

Neurodevelopmental and Growth Outcomes in Children Breastfed by Lactating Individuals Who Used Cannabis

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Cannabis in Human Milk

- Cannabis is the most commonly used recreational drug among lactating individuals
- The American Academy of Pediatrics advises against using cannabis during lactation
- Several studies have demonstrated the presence of cannabinoids, including delta-9-tetrahydrocannabinol (THC) in human milk
 - Between 1987-2020, ~185 milk samples with cannabis exposure have been analyzed
 - The interquartile median of THC concentrations range from 9.43 ng/mL to 53.5 ng/mL
 - The duration of detection of THC in milk has ranged from 6 days to greater than 6 weeks
- None of these studies included follow up of the exposed children for neurodevelopment or growth

Previous studies of neurodevelopment in children exposed to cannabis during lactation

- One study investigated the relationship between infant exposure to marijuana via breast milk and infant motor and mental development at one year of age using the Bayley Scales of Infant Development
 - 68 exposed and 68 control infants, N=136
 - Cannabis exposure via breast milk during the 1st month post-partum was associated with a **decrease** in infant motor development at one year of age
- Another study on 27 cannabis exposed and 25 unexposed breastfed infants found that occasional maternal cannabis use during breastfeeding **did not** have any discernable effects on the breastfed infants development at one year of age
- **There is a critical need for information on how this exposure may affect the exposed child's neurodevelopment and growth over time**

Neurodevelopmental Outcomes in Children Exposed to Cannabis through Human Milk in the Mommy's Milk Cohort



Study Population

- Between 2014 -2021, 174 lactating individuals who reported cannabis use were enrolled into Mommy's Milk, a large breast milk biorepository at UCSD focusing on human milk research
- Cannabis exposure types and routes included:
 - THC only, THC/CBD combos, and CBD only products
 - Inhalation, edibles (oral), and topicals
 - 137 of these women had used cannabis in the last 24 hours and they typically use ≥ 1 time per day
- These were frequency matched 1:n on infant/toddler sex and age to children of individuals enrolled in Mommy's Milk who did not report cannabis use during lactation and completed the same neurodevelopmental questionnaires

Study Design and Data Collection

Study Design

- Participants completed child development questionnaires when their child was between 4 months and 36 months of age
- Age-appropriate assessments were completed up to 4 times during this period

Data Collection

- The maternal questionnaires included:
 - Ages and Stages Questionnaires (ASQ): 3-36 mo.
 - Infant Toddler Social Emotional Assessment (ITSEA): 12-36 mo.
 - MacArthur-Bates Communicative Development Inventories (CDI): 12-16 and 16-30 mo.
 - Modified Checklist for Autism in Toddlers (M-CHAT): 12-36 mo.

Statistical Analysis

- Scores for each instrument were compared between cannabis exposed and unexposed children
- Odds ratios (OR's) and 95% confidence intervals (CI's) were obtained from logistic regression of binary scores (critical concern vs no concern for that assessment) on exposure yes/no
 - The model was adjusted using propensity score (PS) for maternal age, education, income, age and sex of the child
- Multiple imputation was conducted to handle the limited number of missing values for covariates

Ages and Stages (ASQ) Results

N = 92 exposed and N = 452 unexposed

	Unadjusted OR (95% CI)	PS-Adjusted OR (95% CI)
ASQ		
Communication: Critical	0.86 (0.35, 2.11)	0.76 (0.24, 2.45)
Gross Motor: Critical	1.79 (0.68, 4.66)	1.55 (0.42, 5.71)
Fine Motor: Critical	2.01 (0.62, 6.55)	3.26 (0.77, 13.81)
Problem Solving: Critical	1.24 (0.34, 4.47)	0.63 (0.10, 3.83)
Personal-Social: Critical	1.31 (0.48, 3.60)	1.90 (0.54, 6.65)

There were no significant group differences in any domain on the Ages and Stages Questionnaire between the cannabis-exposed children and the unexposed children.

Infant and Toddler Social and Emotional Results

N = 75 exposed and N = 416 unexposed

	Unadjusted OR (95% CI)	PS-Adjusted OR (95% CI)
ITSEA		
Externalizing: Critical	2.04 (0.83, 5.00)	1.29 (0.37, 4.44)
Internalizing: Critical	0.92 (0.26, 3.21)	1.08 (0.23, 5.07)
Dysregulation: Critical	2.74 (1.32, 5.70)	1.34 (0.48, 3.75)
Competence: Critical	1.29 (0.36, 4.65)	1.26 (0.24, 6.54)

There was a significant group difference on the ITSEA in the dysregulation domain between the cannabis-exposed and unexposed groups during lactation *prior* to adjustment. After adjustment for maternal age, education and income, this result was no longer significant.

MacArthur Bates CDI Results

N = 52 exposed and N = 378 unexposed for W&G
N = 37 exposed and N = 160 unexposed for W&S

	Unadjusted OR (95% CI)	PS-Adjusted OR (95% CI)
MacArthur-Bates W&G		
First Signs of Understanding: No 1+	0.44 (0.06, 3.42)	0.43 (0.04, 4.70)
Phrases Understood: Critical	0.32 (0.08, 1.36)	0.46 (0.09, 2.26)
Starting to Talk: No 1+	0.54 (0.30, 0.98)	0.82 (0.39, 1.75)
Vocabulary Checklist: Critical	0.46 (0.19, 1.11)	0.65 (0.24, 1.80)
Actions and Gestures: Critical	0.67 (0.25, 1.75)	0.81 (0.26, 2.54)
MacArthur-Bates W&S		
Words Children Use: Critical	1.03 (0.36, 2.95)	0.90 (0.23, 3.44)
How Children Use Words: Critical	1.77 (0.83, 3.75)	1.46 (0.56, 3.78)
Word Forms: <u>Critical^a</u>	----	----
Combining: Critical	0.36 (0.08, 1.60)	0.38 (0.06, 2.37)
Complexity: <u>Critical^a</u>	----	----

There was a significant group difference on the Words and Gestures in the Starting to Talk domain between the cannabis-exposed and unexposed groups during lactation prior to adjustment.

After adjustment for maternal age, education income, sex of infant this result was no longer significant.

M-CHAT Results

N = 45 exposed and N = 170 unexposed

	Unadjusted OR (95% CI)	PS-Adjusted OR (95% CI)
M-CHAT		
Items Failed: Critical	1.53 (0.29, 8.18)	0.40 (0.04, 4.08)

There were no group differences in any domain on the M-CHAT screening instrument for autism between the cannabis-exposed children and the unexposed children.

Growth Outcomes in Infants Exposed to Cannabis through Human Milk in the Mommy's Milk Cohort



Study Design and Data Collection

Study Design

- Breast milk samples from 172 mothers who **reported** cannabis exposure were assayed for metabolites using LC/MS
 - Concentrations for THC, CBD, and CBN were reported
- Level of THC was above the quantification limit (AQL) in **114 samples**
 - **>1 ng/mL of THC**
- Level of THC was below the quantification limit (BQL) in **58 samples**

Data Collection

- Maternal report of the child's weight, length and head circumference at birth and at the time of sample collection were obtained by maternal interview
- Growth percentiles were assigned using WHO growth curves for breastfed children, 0-2 years of age
- Confirmed with pediatric medical records, and additional growth measurements were captured from the records

Statistical Analysis

- For this analysis, we looked at growth within the cannabis exposed group only
- Linear regression models were constructed for each growth parameter (weight, length, OFC) in each child age category
- The dependent variable was ***growth percentile***
- The predictor variable was ***THC concentrations above the level of quantification (AQL) vs those that were below the level of quantification (BQL)***
- Coefficients for each growth measure (AQL vs BQL) were calculated with 95% CIs
- Models were adjusted for maternal age, education and income, exact age of the child, breastfeeding frequency, for alcohol and tobacco exposure during pregnancy (yes/no), and cannabis use in pregnancy: Unexposed, Exposed in First Trimester, Exposed in Second Trimester, and Exposed in Third Trimester

Child Weight Results

Birth Through 24 Months of Age

Effect of AQL on weight measurements of exposed subjects

	AQL Coefficient	95% Confidence Interval	p-Value
Birth (n = 80)	0.72	(-14.31, 15.74)	0.925
6 Months (n = 66)	-8.63	(-28.84, 11.58)	0.396
12 Months (n = 28)	3.90	(-19.21, 27.02)	0.728
24 Months (n = 20)	9.70	(-19.92, 39.32)	0.486

n: Number of observations with covariate data available for each measurement, selecting one record per pregnancy.

After adjustment, there were no significant differences in child weight percentile at any time point between the cannabis exposed AQL children and the cannabis exposed BQL children.

Child Length Results

Birth Through 24 Months of Age

Effect of AQL on length measurements of exposed subjects

	AQL Coefficient	95% Confidence Interval	p-Value
Birth (n = 76)	4.01	(-12.66, 20.69)	0.632
6 Months (n = 55)	0.20	(-26.72, 27.13)	0.988
12 Months (n = 24)	-19.51	(-55.76, 16.74)	0.269
24 Months (n = 19)	-2.72	(-43.10, 37.67)	0.884

n: Number of observations with covariate data available for each measurement, selecting one record per pregnancy.

After adjustment, there were no significant differences in child length percentile at any time point between the cannabis exposed AQL children and the cannabis exposed BQL children.

Child Head Circumference Results Birth Through 24 Months of Age

Effect of AQL on OFC measurements of exposed subjects

	AQL Coefficient	95% Confidence Interval	p-Value
Birth (n = 35)	22.51	(-11.24, 56.25)	0.182
6 Months (n = 47)	17.46	(-8.85, 43.77)	0.187
12 Months (n = 22)	-7.57	(-39.12, 23.97)	0.615
24 Months (n = 15)	23.21	(-21.52, 67.95)	0.259

n: Number of observations with covariate data available for each measurement, selecting one record per pregnancy.

After adjustment, there were no significant differences in child OFC percentile at any time point between the cannabis exposed AQL children and the cannabis exposed BQL children.

Study Limitations

- We relied on maternal report of cannabis exposure. However, all participants completed a 14-day recall guided by trained study staff who prompted for specific daily use with the aid of a calendar.
- The neurodevelopmental data was also maternal report
 - Selection bias
- Small sample sizes
 - The number of children with critical scores or samples AQL within each analysis was small leading to wide CIs

Next Steps

- Completion of face-to-face neurodevelopmental testing for a subset of children in the sample
 - Performing the Mullen Scales of Early Learning or the Wechsler Preschool & Primary Scale of Intelligence (WPPSI) with 75 exposed children and 75 unexposed children
 - AQL vs BQL
- Comparison on growth parameters to an age and sex-matched group of unexposed infants/toddlers in Mommy's Milk study

Summary and Conclusions

- After adjusting for maternal age, education, income, and child age and sex, there were no significant differences between the cannabis-exposed children and the unexposed children on **any** of the maternal report developmental assessments
- After adjusting for maternal age, education, income, child age, breastfeeding frequency, and prenatal substance exposure, there were no significant differences between the AQL cannabis exposed children and the BQL cannabis exposed children on **any** of the growth measurements evaluated

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Questions?

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Learn more about Mommy's Milk:

MommysMilkResearch.org