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# Association of Fatty Acid Ethyl Esters in Meconium with Behavior during Childhood

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## Abstract

**Objective:** To examine associations between amounts of fatty acid ethyl esters (FAEEs) in meconium and behavior in school aged children exposed to alcohol and drugs in utero.

**Methods:** A secondary analysis of a prospective cohort of cocaine, polydrug exposed children, primarily African-American, low socioeconomic status, recruited at birth into a longitudinal study. FAEEs were quantified with gas chromatography via a flame ionization detector. Meconium was analyzed for FAEEs for 216 newborns of whom 194 were assessed with the Child Behavior Checklist (CBCL) at ages 4, 6, 9, 10, 11, and 12. Generalized estimating equation analyses were used to assess the relationship of quantity of FAEEs to outcomes, controlling for maternal psychological distress.

**Results:** Higher concentrations of FAEEs (ethyl myristate, ethyl palmitate, ethyl oleate, ethyl linoleate, and ethyl linolenate) were associated with caregiver reported aggressive and/or delinquent behavior at ages 10 and 12. After control for caregiver psychological distress, and age, significant ($p < 0.05$) FAEE by age interactions were found for ethyl myristate for aggression and for ethyl oleate, ethyl linoleate and ethyl linolenate for delinquency . Thus, higher concentrations of FAEE were related to more caregiver reported aggressive and delinquent behaviors of clinical significance at ages 10 and 12.

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Contributors

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Hasina Momotaz, M.S., performed data analyses Gregory Powers, M. Sc., performed data analyses
Sonia Minnes, Ph.D., supervision of data collection and analysis, interpretation of data and review of manuscript
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**Conflict of Interest** – No conflicts declared

**Conclusion:** Higher concentrations of FAEEs in meconium are potential markers for children at risk for aggressive and delinquent behaviors related to the effects of prenatal alcohol exposure.

**Keywords**

Prenatal alcohol exposure; child aggression; fatty acid ethyl esters; biomarkers; CBCL; delinquency

## 1. Introduction

Approximately 11.5% of pregnant women in the United States reported current drinking and 3.9% reported binge drinking during the past 30 days in a survey conducted between 2015–2017 (Denny et al., 2019). Prenatal alcohol exposure (PAE) from maternal drinking can result in a wide range of child impairments due to its effects on the developing fetal brain, conceptualized as fetal alcohol spectrum disorders (FASD) (Mattson et al., 2011). These impairments range from the most severe, i.e. fetal alcohol syndrome (FAS), identified by characteristic physical, growth, and central nervous system impairments to alcohol related neurodevelopmental deficits (ARND), which encompass milder deficits of learning, memory, attention, and behavior that may not manifest until older ages (Riley et al., 2011).

Current estimates indicate that FASDs occur globally in 7.7 per 1,000 of the general population of young children and youth (Lange et al., 2017), while a U.S. study found a conservative prevalence rate from 1.1 to 5% in four communities of first graders, exceeding previous estimates (May et al., 2018).

Early identification and intervention for PAE are key to mitigating secondary disabilities, and may be instrumental in preventing subsequent recurrences of maternal drinking during pregnancy. However, timely diagnosis of PAE is impeded by the lack of reliable clinical diagnostic tools (Chiandetti et al., 2017). Although regular prenatal interviews regarding alcohol consumption have been shown to be valid predictors of outcome (Jacobson et al., 2002), they are infrequently done due to cost (Chang, 2001). Additionally, many pregnant women are likely to deny or minimize their drinking due to social desirability (Morrow-Tlucak et al., 1989).

Fatty acid ethyl esters (FAEE), the non-oxidative metabolites of ethanol analyzed in meconium, have been investigated as potential biomarkers for children's risk status secondary to PAE in U.S. and international populations (Bearer et al., 1999; Bearer et al., 2003; Bearer et al., 2005). Analyses of FAEE in meconium has been highlighted as a potential cost effective, non-invasive screening tool for PAE given the high prevalence of FASD and their lifelong developmental effects (Lange et al., 2014; Janczewska et al., 2019).

We previously established that higher concentrations of FAEEs in meconium were related to maternal reports of higher alcohol consumption during pregnancy in a high-risk population (Bearer et al., 1999; Bearer et al., 2005). Further, in follow-up of this cohort, better mental and motor developmental outcomes at two years of age were inversely related to concentration levels of several FAEEs (ethyl myristate, ethyl oleate, ethyl linoleate, and ethyl linolenate) in meconium at birth (Peterson et al., 2008). At older ages, elevated levels

of FAEEs were also related to lower WISC-IV Verbal Comprehension, Working Memory, and Full-Scale IQ (Wechsler, 2003) at school ages of 9, 11, and 15 years (Min et al., 2015) and to increased likelihood of marijuana use at 15 (Min et al., 2020). The present study sought to explore further validation of FAEEs as biomarkers by seeking to determine whether the concentration of FAEEs in infant meconium in the same high-risk sample was also related to behavioral problems frequently noted in prior studies of children with PAE (Khoury et al., 2018).

