



Quality of Maternal Interaction Ameliorates the Effects of Prenatal Alcohol and/or Opioid Exposures on Infant's Emotional Regulation at 6 Month of Age

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Background

- Delayed/inaccurate diagnosis of children with FASD
- Age of diagnosis < 6 yoa – resilience factor (Streissguth, 1996)
- **Pressing need to focus on:**
 - **Early bio-behavioral measures (1st year of life)**
 - **Modifiable resilience factors to improved long-term outcomes**
- Emotional dysregulation, impulse controls, ‘negative affectivity’, irritability – key behavior domains (Kable, 2015)
- Dysregulation of HPA function following PAE
- Higher levels of maternal sensitivity are associated with more regulated infant behaviors (Cunning, 2013)
- Supportive parenting style as a resilience factor in FASD

Goal of this Study

- In ENRICH birth cohort, evaluate the role of:
 - a) prenatal exposures (to alcohol, opioids, and their combination)
 - b) postnatal environment (maternal contingent responsiveness)on infant affect at 6 months of age



ENRICH Study

Ethanol Neurodevelopment Infant and Child Health



NIAAA 1 R01 AA021771 (2013-2018)

MPIs: Ludmila Bakhireva (UNM) / Julia Stephen (MRN)

“Early Indices of Atypical Neurodevelopment Associated with Fetal Alcohol Exposure”

Co-Investigators: Jean Lowe, Dan Savage, William Rayburn, Larry Leeman

Main Goal & Study Groups

Main goal: Identify neurophysiological indices of sensorimotor deficits in 6- & 20-month-old infants associated with PAE using:

- magnetoencephalography (MEG) & EEG
- behavioral measures of self-regulation & early working memory.

Study groups (total n=160 maternal-infant pairs):

- Alcohol
 - MAT
 - Alcohol+MAT
 - HC (frequency match by SES)
- No methamphetamines, cocaine, MDMA (ecstasy)
- Adjust for tobacco, marijuana & other co-exposures
- Lifelong abstainer from illicit drugs & tobacco
Negative on a battery of ethanol biomarkers, urine drug tests (prospective, repeated measures)

Key Assessments in ENRICH

V1 (prenatal)	V2 (after delivery)	V3 (6 months)	V4 (20 months)
Demographics	Pregnancy complications & outcomes	Sensory processing	
Medical & reproductive health	Nutrition: Block FFQ	MEG sensory* Sensory Profile	MEG sensory* Sensory Profile
Maternal biomarkers: GGT, %CDT, PEth, uEtG, uEtS	Maternal biomarkers: GGT, %CDT, PEth, uEtG, uEtS	Cognitive & early working memory	
Alcohol use: TLFB ₁ , TLFB ₂	Alcohol use: TLFB ₃	BSID-III	BSID –III A-not-B task*
Smoking (self-report, urine nicotine & metabolites)	Smoking (any changes since V1)	Self-regulation	
Drug use (self-report, urine drug screen, medical records)	Drug use (self-report, urine drug screen, medical records)	Still-face paradigm* IBQ-R	C-CARES* Snack Delay* ECBQ
	Newborn biomarker: PEth-DBS	Motor & cortical connectivity	
	Growth measures	MEG (mu rhythm)* BSID-III Motor Scale	MEG (mu rhythm)* BSID- III Motor Scale

*Experimental paradigms

V3, V4 Also include assessments of depression (DBI), stress (Parenting stress index), maternal language (C-CARES), breastfeeding, family SES & postnatal environment

The Still-Face Paradigm (SFP): Overview

- SFP developed by Tronick et al to measure infants' role in social interactions & infant/maternal responses to interruptions in play
- Social stressor & proxy measure of:
 - Infant emotional development & regulation
 - mother-infant interactions
- Modified SFP (5 episodes):
 - Episode 1: Baseline interaction (play)
 - Episode 2: **SFP-1**
 - Episode 3: Reunion 1 (play)
 - Episode 4: **SFP-2**
 - Episode 5: Reunion-2 (play)



