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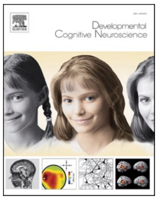

Resting brain activity in early childhood predicts IQ at 18 years

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ABSTRACT

Resting brain activity has been widely used as an index of brain development in neuroscience and clinical research. However, it remains unclear whether early differences in resting brain activity have meaningful implications for predicting long-term cognitive outcomes. Using data from the Bucharest Early Intervention Project (Zeanah et al., 2003), we examined the impact of institutional rearing and the consequences of early foster care intervention on 18-year IQ. We found that higher resting theta electroencephalogram (EEG) power, reflecting atypical neurodevelopment, across three assessments from 22 to 42 months predicted lower full-scale IQ at 18 years, providing the first evidence that brain activity in early childhood predicts cognitive outcomes into adulthood. In addition, both institutional rearing and later (vs. earlier) foster care intervention predicted higher resting theta power in early childhood, which in turn predicted lower IQ at 18 years. These findings demonstrate that experientially-induced changes in brain activity early in life have profound impact on long-term cognitive development, highlighting the importance of early intervention for promoting healthy development among children living in disadvantaged environments.

1. Introduction

A fundamental question in developmental cognitive neuroscience is whether long-term cognitive outcomes can be explained by observable differences in brain activity early in life. Resting brain activity is thought to reflect the brain's intrinsic dynamics (Anderson and Perone, 2018) and has been widely used as a biomarker of brain functioning in large-scale longitudinal studies (Jensen et al., 2021; Marshall et al., 2008; Norton et al., 2021; Troller-Renfree et al., 2022). However, it remains unclear whether individual differences in resting brain activity early in life are meaningfully related to long-term cognitive outcomes. Here we addressed this question, examining the effects of early psychosocial deprivation and an intervention to remove children from deprivation on long-term cognitive development.

The first years of human life represent the fastest pace of brain development during the life span. A lack of expected environmental inputs during this critical period has long-lasting effects on neurocognitive development (Fox et al., 2010). Among various forms of early adversity, psychosocial deprivation due to institutional rearing—which affects millions of children across the globe (Hillis et al., 2021)—is particularly detrimental. Institutional care is characterized by inadequate social and cognitive stimulation, high child-to-caregiver ratios, and limited emotional support (Mason and Narad, 2005; Smyke et al., 2007). To evaluate the efficacy of foster care as an alternative to institutional care, the Bucharest Early Intervention Project (BEIP) (Nelson, 2014; Zeanah et al., 2003) recruited abandoned children living in institutions in Romania and randomly assigned them to either continued usual care (care as usual group; CAUG) or to be removed and placed in foster care (foster care group; FCG). A demographically matched group of never-institutionalized children (never-institutionalized group; NIG)

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were recruited to serve as a community comparison group. The randomized controlled trial (RCT) design of the BEIP allowed causal inferences to be made about the effects of the foster care intervention.

Using this unique sample, previous research found that ever-institutionalized (EIG) children had lower intelligence quotient (IQ) scores compared with NIG children, and that foster care intervention resulted in improved IQ from early childhood through age 18 years. Among children in the FCG, earlier (vs. later) placement into foster care was associated with greater gains in IQ, and caregiving quality emerged as an important factor explaining the effects of the intervention (Almas et al., 2016; Bos et al., 2009; Fox et al., 2011; Humphreys et al., 2022; Nelson et al., 2007; Wade et al., 2019). Together, these findings highlight the far-reaching impact of the early environment on cognitive development.

In addition to lower IQ, EIG children also exhibited brain activity patterns that differed from those observed among NIG children. In typically developing children, resting brain activity is characterized by a decrease in lower-frequency (e.g., theta) electroencephalogram (EEG) power and an increase in higher-frequency (e.g., alpha, beta, and gamma) power from infancy to middle childhood (Marshall et al., 2002; Uhlhaas et al., 2010). This age-related change is thought to be related to cortical maturation and synaptic pruning (Corning et al., 1982; Whitford et al., 2007). Past BEIP research found that, at baseline, EIG (vs. NIG) children showed higher resting EEG power in the theta band and lower power in the alpha and beta bands (Marshall et al., 2004). This brain activity pattern is thought to reflect a maturational lag in functional brain development and has been associated with attention and learning problems (Barry et al., 2003; Perone et al., 2018). At 42 months, although no EEG power differences were found between the FCG and CAUG, children placed into foster care earlier (vs. later) showed neural activity patterns more similar to those observed in NIG children (Marshall et al., 2008), underscoring the importance of early intervention.