## 2. Methods

The present study included 194 children (86 boys, 108 girls) recruited at birth from a large, urban, teaching hospital for a longitudinal study on the developmental sequelae of prenatal cocaine exposure (Singer et al., 2002). We recruited pregnant women considered to be at high risk for drug use due to lack of prenatal care, behavior suggesting intoxication, a history of involvement with the Department of Human Services, or self-admitted substance use, had drug toxicology screenings at delivery. Exclusions included women with a psychiatric history (major depression, bipolar disorder, or schizophrenia), low intellectual functioning (diagnosis of mental retardation indicated in medical chart review), HIV-positive status, or chronic medical illness and infants with Down Syndrome, FAS, or congenital heart defects. Random samples of meconium were collected from 248 newborns following informed consent, and 216 had adequate analysis of meconium. Of the 216 children, 11 had missing interview data, 2 children died, and 9 dropped out or were lost to contact, yielding the current sample of 194 (90% retention rate for living children with adequate analysis of meconium). Follow-up rates for the sample for this study ranged from 99–84% for ages 4–12, with 91% ($n$=176) assessed ≥ 4 time points.

### 2.1 Procedures

Children and their caregivers were seen by separate examiners at the developmental research laboratory for approximately 5 hours at each follow-up visit at ages 4, 6, 9, 10, 11, and 12 years. Children were assessed by a clinical psychologist or master's level research assistant; caregivers were seen by a social worker or trained research assistant, supervised by a licensed clinical psychologist. Examiners were blinded to infant alcohol and drug exposure status. All participants were given a monetary stipend, lunch and transportation costs. This study was approved by the Institutional Review Board of the participating hospital. Parental/caregiver written informed consent and child assent at appropriate ages were obtained. A Certificate of Confidentiality (DA-98–91) was obtained from the Department of Health and Human Services.

Meconium was collected shortly after birth and stored at −70°C until analysis. FAEEs were extracted with acetone/hexane and isolated using silica gel chromatography. Isolated FAEEs were identified and quantitated by gas chromatography using a flame ionization detector (GC/FID). Six FAEE analytes were examined: ethyl myristate, ethyl palmitate, ethyl oleate, ethyl linoleate, ethyl linolenate, and ethyl arachidonate. Ethyl stearate was not analyzed due to background noise on the chromatograms, and ethyl palmitoleate was excluded as it did

not correlate with alcohol exposure in humans or sheep. Meconium analyses were performed by investigators blinded to infant alcohol exposure status.

At the newborn visit, birth mothers were asked to recall frequency and amount of alcohol and drug use for the month prior to and for each trimester of pregnancy (Singer, Salvator et al., 2002). Women were asked the number of drinks consumed per drinking day and what size serving they had. The number of standard drinks (0.5 oz. of absolute alcohol) of beer, wine, or hard liquor per drinking day was computed. Frequency of drinking was recorded on a Likert-type scale ranging from 1 (less than once a month) to 7 (daily use) and converted to reflect the average number of drinking days per week. Number of drinking days per week was multiplied by the number of drinks per drinking day to compute an average number of alcohol drinks per week in the month prior to pregnancy and in each trimester, which were then averaged to obtain a total average drinks per week over the four periods of time. Birth mothers were also asked to recall more than the usual number of drinks ("On the days that you drank more than the usual number of drinks, how many drinks do you have?"). Risk drinking during pregnancy was assessed with TWEAK (Russell, 1994), with a total score of ≥ 2 indicating pregnancy risk drinking. Other substance use during pregnancy, number of tobacco cigarettes, marijuana joints smoked, and crack cocaine "rocks" consumed and the amount of money spent per day, were also collected along with the frequency of use, computing a total average score for each substance (cigarettes, marijuana, and cocaine). The alcohol and drug assessments were updated with the child's current caregiver at all follow-up visits to measure recent (prior 30-day period) caregiver alcohol and drug use.