Tronick, E., Als, H., Adamson, L., Wise, S., & Brazelton, T. B. (1978). Infants response to entrapment between contradictory messages in face-to-face interaction. *Journal of the American Academy of Child and Adolescent Psychiatry*, 17, 1–13

The SFP: Infant Affect

- **Infant Affect** (120 second within each episode)

-3	-2	-1	0	1	2	3
rhythmic crying	shorter cry, protest or yell	mild fuss, frown	neutral	corners of the mouth straight, soft coo	corners of the mouth go up, chuckle or small giggle	Laugh
Negative affect				Positive affect		



- Outcome:
 - % of time the infant displayed positive/negative affect over the duration of each 120-second episode

The SFP: Types of Maternal Responsiveness

- **Maternal Interaction** (during 'play' episodes 1,3,5):
 - **Contingent Responsiveness** (mother mimics infant's behavior or plays interactive game)
 - **Watching**
 - **Attention Seeking**
- Videos are coded by 2 independent raters
- Inter-rater reliability:
 - 0.76-0.91 for infant affect
 - 0.94-0.99 for maternal interaction



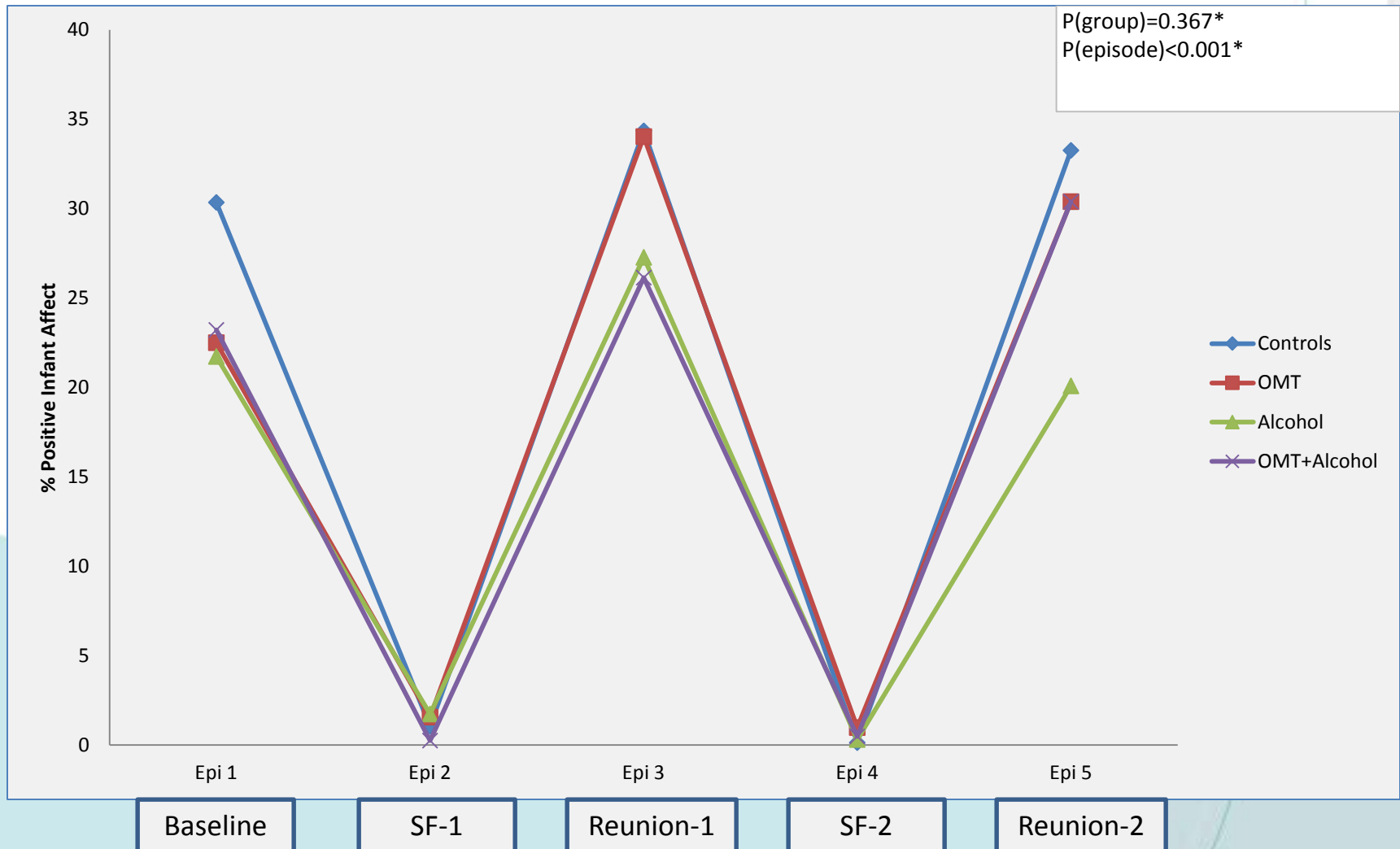
Study Sample: Demographics

- 88 subjects who completed the three study visits
- LTFU rate: *only 4.2% between V1 & V3!*
- Mean gestational age at recruitment: 24.6±8.1 weeks
- Race/ethnicity:
 - 61.4% Hispanic/Latina
 - 4.6% African American
 - 4.6% American Indian
- Maternal education:
 - 29.6% < high school education
 - 54.6% high school/ some college
 - 15.9% college degree or above

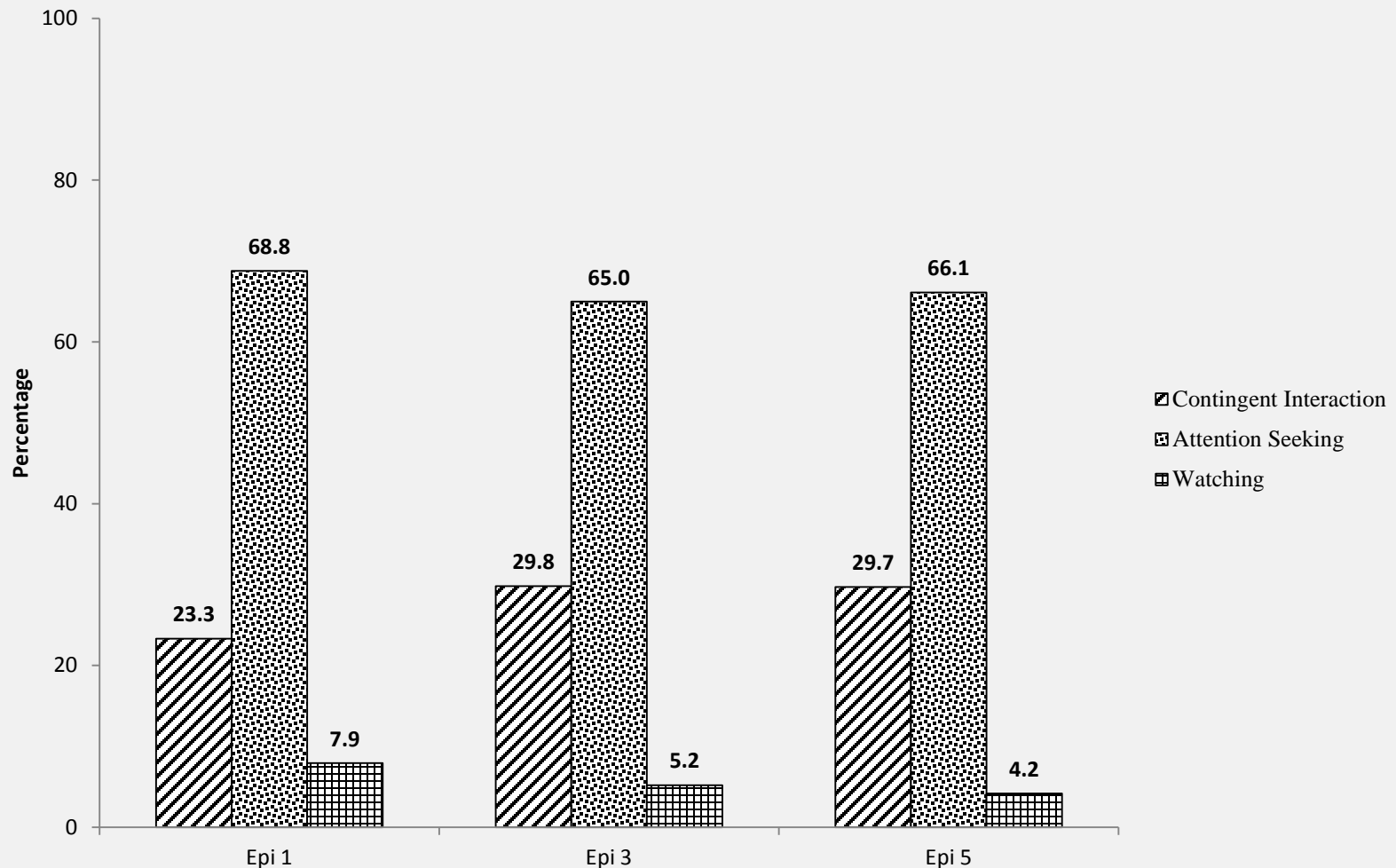
Study Sample: Substance Use Patterns

- Cohort with “moderate” PAE by design
- All PAE subjects meet or exceed the “more than minimal exposure” (≥ 13 SDUs in any 30-day period of pregnancy) criterion specified in the DSM-5 guidelines for ND-PAE
- Majority tested positive for at least one ethanol biomarker:
 - 53.8% of Alcohol group
 - 59.1% Alcohol+MAT group
- Co-exposure with marijuana was common (33.3%-46.2%) but similar among 3 exposed groups
- Co-exposure with tobacco was common:
 - 72.2% in MAT; 25% in Alcohol; 63.6% in Alcohol+MAT

Variability of Infant Positive Affect during the SFP



Different Types of Maternal Interaction with Infants during the “Reunion Episodes”



Predictors of Positive Infant Affect:

Results of Multivariable Mixed Effect Modelling

Predictors	$\hat{\beta}$	p
Exposure		0.095
MAT	-4.21	0.280
Alcohol+MAT	-8.46	0.017
Alcohol	-5.88	0.138
Controls	Reference	
SF Episode		0.601
5	-1.47	0.389
3	0.22	0.901
1	Reference	
Maternal Contingent Responsiveness	0.87	<.001
Infant age	-0.08	0.946
Infant gender		
Male	-1.68	0.529
Female	Reference	
Maternal education		0.152
College or higher	-8.77	0.054
HS/Some college/vocational	-2.71	0.379
Less than HS	Reference	

Determinants of Explained Variability in Infant Positive Affect

Model	Primary exposure and Independent variables	RSS	R ²
0	Intercept only	153,023	NA
1	Covariates only (SF episode, infant age, infant gender, and maternal education)	139,044	0.09
2	Study group + covariates (SF episode, infant age, infant gender, and maternal education)	136,771	0.11
3	Maternal Contingent Responsiveness + covariates (SF episode, infant age, infant gender, and maternal education)	45,882	0.70

Summary

- Polysubstance use (PAE+MAT) was associated with reduced infant positive affect in response to a social stressor.
- Supportive maternal interaction style had a much stronger effect on infant emotional regulation than prenatal exposures to alcohol and/or opioids.
- Implications for future interventions focusing on specific parenting strategies.

Discussion & Future Directions

Limitations:

- SF is a proxy of stress reactivity
- Relatively small N
- Stronger group effect could be observed with higher PAE
- Tobacco, marijuana co-exposures were prevalent
- Maternal behavior is a more proximal measure of infant behavior than prenatal exposures

Strengths:

- Prospective cohort
- Prospective repeated measures of substance use
- Direct observation of mother-child interaction
- Comparison of PAE & opioid-exposed (similar pre-/postnatal environment) vs HC
- Effect of polysubstance use minimized (no stimulants)

Future Directions

- Effect of maternal contingent responsiveness on other outcomes
- Maternal responsiveness at 6-m vs ND outcomes at 20-m
- Development of early intervention programs: incorporate parenting strategies to encourage maternal contingent responsiveness

ENRICH Team

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