Do early changes in brain activity predict long-term cognitive outcomes? Past BEIP research has found that higher resting alpha power at 42 months was associated with higher concurrent cognitive functioning among children in the FCG (Marshall et al., 2008), and that higher resting alpha power at age 8 years predicted better executive functioning at ages 8, 12, and 16 years across groups (Wade et al., 2019). However, it remains unclear whether differences in resting brain activity during the first years of life predict long-term cognitive outcomes, and whether these differences explain the effects of institutional rearing and foster care on cognitive outcomes. Evidence for mediation via brain activity may unfold over time, and earlier changes in brain functioning may result in cognitive changes later in life. To clarify how early differences in brain activity are related to long-term cognitive development, it is important to examine the interplay between cognitive and brain activity across multiple timepoints.

The current study leveraged data from the BEIP to examine the downstream effects of experiential factors (i.e., institutional care, foster care intervention, age of placement in foster care) on neural and cognitive development from early childhood to adulthood. To examine how neurocognitive development during early critical periods is associated with long-term cognitive outcome, we selected neurocognitive measures from the first years of life (i.e., baseline, 30 months, and 42 months) and outcome measures from adulthood. The use of multiple assessments in early childhood and the large time span across measures (from early childhood to adulthood) distinguish the current study from prior research. Additionally, we extended prior studies (Marshall et al., 2008; Wade et al., 2019) to examine whether (and how) differences in early brain activity mediated the effects of experiential factors on long-term cognitive outcome in adulthood. At baseline, 30 months, and 42 months, resting EEG power (in the theta, alpha, beta, and gamma bands) and cognitive skills (using the Bayley Scales of Infant Development) were assessed. At 18 years, cognitive ability was measured using the Weschler Intelligence Scale for Children (WISC-IV); we administered the WISC-IV rather than the Weschler Adult Intelligence Scale in order to prevent potential floor effects in the EIG (Humphreys et al., 2022). Group differences in these brain activity and cognitive measures (Supplementary Material; SM 1) have been reported previously (Humphreys et al., 2022; Marshall et al., 2004, 2008; Nelson et al., 2007).

We hypothesized that differences in brain activity (indexed by resting EEG power) during early childhood would predict long-term cognitive outcome. To test this hypothesis, we calculated composite scores for relative theta, alpha, beta, and gamma power across baseline, 30-, and 42-month assessments, and examined the correlations between these composite scores and 18-year IQ. We also hypothesized that experiential factors would influence early brain activity, and that differences in early brain activity would in turn predict subsequent cognitive functioning. To test this hypothesis, we examined whether early differences in brain activity mediated the downstream effects of experiential factors on 18-year IQ. A series of cross-lagged panel models (CLPMs) were tested to explore the dynamics of neurocognitive development across timepoints.

2. Materials and methods

2.1. Participants

Participants were 202 children (51.49% female; 67.33% Romanian; 21.29% Romani; 11.39% Unknown/Other) from the BEIP study (ClinicalTrials.gov, NCT00747396). This sample size was sufficient for the statistical tests used in the current study, including CLPMs (Bentler and Chou, 1987; Jackson, 2001; Tanaka, 1987) and bootstrap tests of indirect effects (Tofighi and MacKinnon, 2016). Details of study design and participant selection have been previously reported (Zeanah et al., 2003). For the EIG, 136 children (ages 6–31 months, $M_{age} = 22$ months) were recruited from six institutions in Bucharest, Romania. These children had spent between 51% and 100% ($M = 89\%$) of their lives under institutional care, characterized by limited caregiver-child interactions, inadequate sensory and cognitive input, and profound psychosocial deprivation. An additional 51 infants were excluded due to serious medical conditions (e.g., genetic syndromes, fetal alcohol syndromes, micro- or macrocephaly). At baseline, children's physical, cognitive, and socioemotional functioning was assessed. Following baseline assessment, children were randomly assigned to either a CAUG ($N = 68$) or a FCG ($N = 68$). Random assignment was achieved by randomly drawing participant numbers from a hat. Children in the CAUG remained in institutional care, and children in the FCG were taken out of institutions and placed into foster care families. The mean age of foster care placement was 22.63 months ($SD = 7.33$ months, range = 6.81–33.01 months). Foster parents received specialized training in child rearing as well as ongoing support from social workers (Smyke et al., 2009; Zeanah et al., 2003). No baseline differences were found between the CAUG and the FCG in sex assigned at birth, age, or birth weight. At baseline, a group of age- and sex-matched NIG children ($N = 66$) were recruited from the community to serve as a comparison sample. The intervention formally ended when children were 54 months of age.

Due to cultural, political, and policy changes in Romania, there were instances of change in participants' group assignment over the course of the study. Several children in the CAUG and FCG were adopted domestically, moved into government foster care, or returned to their biological families. Consistent with prior studies using the BEIP sample (Debnath, Tang et al., 2020; Nelson et al., 2007; Vanderwert et al., 2016), the current study used an intent-to-treat approach, whereby the data were analyzed based on children's original group assignment. As a result, the findings reported here represent a conservative estimate of the effects of foster care intervention. The protocol of the study was approved by the institutional review boards at the principal investigators' universities, and by the National Authority of Child Protection and the Ministry of Health in Romania. Informed written consent was obtained from biological parents and/or from the local

Commissions for Child Protection in Bucharest. At the 18-year assessment, informed consent was obtained from all participants. The ethical issues of the BEIP study have been previously discussed (Millum and Emanuel, 2007; Wassenaar, 2006; Zeanah et al., 2006).

2.2. Resting EEG power at baseline, 30 months, and 42 months

2.2.1. EEG recording

Resting-state EEG was collected at baseline ($M_{\text{age}} = 20.40$ months; $SD = 7.20$ months), 30 months ($M_{\text{age}} = 30.84$ months; $SD = 2.04$ months), and 42 months ($M_{\text{age}} = 42.36$ months; $SD = 1.44$ months). Participants who completed the EEG assessments included $N = 185$ (CAUG $N = 67$, FCG $N = 66$, NIG $N = 52$) at baseline, $N = 161$ (CAUG $N = 61$, FCG $N = 61$, NIG $N = 39$) at 30 months, and $N = 139$ (CAUG $N = 53$, FCG $N = 56$, NIG $N = 30$) at 42 months. Resting EEG was collected while participants were watching a spinning bingo wheel (Calkins et al., 1996). The wheel contained numerous brightly colored balls and was spun by an experimenter for a series of nine trials (each 10 s in length). After each trial, the experimenter stopped the spinning wheel and changed the balls in the wheel to maintain children's attention for another 10 s. Although children's brain activity was recorded for the entire task, data analysis was performed only using epochs in which the wheel was being spun (Marshall et al., 2004, 2008; McLaughlin et al., 2010, 2011).

EEG signals were collected using a lycra Electro-Cap (Electro-Cap International Inc., Eaton, OH) with sewn-in tin electrodes and the EEG Analysis System from the James Long Company (Caroga Lake, NY). Left and right frontal (F3, F4), central (C3, C4), parietal (P3, P4), occipital (O1, O2), and midline (Fz, Cz, Pz) electrodes were positioned according to the 10/20 Electrode System (Jasper, 1958). The vertex electrode (Cz) served as the reference, and an anterior midline electrode (AFz) served as the ground. Impedances of all sensors were kept below 10 kΩ. EEG signals were digitized at a sampling rate of 512 Hz, and amplifier filter settings for all channels were 0.1 Hz (high pass) and 100 Hz (low pass). For a detailed description of the EEG recording procedure, see past reports (Marshall et al., 2004, 2008).

2.2.2. EEG data reduction and spectral analysis

EEG data were preprocessed using EEGLAB, an open-source analysis toolbox (Delorme and Makeig, 2004), as well as custom written MATLAB (2017a) scripts. EEG data were down sampled to 250 Hz and bandpass filtered (0.3–50 Hz). Continuous EEG data were then segmented into 2-second epochs with 1-second (50%) overlap. Epochs containing artifacts (e.g., eye blinks, movement) were identified using a voltage threshold of ± 150 μV and rejected from analysis. Down-sampling, filtering, and artifact rejection parameters were based on the parameters used in the Maryland analysis of developmental EEG (MADE) pipeline (Debnath, Buzzell et al., 2020). Participants included in the final analysis all had more than 20 s of artifact-free data. Epoched data were re-referenced to the average of two mastoid electrodes. A fast Fourier transform (FFT) with a 2-second Hanning window and 50% overlap was performed on the clean epoched data.

Absolute power (μV^2) was computed in theta (baseline: 3–5 Hz; 30 months: 3–5 Hz; 42 months: 3–5 Hz;), alpha (baseline: 6–9 Hz; 30 months: 6–10 Hz; 42 months: 6–10 Hz), beta (baseline:10–18 Hz; 30 months: 11–18 Hz; 42 months: 13–20 Hz), and gamma (baseline: 19–50 Hz; 30 months: 19–50 Hz; 42 months: 21–50 Hz) frequency bands. The frequency ranges were based on prior EEG studies using this sample (Marshall et al., 2004, 2008); different frequency ranges were used for different ages because the frequency composition of power spectra changes across development (Isler et al., 2022; Marshall et al., 2002). To reduce data skewness, a natural log transformation was applied on the EEG power values.

For each epoch, relative power (i.e., absolute power of each frequency band divided by total absolute power across all frequency bands) was computed and averaged over F3, F4, Fz, C3, C4, P3, P4, Pz, O1, O2 electrodes to generate relative power values covering the whole head. Consistent with past research (Debnath, Tang et al., 2020; Pierce et al., 2021), we chose to focus on relative power in our longitudinal data analysis because relative power has better test-retest consistency (John et al., 1980) and is more reliable (Fernández et al., 1993) compared with absolute power. Moreover, relative power is relatively unaffected by individual differences in impedance and skull thickness, which can change over time (Benninger et al., 1984), and is more sensitive to developmental changes in the frequency composition of EEG (Clarke et al., 2001).

2.3. Cognitive functioning at baseline, 30 months, and 42 months

Children's cognitive ability was assessed at baseline, 30 months, and 42 months by trained Romanian psychologists using the Bayley Scales of Infant Development (BSID-II) (Bayley, 1993). Participants who completed the BSID-II included $N = 201$ (CAUG $N = 68$, FCG $N = 67$, NIG $N = 66$) at baseline, $N = 186$ (CAUG $N = 65$, FCG $N = 64$, NIG $N = 57$) at 30 months, and $N = 179$ (CAUG $N = 62$, FCG $N = 65$, NIG $N = 52$) at 42 months. The BSID-II is widely used in both clinical and research settings to provide reliable measures of cognitive, motor, and behavioral development in infants between 1 and 42 months of age. The current study focused on the mental subscale, which measures cognitive skills including perceptual acuities, discriminations, memory, learning, communication, and abstract thinking skills. Raw scores on the mental scale were assigned an age-equivalent score (Lindsey and Brouwers, 1999), and developmental quotients (DQs; [age-equivalent score/chronological age] × 100) were calculated for each participant. The effects of institutional rearing and foster care intervention on this measure have been reported in prior studies (Nelson et al., 2007; Smyke et al., 2007; Windsor et al., 2007).

2.4. Cognitive outcome at 18 years

Children's cognitive functioning at 18 years was measured using the Weschler Intelligence Scale for Children, fourth edition (WISC-IV) (Wechsler, 2004). Participants who completed the WISC-IV included $N = 46$ for the CAUG, $N = 49$ for the FCG, and $N = 26$ for the NIG. Within each group, there were no differences between participants who did versus did not complete the WISC-IV in terms of sex assigned at birth, baseline age, baseline DQ, or baseline EEG power in the theta, alpha, beta, and gamma bands, $ps > 0.05$, suggesting that children who contributed data to 18-year IQ were representative of the original sample. We administered the WISC-IV rather than the Weschler Adult Intelligence Scale (Wechsler, 2008) in order to prevent potential floor effects in the EIG. The use of WISC-IV for the 18-year assessment in BEIP, and the effects of institutional rearing and foster care intervention on this measure have been reported and discussed in prior report (Humphreys et al., 2022). The WISC-IV consists of 10 subtests (with 5 additional supplemental subtests) measuring cognitive skills in four domains, including perceptual reasoning, verbal comprehension, working memory, and processing speed. The WISC-IV generates composite scores for the four domains, as well as a full-scale IQ score representing the overall level of intelligence across domains. Five participants were identified by researchers as too cognitive impaired to complete the WISC-IV. These participants were assigned a score of 40 (the lowest score available). The perceptual reasoning domain includes Block Design, Picture Concepts, Picture Completion, and Matrix Reasoning tasks. The verbal comprehension domain includes Vocabulary, Similarities, Comprehension, Information and Word Reasoning tasks. The working memory domain includes Digit Span, Arithmetic, and Letter-Number Sequencing tasks. The processing speed domain includes Coding, Cancelation, and Symbol Search tasks.

2.5. Data analysis

2.5.1. Predicting 18-year IQ from resting EEG across early childhood

To examine the correlations between resting EEG power in early childhood and 18-year IQ, we calculated composite scores for relative theta, alpha, beta, and gamma power by averaging standardized scores across baseline, 30-, and 42-month measures. Because 18-year IQ violated normality, we report Spearman's correlation coefficients. Pearson's correlation coefficients showed similar results.

2.5.2. Cross-lagged panel models

We tested a series of CLPMs with experiential factors (institutional rearing, foster care intervention, age of placement in foster care) as predictors of cognitive ability and neural functioning (indexed by resting EEG power). The CLPM is the most widely used cross-lagged model in longitudinal research (Orth et al., 2021; Usami et al., 2019). Given our focus on between-person and between-group differences, we chose to use traditional CLPM (Lüdtke and Robitzsch, 2021; Orth et al., 2021, 2022).

For each of the three experiential factors, one CLPM was fit for each of the four frequency bands (theta, alpha, beta, gamma), resulting in 12 CLPMs in total. Specifically, to examine the effects of institutional rearing, group (1 =EIG, 0 =NIG) was entered into the first set of CLPMs as a predictor of DQ and resting EEG power at baseline, 30 months, and 42 months. To examine the effects of foster care intervention, intervention group (1 =FCG, 0 =CAUG) was entered into the second set of CLPMs as a predictor of DQ and resting EEG power at 30 months and 42 months. To examine the effects of age of foster care placement, age of foster entry was entered into the third set of CLPMs as a predictor of DQ and resting EEG power at 30 months and 42 months. Note that the second and third sets of models did not include the main effects of group on DQ and EEG power at baseline, because foster care intervention took place after baseline assessment and should only have effects on subsequent measures. Across all models, we tested whether 18-year cognitive outcome (IQ) was predicted by 42-month DQ and EEG power.

Data analyses were performed using R (version 4.2.0). CLPMs were estimated using the Lavaan package (version 0.6–11) (Rosseel, 2012). For model fit indices, we report comparative fit index (CFI), Tucker-Lewis index (TLI), root mean square error of approximation (RMSEA), and standardized root mean residual (SRMR). CFI and TLI values ≥ 0.95, SRMR values ≤ 0.08, and RMSEA values ≤ 0.06 represent a good fit to the data (Hu and Bentler, 1999; Little, 2013). Because CFI and SRMR are more robust than TLI and RMSEA when sample size is small ($N \leq 250$), the interpretation of model fit was mainly based on CFI and SRMR (Hu and Bentler, 1999). All variables in the models were mean-centered. Full information maximum likelihood (FIML) estimation was used for handling missing data (Enders and Bandalos, 2001). To test whether early individual differences in neural functioning mediate the effects of experiential factors on 18-year cognitive outcome, indirect effects were evaluated using bootstrapped confidence intervals (CIs) (MacKinnon et al., 2004). Statistical significance of indirect effects was determined by 95% CIs from 20,000 Monte Carlo bootstrap resamples using the R package semTools (Jorgensen et al., 2022).

2.6. Data and code availability

All code and deidentified data (except the age of placement into foster care which may allow for the identification of participants) can be found at Open Science Framework (OSF): https://osf.io/4hfc7/?view_only=ef472f2be36a4ce68b5fbb54f1459c8a.

3. Results

3.1. Early brain activity predicts 18-year IQ

Across groups, 18-year IQ was predicted by resting EEG power in the theta band across baseline, 30-month, and 42-month assessments, $r_{Spearman} = -0.22$, two-sided $p = .016$), Fig. 1. No significant correlations were found for other frequency bands. Post-hoc analysis on different domains of the WISC-IV revealed that early resting theta activity was significantly associated with 18-year perceptual reasoning, working memory, and processing speed, but not with verbal comprehension (see SM 2). These findings provide the first evidence that resting brain activity (indexed by theta power) during early childhood predicts long-term cognitive outcomes even into adulthood.

3.2. Experiential effects

We next examined whether differences in early brain activity serve as a mechanism explaining the effects of institutional rearing on long-term cognitive development. The effects of institutional rearing on 18-year IQ were mediated by resting EEG power in the theta band (Fig. 2). Specifically, institutional rearing predicted higher resting theta power (suggestive of atypical neurodevelopment) at baseline, which in turn predicted lower DQ at 30 and 42 months, and subsequently lower IQ at 18 years, serial indirect effect $\beta = -0.014$, 95% CI $[-0.032, -0.002]$. Supplementary analysis revealed that these mediation effects still held when the direct effect of institutional rearing on 18-year IQ was included in the model (SM 3). No mediation effects were found for the alpha, beta, and gamma bands (for full results, see SM 4). Importantly, resting theta power at baseline predicted 30-month DQ even with baseline DQ and the direct effects of institutional rearing accounted for. In addition, institutional rearing did not predict any 42-month measures when we adjusted for earlier effects, suggesting that group differences in cognitive and neural functioning observed at 42 months (Marshall et al., 2008; Nelson et al., 2007) reflect downstream effects from earlier periods. Post-hoc analysis on different domains of the WISC-IV replicated the effects found with full-scale IQ within the perceptual reasoning, working memory, and processing speed domains (SM 5). Together, these findings suggest that institutional rearing may have resulted in lower IQ scores at age 18 years via changes in resting theta power in early childhood.

Next, we explored whether differences in early brain activity

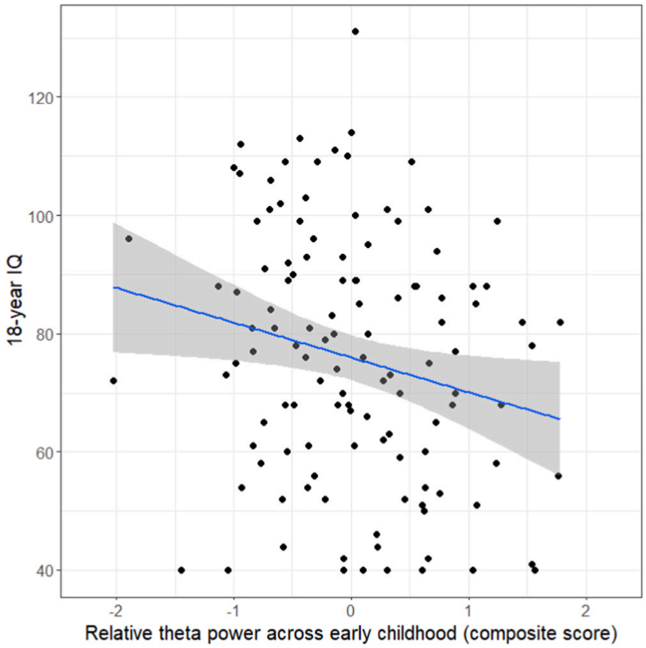

Fig. 1. Resting theta power across early childhood predicted 18-year IQ. Composite scores for resting theta power were calculated by averaging standardized scores across baseline, 30 months, and 42 months. The grey area represents 95% confidence intervals of the trend line.

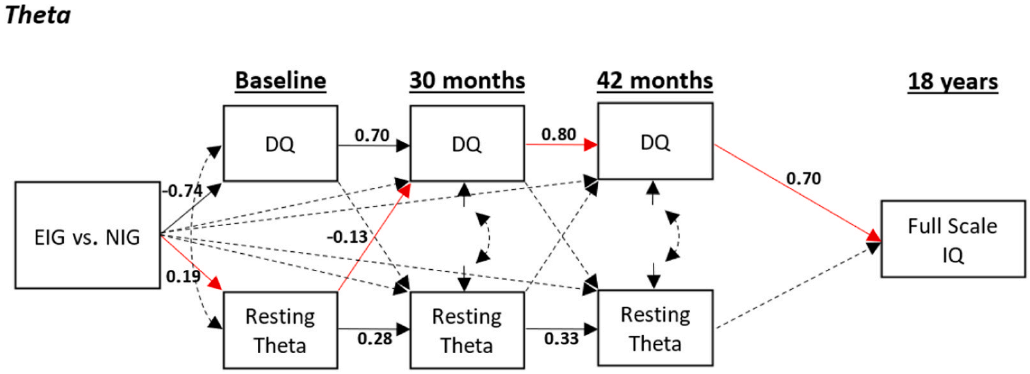

Fig. 2. Resting theta power at baseline mediated the effects of institutional rearing on 18-year cognitive outcome. Standardized coefficients (βs) are reported for statistically significant paths (solid lines). Dashed lines indicate nonsignificant paths. Red lines represent indirect paths of interest. EIG (coded as 1): ever-institutionalized group. NIG (coded as 0): never-institutionalized group. DQ: developmental quotient.

mediated the effects of foster care intervention on 18-year IQ. Consistent with prior BEIP studies (Debnath, Tang et al., 2020; Nelson et al., 2007; Vanderwert et al., 2016), we used an intent-to-treat approach, whereby the data were analyzed based on children's original group assignment, to facilitate causal inferences about the effects of the intervention. As shown in Fig. 3, foster care intervention predicted higher DQ at 30 months (i.e., at the first post-intervention assessment) but not at 42 months, suggesting that intervention improves cognitive functioning early in life and that group differences observed at 42 may reflect downstream effects from earlier periods. Consistent with past research (Marshall et al., 2008), intervention did not predict resting EEG power (for full results, see SM 6). These results suggest that foster care intervention has a positive effect on cognitive development early in life that could be observed behaviorally; though in examining foster care children as a group, they did not show significant differences in resting EEG power compared with the CAUG.

In the final set of analyses, we examined whether the effects of age of foster care placement on 18-year cognitive outcome were mediated by early differences in brain activity. Results show that later (vs. earlier) foster care placement predicted higher resting theta power (suggestive of atypical neurodevelopment) at 30 months, which in turn predicted lower DQ at 42 months and subsequently lower IQ at 18 years (Fig. 4), serial indirect effect $\beta = -0.071$, 95% CI [-0.153, -0.006]. Supplementary analysis revealed that the mediation effects still held when the direct effect of age of foster care placement on 18-year IQ was included in the model (SM 7), and that the effects were fully mediated by 30-month theta power. No mediation effects were found for the alpha, beta, and gamma bands (for full results, see SM 8). Post-hoc analysis on different domains of the WISC-IV replicated the effects found with full-scale IQ within the perceptual reasoning, working memory, and processing speed domains (SM 9). These results suggest that, similar to the effects of institutional rearing, the effects of age of foster care placement on 18-year cognitive outcome are also driven by changes in brain functioning (indexed by resting theta power) early in life.

4. Discussion

Resting brain activity early in life predicted cognitive outcome at 18 years, and mediated the effects of psychosocial deprivation on 18-year IQ. These findings not only provide the first evidence that early resting brain activity predicts developmental outcomes into adulthood, but also reveal fine-grained details about the interactions between the environment, the brain, and behavioral/cognitive performance from infancy to adulthood. The significant correlations between early brain activity and young adult IQ are particularly striking, considering that brain activity was measured during resting state (vs. during cognitive tasks), and considering the long time span between measures and the number of personal and environmental factors (e.g., puberty, education) that could affect the trajectory of cognitive development during this time span.

Our data provide unique insights into how the effects of institutional rearing and foster care intervention unfold over time. These insights are gleaned from two consistent patterns across analyses. First, institutional rearing and foster care intervention had direct effects on DQ early in life (i.e., at baseline or at the first post-intervention assessment), but had no direct effects on 42-month DQ when earlier effects were accounted for. These findings demonstrate that the effects of institutional rearing and foster care intervention on cognitive development emerge early in life, and that group differences in cognitive functioning observed at 42 months may reflect downstream effects from earlier periods. Second, the indirect effects of institutional rearing and age of foster care placement on 18-year IQ were both mediated by early (but not later) EEG measures, suggesting that early (vs. later) differences in neural functioning play a particularly important role in determining long-term cognitive outcomes. Together, these findings highlight the profound impact of early experiential influences on long-term neurocognitive development.

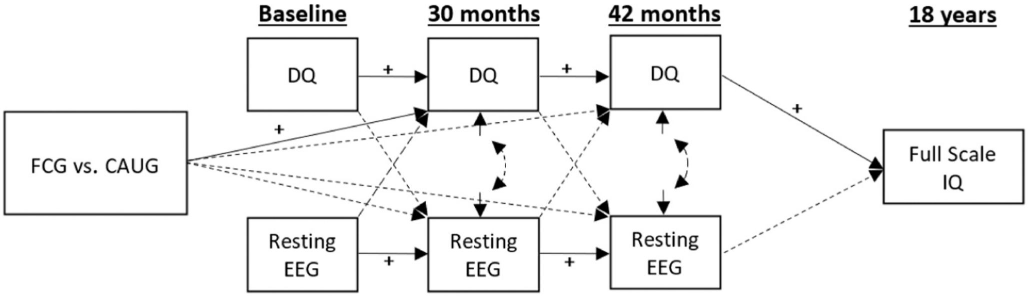

Fig. 3. The effects of foster care intervention (CAUG vs. FCG) on resting EEG and cognitive ability. Solid lines indicate statistically significant paths. Plus signs (+) indicate positive associations. Dashed lines indicate nonsignificant paths. FCG (coded as 1): foster care group. CAUG (coded as 0): care as usual group. DQ: developmental quotient. Resting EEG: resting-state EEG power in the theta, alpha, beta, and gamma bands. Note that foster care intervention took place after baseline and should only have effects on subsequent measures.

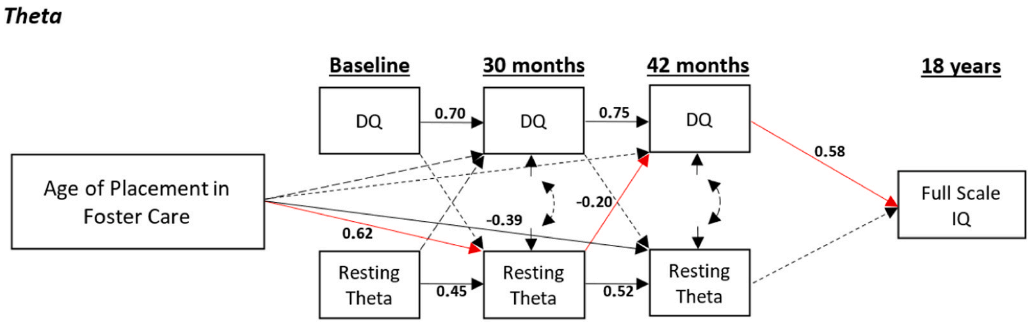

Fig. 4. Resting theta power at 30 months mediated the effects of age of placement in foster care on 18-year cognitive outcome. Standardized coefficients (βs) are reported for statistically significant paths (solid lines). Dashed lines indicate nonsignificant paths. Red lines represent indirect paths of interest. DQ: developmental quotient. Note that foster care intervention took place after baseline and should only have effects on subsequent measures.

The human brain undergoes considerable changes during the first years of life (Gilmore et al., 2018; Hadders-Algra, 2018), and normal brain development requires expected inputs to guide neural pruning and cortical specialization (Black et al., 1998; Fox et al., 2010; Greenough et al., 2002). Inadequate environmental inputs during critical periods can fundamentally change the dynamics of neurocognitive development (McLaughlin et al., 2017; Nelson and Gabard-Durnam, 2020), affecting long-term cognitive outcomes. Indeed, past research has shown that early institutional rearing was associated with widespread cortical thinning, and that cortical thinning across multiple brain areas (e.g., the inferior parietal cortex, precuneus, and superior temporal cortex) mediated the associations between early institutional rearing and attentional problems at ages 8–10 years (McLaughlin et al., 2014). Children with a history of institutional rearing also showed lower white matter directional organization in the prefrontal cortex (PFC) and in white matter tracts connecting the PFC and temporal lobe, and these alterations predicted lower cognitive functioning at ages 9–14 years (Hanson et al., 2013). In addition to cortical thickness and white matter organization, early adversity has also been associated with alterations in the volume of cortical (e.g., inferior frontal gyrus) and subcortical (e.g., ventral striatum) structures, which in turn predicted emotional and behavioral problems in adolescence (Luby et al., 2017; Mackey et al., 2017). The current study provides new evidence that early adversity influences long-term cognitive development through changes in early brain activity. We call for future research to examine how these changes are related to structural, physiological, and functional changes of the brain.

