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Full Length Article

Caregiving and infants' neurodevelopment in rural Costa Rica: Results from the Infants' Environmental Health Study (ISA)

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ABSTRACT

Early caregiving is one of the strongest influences on children's development, and among the most significant modifiable environmental factor. The aim of this study was to explore the association between quality of caregiver-infant interactions and neurodevelopment of infants living in banana-growing communities in rural Costa Rica characterized as having environmental toxic exposures. Home visits were conducted with 94 caregiver-infant dyads from the Infants' Environmental Health Study (ISA), living within Matina county, Limón province. One-year infant neurodevelopmental outcomes were assessed using the Bayley Scales of Infant and Toddler Development®, Third Edition *(Bayley-III)*. Quality of caregiver-infant interaction was assessed with a standardized observational task: *Nursing Child Assessment Satellite Training Teaching scale (NCATS)* at around two years of age. Multiple regression analyses examined associations between components of caregiver-infant interactions and neurodevelopmental outcomes, adjusting for mancozeb and manganese exposure and other potential confounders. Compared to *NCATS* normative data for U.S. Hispanic mothers, 35% of the sample had overall caregiving interaction scores ≤10th percentile cut-off, indicating less than optimal interactions. Higher quality of caregiver-infant interaction was associated with higher expressive communication ability in infants [ß = 0.03 (95% CI: 0.01, 0.06)], controlling for pesticide exposure and confounders. Aspects of caregiving such as stimulation and growth-fostering of infants were most strongly associated with language outcomes. Results suggest an association between positive caregiving on language development for infants living in a rural agricultural area in Costa Rica, and highlight aspects of caregiving that could be targeted to improve resilience of these children who live in vulnerable conditions.

1. Introduction

The impact of prenatal and early life pesticide exposure on neurodevelopment is a public health concern (London et al., 2012), particularly in poverty-stricken, agricultural communities, such as the banana-growing areas in Costa Rica (van Wendel de Joode et al., 2012, 2014; Mora et al., 2014). The use of synthetic pesticides by banana-growing plantations in Costa Rica is among the highest in Central America (Bravo et al., 2011, 2013). The province of Limon, in Costa Rica, accounting for 99% of the national banana production, is one of the poorest regions in the country (Costa Rican Institute of Statistics and Census 2011). Many pesticides are applied in this region, including chlorpyrifos and manganese-containing fungicides such as mancozeb (Mora et al., 2014, 2015; van Wendel de Joode et al., 2012; 2014; 2016a); chlorpyrifos and manganese are known neurotoxins, and chlorpyrifos, manganese and mancozeb are suspected endocrine

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disruptors (Eaton et al., 2008; Saunders et al., 2012; Wesseling et al., 2001; van Wendel de Joode et al., 2016b; Rauh et al., 2011). The double burden of impoverished living conditions combined with the relatively high level of pesticide and manganese exposure may increase risk for neurodevelopmental problems (Keifer and Firestone, 2007; Lucio, 2008; Rice and Barone, 2000; Gunier et al., 2015; Mora et al., 2018).

The influence of modifiable environmental factors, such as the child's rearing environment, on developmental outcomes for children exposed to chemical substances has received little attention in the paediatric environmental health literature. Of the few studies conducted in child populations exposed prenatally to neurotoxins, including lead, methylmercury, chlorpyrifos, and polychlorinated biphenyls (PCBs), associations have been demonstrated between the quality of stimulation in the home environment and children's developmental outcomes (Davidson et al., 2004; Horton et al., 2012; Koller et al., 2004; Walkowiak et al., 2001; Torres-Sánchez et al. (2009)). It has been purported that within the context of neurotoxic exposure, social and parenting factors account for 40% or more of the variance in children's neurocognitive outcomes (Weiss, 2000), emphasizing the importance of the home environment on neurodevelopmental outcomes.

Animal studies conducted in rats show that maternal nurturing in early life has the potential to reverse the negative effects of prenatal adversity (Kappeler and Meaney, 2010). In humans, the World Health Organization has stated that the quality of early caregiver-infant interactions is one of the most significant modifiable environmental factors contributing to children's development and attachment security, and this relationship is observed across cultures and socioeconomic strata (Richter, 2004). Children whose caregivers provide nurturing and stimulating care in early life show better neurodevelopmental outcomes, irrespective of level of socioeconomic disadvantage (Bradley et al., 1989; Richter, 2004). Moreover, in the context of poverty and other adverse environmental conditions, positive caregiver-infant interactions are shown to act as a buffer against the negative impact of these conditions, and contribute to increased resilience (Barnard and Eyres, 1979; Richter, 2004; Shonkoff and Phillips, 2000). Thus, positive and stimulating caregiver-child interactions in early life have the potential to alter the course of development of children, especially in high risk populations (Brooks-Gunn et al., 2002; McCain et al., 2011).