**2.1.1. Measures—**Demographic and medical characteristics, maternal age at birth, gestational age, birth weight and length, head circumference, and Hobel Neonatal Risk score (Hobel et al., 1979), were extracted from the medical records of the mothers and infants. Socioeconomic status was calculated using the Hollingshead Index (Hollingshead, 2011). Maternal vocabulary was assessed at birth using the Peabody Picture Vocabulary Test-Revised (PPVT-R) (Dunn and Dunn, 1981), and updated using its third edition (PPVT-III) (Dunn et al., 1997) at later assessments. The Block Design and Picture Completion subtests of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler, 2003) were used to estimate maternal non-verbal intelligence at infant birth. Maternal psychological distress was measured with the Global Severity Index ($\alpha = 0.95$), a summary scale of the Brief Symptom Inventory (Derogatis, 1992), at birth and at each follow-up visit. At each visit, child placement (with either biological mother/relative or adoptive/foster caregiver) was noted and data on the current caregiver updated to provide concurrent assessment of caregiver intelligence, psychological distress, and drug use.

Infants were followed to 4, 6, 9, 10, 11, and 12 years of age and their mothers or current caregivers completed the Child Behavior Checklist (CBCL – 4–18) (Achenbach, 1991). The CBCL is a standardized, reliable and valid observational checklist widely used in behavioral research. The CBCL yields 8 subscales (Anxious-Depressed, Withdrawn-Depressed, Somatic complaints, Thought problems, Social problems, Attention problems, Aggression, Delinquency). Both continuous (t-score) and categorical measures (≥ 10% frequency) were used in analyses. Due to skewed distribution, syndrome scores were

dichotomized using t-scores ≥ 65, indicating ratings at or above the borderline/clinical cutoff.

**2.1.2. Statistical Analyses—**Data that were positively skewed were normalized using a log transformation (alcohol and drug use, maternal psychological distress) prior to analyses. Means and standard deviations are reported by the variables' original distribution, with transformations used in analyses. Concentrations for each FAEE were transformed by $\log_{10}$ (FAEE+100) to correct skewed distribution.

Generalized estimating equations for correlated binary outcomes with logit link assessed the relationship of FAEE quantity with dichotomous CBCL subscale outcomes over 6 time points, controlling for caregiver psychological distress (GSI), a confounder known to relate to caregiver responses on CBCL outcomes and related to FAEE quantity at birth. Positive FAEE tests were not associated with potentially confounding variables of marijuana, cocaine, or tobacco use at birth (Bearer et al., 1999) nor was the amount of FAEE correlated with severity of use of these substances (Peterson et al., 2008). Maternal age, socioeconomic status, educational level, race, and number of prenatal visits were also not associated with any FAEE (Peterson et al., 2008). Infant gestational age, birthweight, and head circumference were related to quantity of FAEE, but were considered mediating, not confounding variables, based on their demonstrated relationship to alcohol exposure based on maternal report in our sample (Singer, et al., 2002) and in other studies (Bana et al., 2014). Only those behavioral domains occurring with ≥ 10% incidence of clinically significant symptoms (t-score ≥ 65) and were correlated with FAEE quantity in at least 2 out of 6 assessment times were used in multivariate modeling. Main effects and interaction effects for age were examined after control for caregiver psychological distress and its interaction with age. Each FAEE was modeled separately. For those where there were significant effects, gender and gender by GSI interaction terms were also evaluated.

## 3. Results

Table 1 presents demographic and medical characteristics of mothers and infants at birth. Women were primarily African-American (80%), unmarried (87%), with less than a high school education (M = 11.8 ± 1.5), and of low socioeconomic status (100%). Women were on average 27.3 years of age (± 5), and had 2.8 ± 1.7 children. Vocabulary and non-verbal intelligence skills were below average based on standardized assessments, (PPVT-R) (M = 76.8 ± 13; WAIS-R Block Design M = 7 ± 2, Picture Completion M = 6.9 ± 2), possibly reflecting poor education.

About 59 percent of women reported drinking alcohol during pregnancy, averaging 2.1 ± 3 drinks on 1.4 ± 2 drinking days per week, and 63% reported a TWEAK score of ≥ 2, indicating risk. Sixty-one percent of women reported smoking an average of 12.1 ± 11 cigarettes daily while 46% indicated ingesting an average of 24.2 ± 51 units or "rocks" of cocaine weekly. About 24% of women reported smoking an average of 2.9 ± 4.2 joints of marijuana per week. The Global Severity Index mean of the Brief Symptom Inventory was 0.67 ± 0.69, indicating overall psychological distress symptoms in the normative range.

Fifty six percent of infants were female, and about 21% were preterm. Birthweight, length, and head circumference were within normal limits. Eleven percent of children were in foster/kinship/adoptive care at some time during the study (For further description at various time points see (Singer et al., 2004; Linares et al., 2006; Minnes et al., 2008; McLaughlin et al., 2011).

Table 2 presents correlation tables for the logs of each FAEE with the T-scores for the Internalizing/Externalizing scales of the CBCL and with the categorical scores (≥ 10 percentile) for subscales of Aggression, