

PLACENTAL PROGRAMMING OF INFANT NEGATIVE AFFECT: EXAMINING THE ROLE OF INTERLEUKIN-6

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BACKGROUND

- The prenatal environment shapes offspring outcomes, influencing both physical and psychological development.
- Prenatal factors (e.g., maternal stress, dietary quality, body composition, etc.) are linked to infant growth and behavioral health.
- Head circumference is a crude measure of brain growth and alterations in head circumference trajectories are associated with a range of neurodevelopmental disorders.
- Infant negative affect, or propensity to experience a range of negative emotions (irritability, fussiness, difficulty soothing, etc.) can impact parent-child relations, early social development, and long-term emotional well-being, and is an early risk factor for emerging developmental psychopathology.
- Inflammation is a hypothesized mechanism through which risk factors, including the risk for altered growth and psychopathology, are conferred from parent to child.
- The placenta plays a crucial role in fetal development, acting as a barrier and a source of various cytokines.
- Interleukin-6 (IL-6) is an inflammatory cytokine that has been implicated in physiological and pathological processes during pregnancy.

METHODS

Participants:

- $N = 302$ mother-infant dyads (73% White, non-Hispanic; $M_{age} = 31.97$).

Delivery Sample Collection:

- Placentas ($n = 209$) were biopsied following delivery and samples were banked.
- High sensitivity ELISAs were conducted to assess IL-6 levels in placental homogenate.

Head Circumference:

- Captured at birth via Electronic Medical Record review and during in-laboratory assessments at 6 months and 12 months.
- Head circumferences were z-scored, adjusted for age and child sex, and percentiles were calculated using the Cumulative Distribution Function.

Negative Affect Assessment:

- Laboratory observations were coded using the validated, Gentle Arm Restraint Task, consisting of three episodes:

- Baseline** (30 sec): Infant has access to desirable toy
- Restraint** (30 sec): Caregiver gently restrains infant's arms
- Recovery** (30 sec): Infant is given free access to toy

Data Analysis:

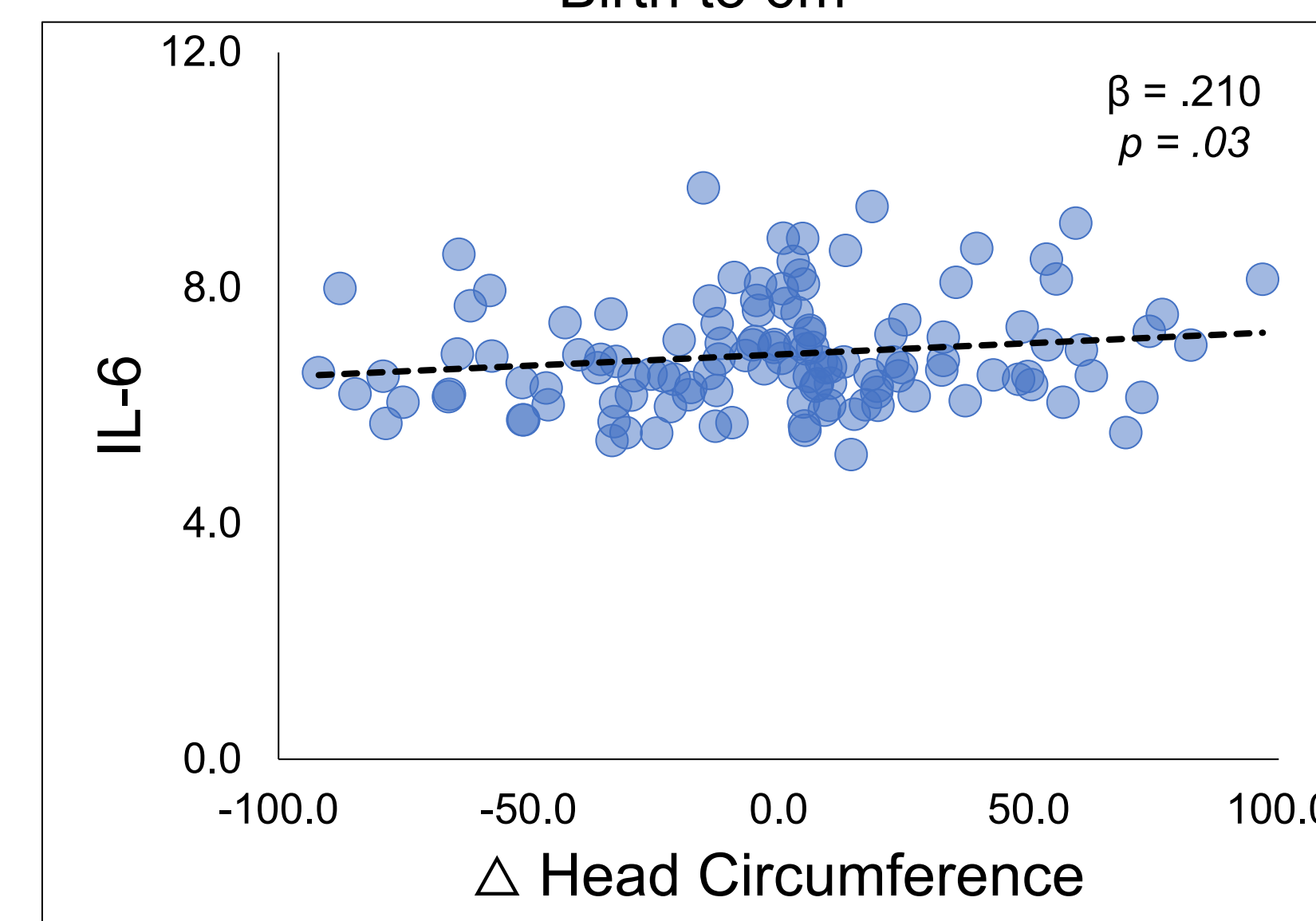
- Structural equation models using robust maximum likelihood estimator were conducted in *Mplus*.
- All models were adjusted for relevant covariates.

RESULTS

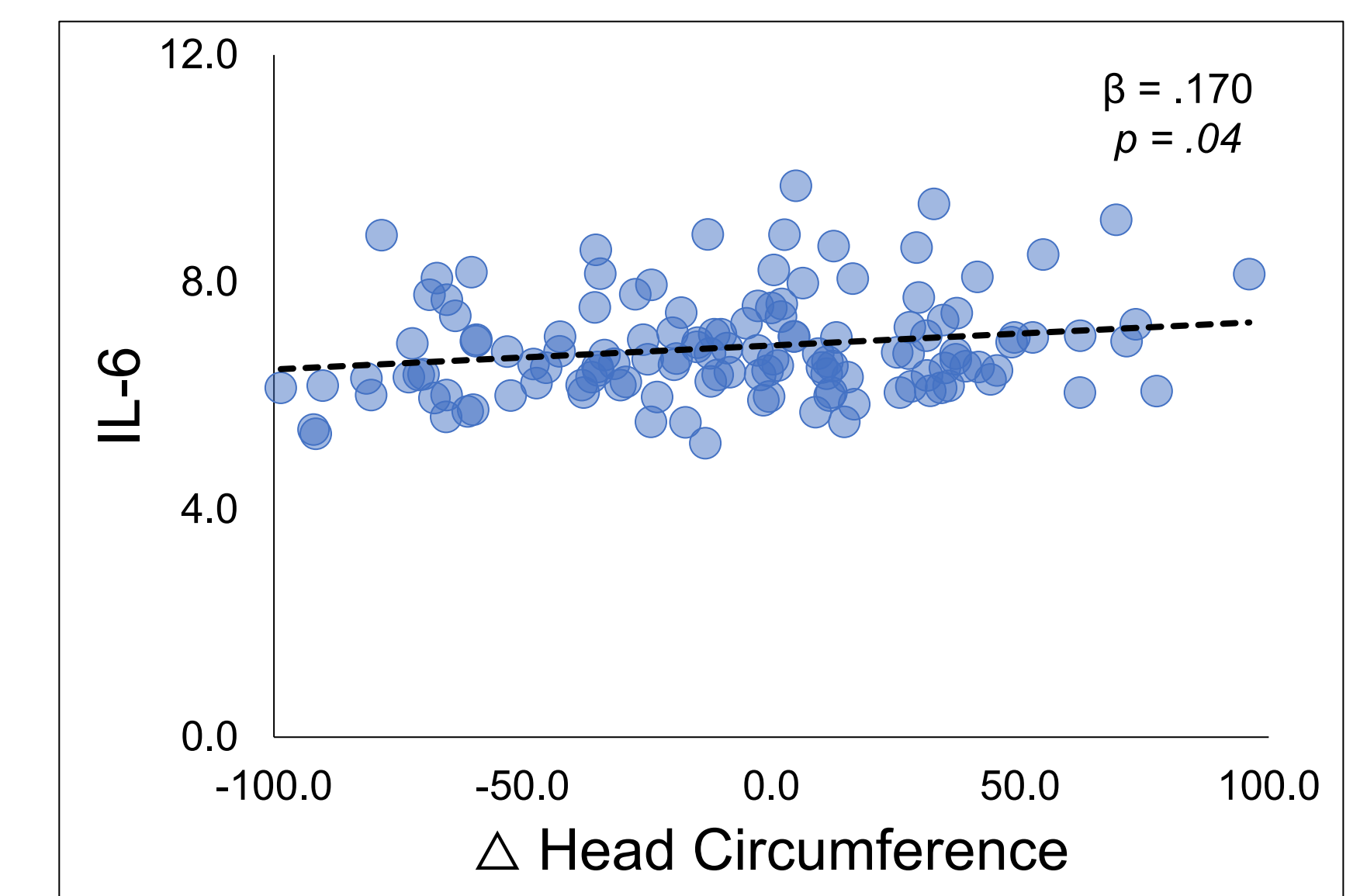
Placental IL-6 and infant head circumference trajectories



Head Circumference Percentile Change from Birth to 6m

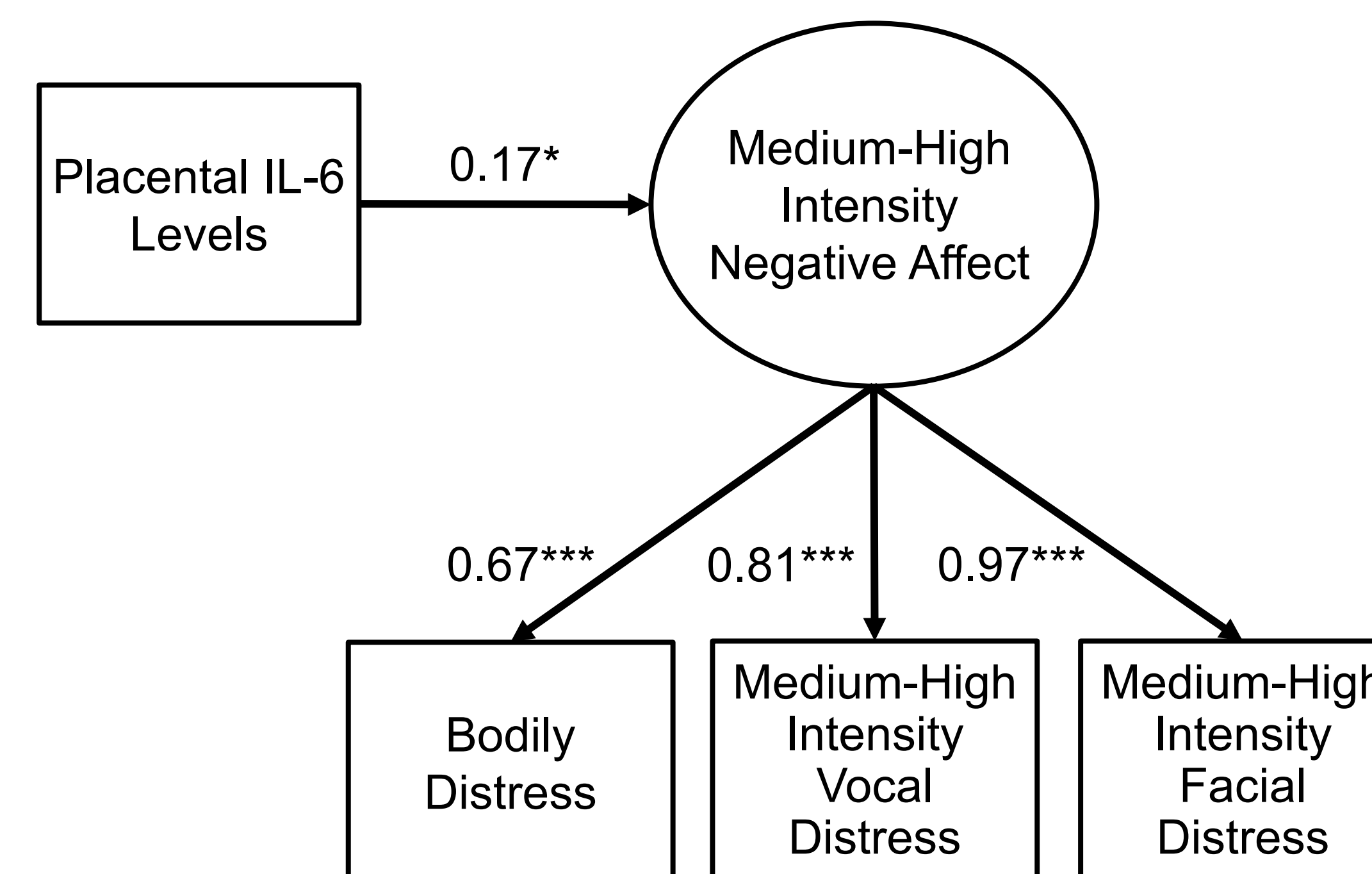
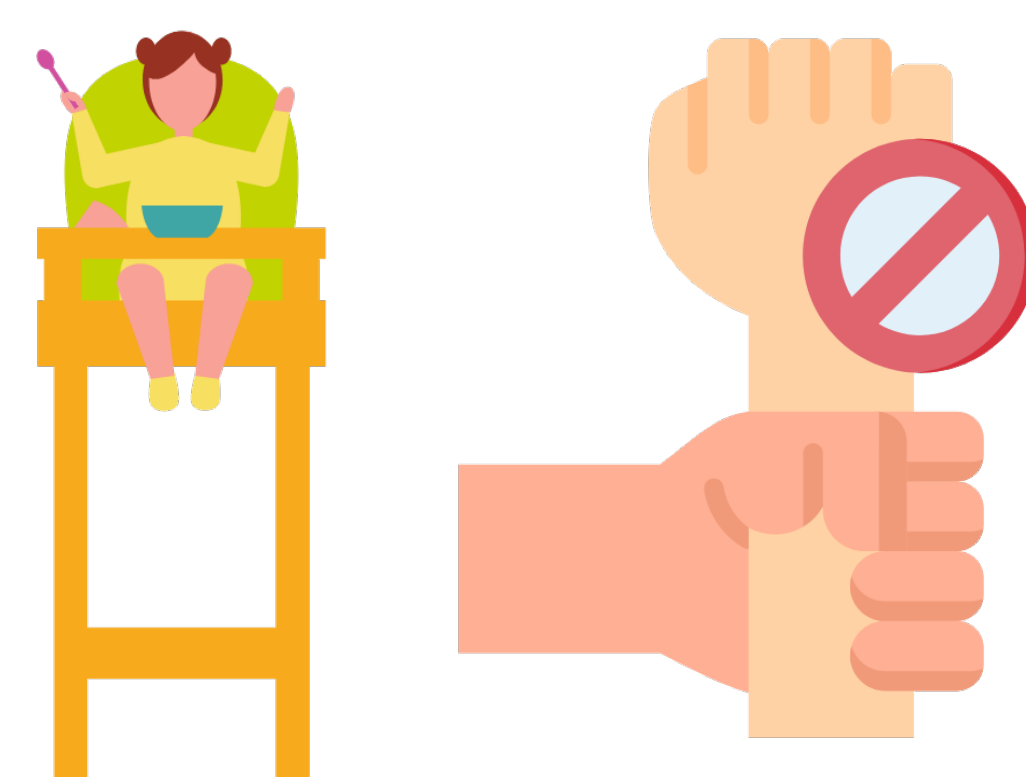
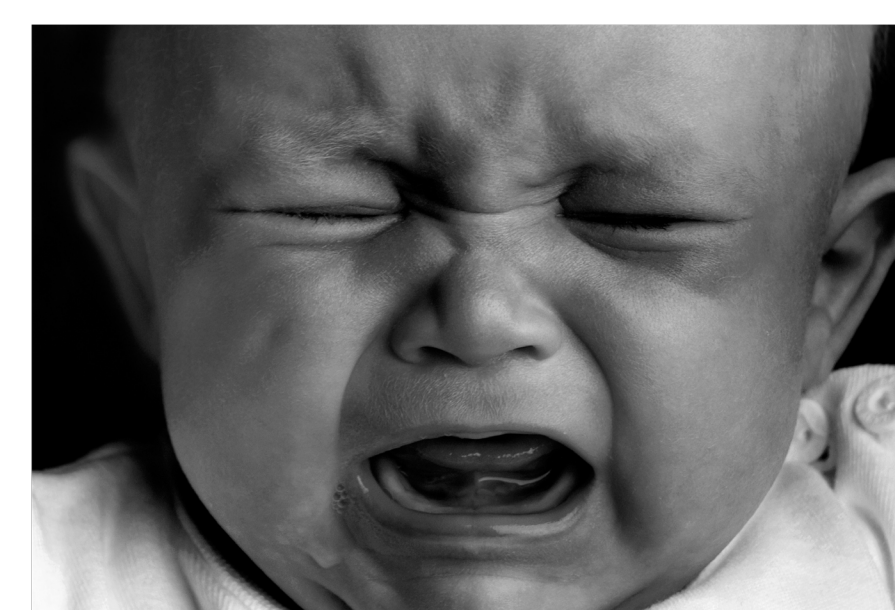


Head Circumference Percentile Change from Birth to 12m



Note. All estimates adjusted for maternal age, child sex, gestational age at birth, race/ethnicity, income, and birthweight.

Placental IL-6 and infant negative affect at 6 months



$\chi^2(10) = 16.03$; CFI = 0.98; TLI = 0.97; RMSEA = 0.05; SRMR = 0.03
Note. Adjusted estimates are depicted.

Predictors of Infant Negative Affect at 6 months

	Estimate	S.E.	P value
Placental IL-6	0.18	0.05	0.04
Maternal Age	-0.01	0.07	0.90
Maternal Race/Ethnicity	0.01	0.07	0.90
Prenatal Vitamin Use	-0.04	0.06	0.50
Household Income	-0.11	0.08	0.16
Pushing Time During Labor	-0.28	0.09	0.002
Child Sex (male)	0.03	0.07	0.79
Gestational Age at Birth	0.15	0.08	0.06
Born Pre-pandemic	-0.07	0.07	0.34
Maternal CES-D ¹	0.07	0.07	0.34
Remote Assessment	-0.09	0.07	0.17

Note. Bolded items indicate significance. ¹Center for Epidemiological Studies Depression Scale.

CONCLUSIONS

- Placental IL-6 levels predicted accelerated head circumference growth over the first year of life and infant negative affect at 6 months of age.
- Effects were robust and survived adjusting for a wide range of relevant covariates, suggesting that the effects independent of other maternal, child, or environmental factors.
- Early identification of biomarkers that predict infant negative affect is a key step toward development of targeted intervention strategies to optimize infant behavioral and mental health outcomes.

Future directions:

- Identifying maternal factors that influence placental IL-6 expression, such as adipose tissue, dietary quality, and emotional health.
- Relating maternal factors to infant behavioral health and testing the mediating role of placental IL-6 in these associations.
- Exploring the role of placental inflammation on other infant outcomes, including cardiometabolic health outcomes.

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