The present study had two main objectives. First, we sought to explore the quality of caregiver-infant interactions in mother-infant pairs from the Infants' Environmental Health Study, situated in a rural banana growing area in Costa Rica. Our second objective was to test whether caregiver-infant interactions are associated with infants' neurodevelopmental outcomes at one year of age, after controlling for mancozeb and manganese exposure level and relevant covariates.

2. Methods

2.1. Study design and recruitment

The present study was carried out with a sub-sample from a larger, community-based, prospective cohort study investigating the impact of prenatal pesticide exposure on the physical and neurodevelopmental outcomes of infants living in Matina county, Limón province, Costa Rica, *The Infants' Environmental Health Study* or *Infantes y Salud Ambiental (ISA)* (Joode et al., 2014). The ISA study evaluates the impact of pesticide exposure and excess manganese on health, and aims to contribute towards risk reduction strategies in these banana-growing communities. Detailed methods for the ISA study have been described elsewhere (see Mora et al., 2014, 2018; Joode et al., 2014). The enrollment of all women from ISA study took place between March 2010 and June 2011. Pregnant women living within five kilometers of banana plantations with large-scale production in Matina County were recruited via communal groups, advertisements and referrals from educational and nutritional centres. Women were eligible for the study if they were at least 15 years old, and were less than 33 weeks pregnant at the time of inclusion. A total of 480 women were identified and, of these, 451 (94%) participated. The women lived in one of 40 villages spread throughout the county of Matina. Written informed consent was obtained from each participant and from her parent or legal guardian for women under 18 years of age who assented their parents/legal guardians' consent.

Women were visited and interviewed at their homes one to three times during pregnancy (between 19 and 33 weeks gestation), and samples of maternal urine, blood and hair were also collected at each visit for pesticide metabolites and manganese, respectively (van Wendel de Joode et al., 2014; Mora et al., 2014). Women were also visited shortly after the birth of their infant for an interview (median = 7 weeks postpartum (Mora et al., 2015). Subsequently, mother-infant dyads were visited when the infant was approximately one year of age to complete interviews and assessments of infant neurodevelopmental outcomes from August 2011 and April 2013.

Infants who had underwent one-year neurodevelopmental evaluations were identified and recruited, and a random sub-sample of 129 participants was selected to examine care-giver child interactions. Every attempt was made to obtain a sub-sample that was representative of the ISA study sample, with respect to village distribution and varying levels of prenatal exposure. Recruitment and data collection were limited, however, by accessibility to villages during the periods of data collection, localization of participants, and convenience of scheduling the home visits. Participants were only excluded if they were unreachable despite several attempts, unable to be located, or no longer living in the study area. Only two participants declined to participate in this study. Further exclusions (n = 4) were made due to poor data quality of the recordings of caregiver-infant interactions. The final study sample consisted of 94 caregiver-infant dyads (see Supplemental Table 1 for flow chart). Assessment of the 94 caregiver-infant interactions took place over two field trips conducted in October 2012 and April 2013. The assessment was conducted in Spanish, during home visits with infants and their primary caregivers. Data were collected by a graduate student (A.D.) and was supported by a research assistant (L.C. or J.C.C.) who had established a good report with the families during previous visits.

2.2. Assessment of one-year infant neurodevelopmental outcomes

Infant neurodevelopmental outcomes were assessed for all infants in the ISA study when infants were one year of age (Mora et al., 2018). Neurodevelopmental outcomes were assessed using the *Bayley Scales of Infant Development-Third Edition (Bayley-III),* a standardized and widely utilized measure of infant neurodevelopment (Bayley, 2006). The *Bayley-III* consists of outcomes across four domains: cognitive, language (receptive and expressive communication), motor (gross and fine motor), and social-emotional development. Social-emotional development is measured via a parent report questionnaire whereas the cognitive and motor domains are assessed with standard, objective tasks.

2.3. Assessment of the quality of caregiver-infant interactions

The evaluations of caregiver-infant interactions for the present study sub-sample took place during home visits with primary caregivers when infants were between one and two years of age. Caregiver-infant interactions were assessed, on average, 8.6 months after infant neurodevelopmental outcomes were assessed with the *Bayley-III*. Quality of parenting behaviors have been shown to display considerable stability over the first 6 years of life (Dallaire and Weinraub, 2005; Landry et al., 2001; Holden and Miller, 1999). Thus, the caregiver-infant interactions that were measured in the current study were used to estimate caregiver-infant behaviors that would have been expected at an earlier age.

The data collector (A.D.) remained blinded to *Bayley-III* scores and prenatal pesticide exposure levels until the data were coded and ready to be analyzed. The quality of caregiver-infant interactions was assessed using the *Parent-Child Interaction Teaching Scale of the Nursing Child Assessment Satellite Training (NCATS*; Sumner and Spitz, 1994), a structured teaching task designed for use with children from birth to 36 months of age, based on Barnard's bidirectional and transactional framework of child development (Guralnick, 1997). The *NCATS* is a practical observational measure of caregiving interactions (Byrne and Keefe, 2003), which has been widely utilized in research and clinical contexts, including several diverse and high-risk populations in the U.S. such as Hispanic immigrants (Fuller et al., 2010; Leidy et al., 2010) and low-income Hispanic communities (Ayala et al., 2010; McCabe et al., 2010). In addition, it is one of the few measures to have been validated with Spanish-speaking populations (Sumner and Spitz, 1994). In this task, caregivers are guided to select a developmentally appropriate task that they have not yet seen their child perform (e.g., stack blocks). Caregivers are then provided with the materials for the task and asked to try and teach the task to their child. Each interaction is scored on 73 items across six subscales, with each item coded in a binary manner (observed/not observed). Four of the subscales measure the caregiver's contribution to the interaction (*Sensitivity to Cues, Response to Distress, Social-Emotional Growth Fostering,* and *Cognitive Growth Fostering*) and two of the subscales measure the child's contribution (*Clarity of Cues* and *Responsiveness to Caregiver*). The number of observed behaviors is summated for each subscale and for the total scales, resulting in an *Overall Caregiver-Child Interaction* score, a *Caregiver Total* score, a *Child Total* score, and individual scores for each of the six subscales with higher scores reflecting more positive interactions.

Each interaction was video-taped and later independently coded by two trained raters, who each underwent a comprehensive training and achieved the required research reliability of 90% in the administration and scoring of the *NCATS* (ICC = 0.89).

2.4. Maternal interviews and assessment of social-environmental factors

Socio-demographic and occupational information, including maternal age, mother and father's years of education, parity, immigrant status (native Costa Rican or immigrant), marital status (married/living together or single), total number of children in household, and total family income, was collected at the baseline interview.

Mother's depression status was assessed via the *Centre for Epidemiological Studies-Depression Scale* (Radloff, 1977) at the same time point. Quality of the home environment, assessed via the *Home Observation for Measurement of the Environment, Short-Form* (Caldwell and Bradley, 1984), and perceived social support, adapted from a version of the *Duke-UNC Functional Social Support Questionnaire* (Broadhead et al., 1988), were also assessed at the one-year visit.

2.5. Adjustment for prenatal mancozeb/ETU and manganese exposures

As part of the ISA cohort, urinary ethylenethiourea (ETU), a specific metabolite of mancozeb, as well as manganese levels in maternal hair and blood (MnH and MnB, respectively) have been used as measures of prenatal mancozeb/ETU and manganese exposures (van Wendel de Joode et al., 2014; Mora et al., 2014). In the current study, to adjust for possible confounding of the associations between caregiver-infant interactions and outcomes of *Bayley-III* by mancozeb/ETU and manganese exposure, we included log10-transformed averaged prenatal urinary ETU and log10 transformed averaged Mn-hair concentrations measured during pregnancy as covariables in our statistical models (see statistical analyses).

We adjusted for these exposures because they have been associated with *Bayley-III* outcomes in our prior work (Mora et al., 2018). In short, in the full ISA cohort sample at 1-year of age, it was found that for girls, higher prenatal urinary ETU was associated with lower social-emotional *Bayley-III* scores [ß per 10-fold increase = −7:4 points (95% CI: −15:2, 0.4)], whilst higher prenatal hair Mn was associated with lower cognitive scores [−3:0 (−6:1, 0.1)]. For boys, higher hair Mn was associated with lower social-emotional scores [−4:6 (−8:5, −0:8)]. We observed null associations for blood Mn, language, and motor outcomes (Mora et al., 2018).

2.6. Statistical analyses

Descriptive and socio-demographic characteristics of participants and quality of caregiver-infant interactions were examined. We identified the items that most contributed to low scores (i.e. negative aspects) and high scores (i.e. positive aspects) on the *NCATS* subscales by determining the behaviors that were observed in less than 50% or in more than 75% of the study sample, respectively. Caregiver-infant interaction scores were compared to the normative data for the U.S. Hispanic population, provided in the *NCATS* manual. The Hispanic normative group was selected as a comparison group in order to obtain a descriptive comparison of caregiving behaviors relative to a Spanish-speaking sample that was as similar as possible to the study sample. The 10th percentile cutoff for the Hispanic sample was used to determine the proportion of dyads with "worrisome scores", indicative of less than optimal interactions (Sumner and Spitz, 1994).

To examine associations between caregiver interactions and neurodevelopmental outcomes, two-tailed Pearson's r correlations were used. We averaged specific gravity-corrected urinary ETU, hair Mn, and blood Mn concentrations across the repeated samples collected for each woman throughout pregnancy. Variables that were not normally distributed, including mean MnH and mean ETU, were $\log_{10}$-transformed. Multiple linear regression analyses were performed separately for each of the *Bayley-III* outcome variables, the four scales and four subtests, to examine associations between the overall quality of caregiver-infant interaction (*NCATS* Overall Interaction score) and each neurodevelopmental outcome, after adjusting for mancozeb and manganese exposures and additional covariates. This resulted in eight distinct regression models designed in the following way: child sex, caregiver age, and maternal education (selected as a proxy for socioeconomic status) were entered as control variables in Block 1; mancozeb metabolite and manganese concentrations (MnH, ETU, and MnB) were entered in Block 2; and the *NCATS* Overall interaction score was entered in Block 3. In addition to the variables deemed to be theoretically important that were included a priori (child sex, caregiver age, maternal education), only those variables that were statistically significant ($p < .05$) at the bivariate level were selected as control variables. Regression diagnostics were run to confirm that there were no collinearity issues in our regression models predicting neurodevelopmental outcome (Variance Inflation Factor < 2 for all covariates retained). All data were analyzed using an alpha level of .05 and effect sizes were tabulated.

3. Results

3.1. Descriptive results

Demographic characteristics of participants are provided in Table 1. The sub-sample was representative of the main ISA study sample in terms of the spread of villages and socioeconomic conditions of mother-infant pairs with respect to family income and parental education levels. There was a tend towards more boys in the sub-sample compared to girls; 50.1% and 49.9% for the full sample versus 60% boys and 40% girls for the sub-samples ($p = 0.10$). At the time of the *Bayley-III* assessment, the infants of the sub-sample (n = 94) had a mean age of 13.1 months of age, 38.3% were first-born, and 88.3% of their primary caregivers were their biological mothers. Mothers and fathers had similar levels of education (mean = 7.2 and 7.1 completed years, respectively) and median reported family income was $120 US per month. Median residential distance to plantation was 267 m, and participants came from 27 different villages throughout the Matina County. All *Bayley-III* scores were normally distributed and, at the

Table 1
Characteristics of study population, a subset from ISA study, at NCATS evaluation (n = 94) unless indicated elsewise.

	n	n (%)	Mean	SD	Min	Percentile 25th	50th	75th	Max
Child Characteristics									
Child's age at time of NCATS (months)	94	–	21.2	3.5	13	19.8	21.0	23.3	30
Child's age at time of Bayley-III (months)	94	–	12.6[c]	1.3	11.4	12.0	12.6	14.0	17.2
Child's sex (% males)	94	56 (60)	–	–	–	–	–	–	–
Child's birth order (% first-born)	94	36 (38.3)	–	–	–	–	–	–	–
Caregiver/parent characteristics									
Proportion of caregivers who were biological mothers	94	83 (88.3)	–	–	–	–	–	–	–
Caregiver's age at time of NCATS (years)	94	–	27.7	9.7	13	21.0	26.0	31.0	70
Mother's age at birth of child (years)	94	–	24.3	6.1	15	19.0	24.0	28.3	41
Mother's marital status (% married or living as married)	94	67 (71.3)	–	–	–	–	–	–	–
Mother's level of education (total years	94	–	7.2	2.5	1	6.0	6.5	9.0	12
Father's level of education (total years)	81	–	7.1	2.9	0	6.0	6.0	9.0	16
Maternal depression (CES-D[a] total score)	93	–	17.2	11.4	0	7.5	14.0	25.0	48
Maternal social support (score out of 50)	93	–	39.3	9.3	15	34	42	47	50
Proportion of mothers who are immigrants (vs. native Costa Rican)	94	17 (18.1%)	–	–	–	–	–	–	–
Proportion of mothers who used any substances (i.e., smoking, drugs or alcohol) during pregnancy	94	8 (8.5%)	–	–	–	–	–	–	–
Proportion of mothers who performed any agricultural work (including work at banana plantation) during pregnancy	94	15 (16.0%)	–	–	–	–	–	–	–
Family income per capita (USD$ per month)	84	–	139.3	78.8	16	82.9	120.0	175.0	380
Quality of home environment (HOME[b] score)	94	–	8.0	1.4	5	7	8	9	11
Distance from residence to banana plantation (metres)	94	–	267.0[c]	736.8	0.3	43.5	266.9	712.3	3131
NCATS outcomes									
Caregiver-infant interaction total score	94	–	49.0	5.7	35	44.0	49.0	53.0	61.0
Caregiver total score	94	–	33.6	4.5	23	31.0	24.0	36.25	44.0
Infant total score	94	–	15.3	3.1	8	14.0	16.0	17.0	23.0
Prenatal biomarkers of exposures									
Log_{10} Hair Mn (μg/g)	94	——	0.23	0.5	−0.8	−0.2	0.2	0.6	1.4
Blood Mn (μg/L)	92	–	24.0	7.2	11.3	18.4	23.3	28.5	49.4
Log_{10} Urinary ETU (μg/L-specific gravity adjusted)	94	–	0.5	0.3	0.01	0.3	0.5	0.7	2.1

Abbreviations: Mn manganese; ETU ethylenethiourea; SD standard deviation; *NCATS* Nursing Child Assessment Satellite Training Teaching Scale.
[a] Center for Epidemiologic Studies Depression Scale (CES-D); scored out of 60.
[b] HOME = Home Observation for the Measurement of the Environment scale; scored out of 12.
[c] Median reported.

Table 2
One-year Bayley-III outcome scores, reported as z-scores and percent falling below the average range, for the study sample.

Bayley-III Scales and Subtests	*n*	Mean (SD)	Range	n (%) < 1 SD[a]
Cognitive scale composite	94	−0.14 (0.88)	−2.54 – 1.87	8 (8.5)
Language scale composite	94	−0.64 (0.38)	−1.73 – 0.40	12 (12.8)
Receptive communication subtest[b]	94	−0.20 (0.81)	−1.56 – 2.38	33 (35.1)
Expressive communication subtest[b]	94	−0.21 (0.89)	−2.07 – 2.01	8 (8.5)
Motor scale composite	91	−0.05 (0.55)	−1.20 – 1.20	3 (3.3)
Fine motor subtest[c]	91	−0.12 (0.89)	−1.35 – 2.87	8 (8.8)
Gross motor subtest[c]	94	−0.19 (0.99)	−2.96 – 1.58	3 (3.2)
Social-emotional scale composite	94	0.09 (0.95)	−2.18 – 2.23	25 (26.6)

Abbreviations: SD = standard deviation.
[a] Percent of sample having a standard or scaled score less than one SD below the mean (i.e., Standard score ≤ 85 or Scaled score ≤ 7).
[b] Correlations between Receptive and Expressive subtests (r=56, $p < .001$); Correlations between the Language scale composite and the Receptive (r=.47, $p < .001$) and Expressive subtests (r = .40, $p < .001$).
[c] Correlations between Fine motor and Gross motor subtests (r = .52, p < .001); Correlations between the Motor scale composite and the Fine motor subtest (r = .62, $p < .001$) and Gross motor subtest (r = .66, $p < .001$).

group level, fell within the average range (Table 2). At the time that the *NCATS* was administered, the infants had a mean age of 21.2 months.

3.2. Quality of caregiver-infant interactions

The average teaching time taken by caregivers on the *NCATS* was around three minutes (mean = 181.6 s, *SD* = 77.1), which is within *NCATS* guidelines (Sumner & Spietz, 1994). A total of 17 caregivers (18%) needed more than one trial to teach the task. This was either because the task they initially chose for their children was too easy or too difficult, or because caregivers were uncertain and were assisted with choosing a task that was developmentally appropriate for the child. In the case that the task was too easy or too difficult, the next task on the list was attempted. The very last trial was coded in every case. The majority of infants (90.4%) were in the "quiet alert" state during the teaching interaction, which is considered the ideal state for the administration of this task. The remaining nine children were in the "active alert" state, which is also considered an acceptable state for this task.

The mean overall Caregiver-Infant Interaction score was 49 out of a maximum score of 73 points. The average Caregiver total score was 33.6 out of a maximum score of 50, and average Infant total score was 15.3 out of a maximum score of 23. Overall, the infants' contribution to the interaction, as represented by the Infant Total score and the infant subscale scores, was higher relative to caregivers' contribution.

For descriptive purposes, the *NCATS* scores of the study sample

Table 3
NCATS scores in the study sample (n = 94).

NCATS contents	Mean (SD) or *n* (%)	Range
Average time teaching (seconds)	181.6 (77.1)	81 to 452
Proportion of infants displaying potent distress	58 (61.7%)	n/a
Caregiver scales		
Sensitivity to cues (maximum = 11)	8.32 (1.00)	6 to 11
Response to distress (maximum = 11)	8.69 (2.09)	5 to 11
Social-emotional growth fostering (maximum = 11)	7.26 (1.30)	4 to 11
Cognitive growth fostering (maximum = 17)	9.36 (2.33)	3 to 15
Caregiver total (maximum = 50)	33.63 (4.47)	23 to 44
Caregiver contingency items total (maximum = 20)	11.44 (3.02)	3 to 18
Proportion with Caregiver total at/below 10th percentile cutoff score (score of 33 out of 50)*	45 (47.9%)	n/a
Infant scales		
Clarity of cues (maximum = 10)	7.94 (1.37)	5 to 10
Responsiveness to caregiver (maximum = 13)	7.38 (2.12)	2 to 13
Infant total (maximum = 23)	15.32 (3.13)	8 to 23
Infant contingency items total (maximum = 12)	6.89 (1.94)	2 to 12
Proportion with Child total at/below 10th percentile cutoff score (score of 11 out of 23)*	17 (18.1%)	n/a
Caregiver-Infant Overall Interaction Total (maximum = 73)	48.95 (5.70)	35 to 61
Caregiver-Infant contingency items total (maximum = 32)	18.70 (4.20)	7 to 29
Proportion with Overall total at/below 10th percentile cutoff score (score of 46 out of 73)*	33 (35.1%)	n/a

NCATS = Nursing Child Assessment Satellite Training Teaching Scale.
* Compared to NCATS U.S. Hispanic normative sub-sample (n = 311); indicates the proportion of caregiver-child dyads most at risk (i.e., with "worrisome scores" or less than optimal interactions).

were compared to the normative data for the *NCATS* U.S. Hispanic subsample. The study sample was similar with the *NCATS* U.S. Hispanic normative sample with respect to child's sex, birth order, caregiver age, and mothers' marital status, but differed with respect to the child's age (i.e., the present study sample was older), and to the mother's level of education (i.e., the present study sample had a lower level of education) (Supplemental Table 1). Relative to this normative sample, approximately 35% of the study sample had overall Caregiver-Infant Interaction scores at or below the 10th percentile cut-off score, indicating less than optimal interactions. A greater proportion of caregivers (47.9%) had less than optimal interactions (i.e., 47.9% of the Caregiver Total scores were at/below the 10th percentile) compared to infants (i.e., 18.1% of the Infant Total scores were at/below the 10th percentile).

An analysis of the items on each of the *NCATS* subscales (Table 3) revealed that caregivers lost the greatest number of points on both the *Cognitive Growth Fostering* subscale, specifically items related to describing perceptual qualities of materials, verbal acknowledgement of improvement, and signalling completion of task to child verbally or non-verbally, and the *Social-Emotional Growth Fostering* subscale, specifically items related to praising or cheerleading of child's effort, displaying non-verbal affection, and appropriate positioning of child. However, most caregivers did respond sensitively to their infants' cues (i.e., *Sensitivity to Cues* subscale), except for two items related to the allowance for exploration prior to the first instruction and the provision of praise for child's successes or partial successes. On the *Response to Child's Distress* subscale, which was scored on 61.7% of children who displayed potent distress cues, fewer than half of the caregivers diverted the child's attention or paused the teaching episode in response to the distress, yet most of the caregivers avoided displaying negative responses to child's distress.

An analysis of the two infant subscales showed that most infants displayed very clear cues during the interaction, including facial cues, motor activity, vocalizations and disengagement cues. With regard to *Infants' Responsiveness to Caregiver*, less than half of the infants in the sample displayed behaviors assessed by items such as: smiling at caregiver, following the caregiver's verbalization or non-verbal behavior, and looking at caregiver when caregiver attempted to establish eye contact. Nevertheless, all but two of the infants were able to follow caregivers' alerting behavior and approximately three-quarters of the infant sample vocalized or babbled in response to caregiver's vocalization or non-verbal behavior.

3.3. Correlations

The *NCATS* Overall Interaction score was significantly associated with the *Bayley Language scale* composite score ($r = .24$, $p < .05$) and the *Expressive Communication* subtest ($r = .29$, $p < .01$). None of the exposure variables were associated with the *Bayley-III* outcomes among the subsample of participants included in the current study, consistent with results of the larger study sample in non-sex-stratified analyses (Mora et al., 2018). Finally, in this subsample of 94 mother-infant dyads, we did not find any association between pesticide exposure and quality of caregiving.

3.4. Multivariate results

The association between the *NCATS* Overall Interaction score and the *Bayley Expressive Communication* subtest was significant in the adjusted regression model. Infants' expressive communication scores were one-third of a standard deviation higher for every 10-point increase in the overall NCATS Overall Interaction score (ß = 0.03, *95% CI* = 0.01, 0.06) (see Table 4). The *NCATS* Overall Interaction score accounted for an additional 3.1% of the total variance in the model above and beyond variance attributed to confounders ($Adj\ R^2 = .40$, $p < .01$). The *NCATS* Overall Interaction score was not associated with any other outcome on the *Bayley-III* after accounting for covariates.

4. Discussion

We examined the association between early caregiving interactions and neurodevelopmental outcomes of infants who live in rural Costa Rica, an area with intensive banana growing. We found that higher quality of caregiving interactions was associated with better expressive language outcomes in infants, after accounting for maternal exposures to mancozeb as well as hair and blood manganese levels during pregnancy.

Delays in language development are among the most consistent and earliest outcomes found among children living in poverty and among pesticide-exposed children (Handal et al., 2008; Perkins et al., 2013). Our findings are particularly relevant when considering the low education levels of the mothers in our sample given that parents with low education are less likely to use complicated syntax and diverse vocabulary (Hart and Risley, 1995). Considering that caregivers' capacity to

Table 4
Adjusted[a] associations between NCATS overall interaction score and Bayley III outcomes, controlling for relevant covariates.

Bayley-III Scale	Overall Interaction total ß (95% CI)
Cognitive	0.00 (−0.04, 0.03)
Language	0.01 (−.002, 0.03)†
Receptive Communication	0.00 (−0.02, 0.3)
Expressive Communication	0.03 (0.01, 0.06)*
Motor	0.02 (−0.01, 0.04)
Fine Motor	0.01 (−0.02, 0.04)
Gross Motor	0.01 (−0.03, 0.05)
Social-emotional	0.02 (−0.01, 0.05)

[a] Adjusted for child sex, child age at Bayley testing, caregiver age, prenatal logETU (μg/L), MnB (μg/L), and logMnH (μg/g) concentrations.
* $p < .05$.
† $p < .10$.

foster cognitive and social-emotional growth in their children may also be attenuated by the effects of their exposure to contaminants, lower education, long workdays, and poverty induced stressors, makes these areas especially worthy of interventions.

The *Cognitive growth-fostering* and *Social-emotional growth fostering* subscales of the *NCATS* contributed most to Expressive language outcomes in infants; both of these subscales emphasize parents' ability to provide verbal and nonverbal stimulating experiences for the infant (Sumner and Spitz, 1994). These findings suggest that stimulation and growth-fostering behaviors, such as encouraging and praising children's efforts, may be important areas to target when developing interventions with this population. Both verbal and nonverbal stimulation are strongly related to the development of cognitive and language abilities in children growing up in poverty (Allhusen et al., 2001; Brooks-Gunn et al., 2002) and help to develop the attachment security and self-esteem of children facing environmental stressors (e.g., Bakeman and Brown, 1980; van Ijzendoorn, 2005).

Infants in our sample displayed clear verbal and non-verbal cues and appropriately responded to caregivers, a finding that was consistent with infants' one-year neurodevelopmental outcomes (as measured by the *Bayley-III*), which were within the average range for the majority of the group. Further, most caregivers displayed sensitivity to infants' cues and responsiveness to infants' distress. However, many caregivers in the study sample struggled with some aspects of caregiving, especially those involving stimulation and the fostering of infants' cognitive and social-emotional development. Caregivers tended to provide insufficient praise to their child, limited face-to-face contact, limited use of a variety of descriptive words during the task, and infrequent allowance for task exploration. Most caregivers in our sample were responsive to children when they showed distress cues, but had difficulty responding immediately to infants' non-distress cues. Specifically, caregivers obtained lower scores on behaviors that are contingent upon timely responsiveness to infant cues (i.e., contingency items on the Caregiver subscales). The developers of the *NCATS* identify contingency as a major component of caregiving and a key process in the shaping of behavior (Sumner and Spitz, 1994). Positive contingent responses are seen to help create behavioral patterns by providing a mechanism by which children begin to understand the relationship between behavior and environment. On the other hand, infants' responsiveness to caregivers might have also contributed to the interactions since the *Responsiveness to Caregiver* subscale consists almost exclusively of contingency items, reflecting the bi-directional transactional nature of caregiving. Moreover, infants' responsiveness to their caregivers was moderately associated with caregivers' ability to foster social-emotional growth, suggesting that infant behaviors contribute to and are dependent to some extent on the caregiver's capacity to stimulate the infant.

Our sample was compared to the cut-off scores (i.e., the score obtained by ten percent or less of the subsample) provided in the *NCATS* manual for the U.S. Hispanic subsample; scores below this cut-off indicate the proportion of the study sample at highest risk of poor quality of caregiver-infant interactions. We found that over one-third of the overall caregiver-infant interaction scores in our sample were at or below the cut-off score, and about half of the scores representing the caregivers' contribution were at or below the cut-off, compared to only 18% of the scores reflecting the infants' contribution. These results suggest that caregiver behaviors contributed most to the overall interaction quality. Although the U.S. Hispanic subsample was chosen as the comparison group, they differed from the present study sample on two important characteristics: the age of children at the time of the *NCATS* assessment (i.e., the U.S. Hispanic infants were younger by about seven months), and the level of education of the mothers (i.e., the U.S. Hispanic mothers had an average of 12 years of education, compared to an average of seven years in our sample). Thus, the low scores in the current sample should be interpreted with caution because these are relative to the Hispanic normative group to which it was compared. If the higher cutoff scores from the other *NCATS* ethnic subsamples (i.e., U.S. Caucasians and African-Americans) were used instead, then an even greater number of individuals in the current sample would have been identified as having "worrisome" scores.

A mayor methodological constraint of this study is that quality of caregiver-infant interaction was assessed about eight months after measuring infant development. It is possible that interaction changed in the eight months after *Bayley-III* assessment. Thus, the current design of this study cannot demonstrate causation because the modifier of interest (caregiving) was not measured prior to the neurodevelopmental evaluation. That said, quality of parenting behaviors has been shown to display considerable stability over the first six years of life (Dallaire and Weinraub, 2005; Landry et al., 2001; Holden and Miller, 1999). A prior study (Dallaire and Weinraub, 2005) examining sensitive and responsive parenting behaviors over a time period of six years, reported correlation coefficients in the range of .30-.35, suggesting that our measure of parent-child interaction is a reliable proxy for behaviors that would have been exhibited eight months before.

Another limitation of this study is its relatively small sample size. In the full sample of the ISA cohort at one year of age that included 355 mother-infant pairs, sex-specific effects were observed for the associations of urinary ETU and hair manganese concentrations with infant cognitive and socioemotional development; these associations were weaker, or absent, when considering boys and girls together (Mora et al., 2018). Yet, in the current study we were unable to study possible effect modification by infants' sex, whereas quality of caregiving interactions might have different effects on development of boys and girls. This limited our ability to draw conclusions about any potential buffering effect of caregiver-infant interaction. Finally, our analysis did not include other biomarkers of pesticide exposure that have been associated with neurotoxicity, such as chlorpyrifos. Consideration of overall burden of exposure could indicate an even greater potential for the caregiving environment because there may be more potential for amelioration based on adverse effects from multiple neurotoxic exposures. Future studies should look at the role of caregiving in association with the potential synergistic effects of multiple chemical exposures.

Overall, our results are comparable to other studies' findings that have evaluated caregiving using the *NCATS* with other ethnic groups, such as Native Americans (Seideman et al., 1992), Alaskan Inuit (MacDonald-Clark and Harney-Boffman, 1994), and Canadian Aboriginals (Letourneau et al., 2005). These studies also documented lower than average quality of interaction when compared to *NCATS* normative data, perhaps reflecting cultural differences in caregiving and the lower socioeconomic status of the study samples, which may also be the case in our study. Certain cultural modifications needed to be made to the *NCATS* (i.e., changing some words to more culturally and regionally relevant words, and elaborating on instructions) in order to adapt the task to the cultural context of Costa Rica, and of Limon in particular. Factors such as maternal education and availability of stimulating materials, which are intrinsically linked with socioeconomic status, might have also impacted the results.

In summary, our findings suggest that aspects of caregiver-infant interactions are associated with early neurodevelopmental outcomes after accounting for important confounds and controlling for pesticide exposure. A prospective design is necessary to determine whether high-quality caregiver-child interactions in the early years can help to mitigate the impact of poverty and prenatal exposure to neurotoxins on cognitive and socioemotional outcomes, and foster the underlying skills required for language development.

Conflict of interest

The authors declare no conflict of interest.

Transparency document

The Transparency document associated with this article can be found in the online version.

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Appendix A. Supplementary data

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