted trajectories of CNS Functioning given perinatal adversity and relational health.
Note. The High Adversity group is comprised of children across all age categories in the NMT Metric database ages 0 to 216 months (comprised of metrics of raters with "Acceptable" or "High" fidelity, $N = 15{,}140$) with scores ranging from four to six on the AE (adverse experiences) severity variable during the perinatal period (0 to 2 months), but not on the RH (relational health) severity variable during the perinatal period ($n = 1433$). The Low RH group is the opposite ($n = 2440$). The Typical group is comprised of individuals whom clinicians have deemed to have "typical" functioning on whom they completed metrics. "Typical" children and adults may have had some developmental adversity; the selection of "typical" is based upon the clinician's impression that this individual's current functioning is within a non-clinical range ($n = 945$).

from relationally impoverished environments, and their current more relationally positive context may be promoting their growth or providing a regulating environment. Impressively, despite children's adversity histories, RH later in life may have meaningful implications for functioning. Theories of developmental psychopathology posit that not only what happened matters, but the context in which it occurs matters (Cicchetti & Toth, 1995; Ludy-Dobson & Perry, 2010). Indeed, the relational context in which trauma occurs as well as the quality of subsequent relational environments may have powerful implications for children (Schumm et al., 2006). While this finding may provide a message of hope regarding ways to remediate developmental trauma, the current RH variable may be a proxy for several unmeasured variables, including a child's degree of relational adeptness, or their lack of behavioral concerns that make them easily relatable.

Despite the strength of the current RH finding, several of the indicators of developmental experience also evidenced strong associations with a child's degree of functioning. Both severe AE and extremely poor RH during the perinatal period were most strongly associated with negative outcomes, consistent with organizational theories of development (Cicchetti & Toth, 1995; Perry, 2001; Tronick & Perry, 2015) and research suggesting that the brain is most plastic during the few weeks following birth (Ishii et al., 2015; Paredes et al., 2016). Interestingly, severity of RH during the perinatal period was a stronger predictor of negative outcomes than severity of AE, the predictor variable that we used that is most similar to traditionally-utilized scales of "adverse childhood experiences." This suggests that the context and quality of early experiences (somatosensory, interactional, attunement, affective, safety, etc.) have a profound influence on subsequent development in multiple domains. The dependence of newborns on consistent, predictable caregivers to provide basic physical and emotional needs and thereby shape their developing stress response capabilities may contribute to this strong finding (Beeghly et al., 2016; Brandt, 2008). Although potentially traumatic events, such as domestic violence, are also impactful during this time, it is important to reflect on which developmental capacities are forming at a given time in development, and how these might dictate which types of experiences are most impactful. Newborns settle into their developmental context and are fully dependent on caregivers to regulate their temperature, relieve hunger, help regulate them, and soothe their primitive stress response systems. As a result, systems involved in reward, pleasure, safety, hunger, satiety, thermoregulation, transitions, organization of motor systems, state regulation, etc. are under development, and highly sensitive to and influenced by early experiences.

Following the perinatal period, the association between RH and outcomes significantly diminishes. This is not to say that connectedness does not continue to matter; indeed, we see that strong RH in a child's current environment matters greatly. Yet, holding all else equal – AE seem to take over in importance as a child ages, particularly in infancy and early childhood. The finding that AE are strong predictors of outcomes up until four years of age also fits with current understandings of the role of early life experiences in influencing outcomes. Infants are building a relational template that helps them determine if people are ultimately trustworthy and are working to determine if their world is safe (Narayan, Rivera, Bernstein, Harris, & Lieberman, 2018). Receipt of consistent messages that they are not safe during this sensitive developmental phase may result in significant neurodevelopmental alterations in attachment and in stress response systems that can have persistent implications.

We see evidence of this persistence, or what we informally call a "developmental echo" or lag in the current analysis. The idea that once a child is moved off of a typical developmental trajectory, they tend to appear further and further from age typical with time is not new (Font & Berger, 2015). A visual indication of this developmental echo is seen in Fig. 2, where we plot expected CNS Functioning over time in the sample of typical children, (ages 0 to 18) and in children whose perinatal experience included either significant AH or significant RH, and see an increasingly widening gap.

In sum, the current results are consistent with what researchers and clinicians have largely assumed: that early developmental experiences have a significant impact on development. Yet, the relatively more powerful impact of developmental disruptions in connectedness and adversity in the first two months of life is a striking finding with significant practice and policy implications. Other studies examining, for example, the impact of extreme early-life deprivation during the first three years of life have noted that deficits can persist into adulthood (Sonuga-Barke et al., 2017). And, emerging research also suggests that positive relational experiences, such as perceived family, peer, school, and community support, may buffer negative outcomes (Saeri, Cruwys, Barlow, Stronge, & Sibley, 2018; Sege et al., 2017).

Study strengths, limitations, and future research directions

Results must be interpreted in light of study strengths and limitations. One limitation was reliance on clinician report. Clinicians likely varied in the degree and quality of information available to them regarding a child's life experiences. Some clinicians may not have had

access to either child welfare records or a reliable reporter of the child's history. Use of retrospective reports of developmental histories in the study of how trauma influences functioning is a debated practice (Greenhoot, 2013) given that retrospective reports often differ from actuarial reports (Hambrick, Tunno, Gabrielli, Jackson, & Belz, 2014). Yet, aspects of NMT training may have mitigated the impact of retrospection on the current study.

Clinicians using the NMT Metrics have completed over 150 h of training, and have passed fidelity exercises to demonstrate competence and inter-rater reliability with these tools. When scoring, they are instructed to use all evidence available to them, including multiple reporters, case files, psychological assessments, and medical records. Allowing clinicians to use all information available to them may be a useful way to obtain the fullest picture possible about a child's developmental experience. Additionally, the scoring schema is designed to accommodate information gaps and neither add nor reduce risk beyond a neutral score to prevent a retrospective reporting bias. Clinicians are asked to only rate scores in the "severe" category if they have reports from child welfare documents, or reliable child, caregiver/case manager reports indicative of severe adversity during a specific developmental period. Regardless, prospective, longitudinal studies that track multiple dimensions of adverse experiences and their associations with functioning over time are needed.

Another study limitation was the monomethod, monoreporter design, which may have resulted in inflated correlations between variables (Podsakoff, MacKenzie, Lee, & Podsakoff, 2003). We sought to address this statistically. Ridge regularization in tandem with cross-validation is an effective method for addressing multicollinearity to learn generalizable and stable estimates from the data, while still permitting statistical inference.

Future research directions using the current dataset include evaluating which types of adversity or relational poverty are most associated with neurodevelopmental functioning, and which specific functional domains are most affected by various dimensions of adversity, including timing, type, frequency/chronicity, and severity. There are likely key domains, such as attention, arousal, sleep, and mood, that are affected by certain types of experiences during specific developmental periods. Interactions between risk trajectories and current functioning also need to be explored, when sample sizes are large enough, as does the association between the timing of various protective experiences and specific brain-mediated developmental functions.

We are aware that the utility of the current dataset will be vastly improved when it is linked to other indicators of children's functioning. Currently, we are scaling up clinical sites using the NMT to collect additional data, such as expanded demographic information (e.g., placement type, indicators of which sources were used to inform the developmental history reports, caregiver and clinician information), standardized measures of behavioral, social, cognitive, and neuropsychological function, and detailed information about the sequence and type of intervention children are receiving.

Conclusions

Findings indicate that the impact of highly traumatic and relationally impoverished experiences, particularly when occurring during the first few months of life, can be enduring. Conversely, relationally rich contexts at any point in a child's life may serve as a buffer. From either perspective, the potential for prevention and early intervention to address risk, reduce future morbidity, and enhance the lives of children is unmistakable.

Every provider coming into contact with pregnant women, or newborns and their families, can and should play a pivotal role in identification of families at risk and early intervention. Physicians, nurses, midwives, doulas, infant mental health specialists, home visitors, lactation consultants, etc. can inquire about the family's living conditions, adjustment to parenthood, stress levels, family violence, caregiver depression, substance use, economic stability, etc., and either intervene or provide a referral for support. They can provide anticipatory guidance regarding the the lasting effects of both early adversity and neglect, and the buffering impact of safety, protection, loving and attuned caregiving, and a developmentally rich environment. While the use of standardized screening and intervention tools may support this work, they cannot substitute for a conversation with a sincerely interested provider. Any program that decreases the isolation of caregivers during pregnancy and early childhood may significantly mitigate children's risk. Such efforts must also be paired with advocacy work to move local, state, and federal policies into greater alignment with these scientific findings.

Depending on the training, context and inclination of the provider, other preventive approaches can include simply observing the level of relational attunement and reciprocity of interactions between parent and newborn, and providing support or making a referral for a more advanced assessment by an infant mental health specialist if questionable patterns present (Brandt, Perry, Seligman, & Tronick, 2014; Weatherston, 2000). Professionals can also be trained in more advanced skills for supporting parents, such as: a) use of the Newborn Behavioral Observation (NBO), a clinical relationship-building approach for engaging parents in understanding their baby's unique language and behavioral repertoire, reducing parental anxiety, and enhancing parent-child interactions (Nugent, Keefer, Minear, Johnson, & Blanchard, 2007); and, b) the Parent-Child Interaction (PCI) Feeding and Teaching Scales that can be used starting at birth to identify dyads with potentially problematic interactional patterns, and pinpoint areas for intervention and support (Brandt, 2013; Oxford & Findlay, 2013).

Child medical providers typically see infants and their caregivers four times during the first two months of life and eight times during the first year (and even more so when children are preterm or have birth complications), and maternal medical providers typically have two postpartum contacts for checking in with the mother. These contacts afford multiple opportunities to build relationships, check in on family progress, and screen for relational challenges, including parental depression.

The findings reported here suggest the need for communities to organize coordinated efforts that embrace families with newborns and young infants in novel ways to prevent isolation, reduce stress, and promote safe and joyful parent-child relationships. Community based approaches for reduction of child risk include home visiting programs by nurses or other providers that focus on the parent-child relationship, risk reduction, and promotion of child safety and positive parental engagement (Doggett, 2013). The documented efficacy of home visiting programs targeting pregnant and post-partum mothers, such as Healthy Families America, Early Head Start Home Visiting, and Nurse Family Partnership (NFP) (DiLauro, 2012), may be due in part to the fact that the supportive services are provided during a time when we know that experiences, particularly relational experiences, are highly influential for the developing child. Other useful community programs may include lactation support organizations, faith-based congregations, and state and federal programs such as the Women, Infants, and Children (WIC) Supplemental Nutrition Program.

Even if a child's early experiences are poor, improving future relational contexts will likely improve outcome. To do so, however, we must think outside of traditional 50-minute therapy sessions toward ways to enrich a child's entire relational world every hour of the day, from the family context to friends, schools, and community settings. Certainly, these findings highlight the complex pathways through which developmental experience influences children's functioning. We must never underestimate how experiences can both hurt and heal, and how positive experiences early in life can optimize development and be preventive. Continuing to explore associations between experiences and outcomes will allow us to construct and promote clinical work that is more responsive to nuance, patient-centered, and increasingly effective.

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