Our findings also suggest that resting theta power may represent a useful biomarker for indexing the long-term effects of early adversity on neural and cognitive development. Indeed, across four frequency bands, theta was the only one that predicted 18-year IQ across groups, and resting theta mediated the effects of institutional rearing and age of foster care placement on 18-year cognitive outcome. Theta power is particularly salient in EEG power spectra among young (vs. older) children (Cellier et al., 2021; Gibbs and Knott, 1949; Marshall et al., 2002), and past research has shown that resting theta power in children is sensitive to environmental risk factors such as poverty and sociocultural disadvantages (Harmony et al., 1988; Maguire and Schneider, 2019; Otero, 1997; Otero et al., 2003). It is important to note that resting theta and event-related theta have been associated with distinct cognitive outcomes. Although increased theta power and theta/beta ratio during resting state have been associated with lower cognitive functioning (Barry et al., 2003; Corning et al., 1986; Maguire and Schneider, 2019; Perone et al., 2018), increased theta power during tasks (e.g., learning) predicted higher cognitive performance in infants (Begus and Bonawitz, 2020). One possible explanation for this discrepancy is that event-related theta and resting theta may reflect two distinct types of synchronization. For example, Klimesch (1999) proposed that event-related theta may reflect narrow-band synchronization that is closely related to hippocampal theta and the encoding of new information (Herweg et al., 2020). By contrast, resting theta may be related to irregular slow activity (ISA), which leads to a broad-band increase in lower-frequency power but may interfere with information processing (da Silva, 1992). Alternatively, considering that increased theta is typically observed during cognitive processing in children (Begus and Bonawitz, 2020), higher theta power during resting state may suggest the unnecessary engagement of mental effort in the absence of cognitive tasks, and this behavioral tendency may be associated with lower cognitive functioning (Orekhova et al., 2006; Saad et al., 2018). Clarifying these mechanisms is crucial for identifying effective biomarkers of early adversity and long-term cognitive outcomes.

This study has limitations. First, considering that CLPMs typically require large samples, the sample size of this study is sufficient but not ideal. We note that the model fit indices used in this study are robust to small sample sizes (Hu and Bentler, 1999), and according to these indices all models provided good model fit. Second, in order to limit the total number of models tested, we only examined whole-brain EEG activity, without exploring effects at specific brain areas. It is possible that resting EEG in certain brain areas is more sensitive to environmental influences and/or better predicts cognitive outcome. Third, due to participant attrition, the sample size was lower for the 18-year assessment than for prior assessments. That said, supplementary analyses revealed that those who completed the 18-year IQ measures were not different from those who did not on key variables, including baseline EEG power, baseline DQ, and demographic variables. As such, our results are representative of the original cohort. Fourth, the current study used a traditional analysis approach based on predefined frequency bands. Although this approach has provided crucial insights into the development of brain functioning (Cuevas and Bell, 2022), recent research suggests that age-changes in EEG power may be better characterized as changes in peak frequency or aperiodic activity (i.e., the arrhythmic component of neural oscillations) (Cellier et al., 2021; Donoghue et al., 2022). To clarify the relations between early experience, brain activity, and cognitive development, we call for future research to use spectral parameterization approaches to better characterize brain activity (Ostlund et al., 2022).

5. Conclusions

This study provides the first evidence that resting brain activity in early childhood has meaningful implications for predicting long-term cognitive outcomes into adulthood. Given the central role of cognitive functioning in determining a wide range of life outcomes such as academic achievement, income, and mental well-being, these findings provide crucial implications for effective intervention strategies to promote healthy development among children living in disadvantaged environments.

CRediT authorship contribution statement

Enda Tan: Conceptualization, Methodology, Software, Data Curation, Formal analysis, Investigation, Visualization, Writing - Original Draft. **Alva Tang**: Conceptualization, Methodology, Software, Data Curation, Formal analysis, Investigation, Visualization, Writing - Review & Editing. **Ranjan Debnath**: Conceptualization, Methodology, Software, Data Curation. **Kathryn L. Humphreys**: Supervision, Funding acquisition, Conceptualization, Methodology, Resources, Writing - Review & Editing. **Charles H. Zeanah**: Supervision, Funding acquisition, Conceptualization, Methodology, Resources, Writing - Review & Editing. **Charles A. Nelson**: Supervision, Funding acquisition, Conceptualization, Methodology, Resources, Writing - Review & Editing. **Nathan A. Fox**: Supervision, Funding acquisition, Conceptualization, Methodology, Resources, Writing - Review & Editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

I have shared the link to my data and code at the Attach File step.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.dcn.2023.101287.

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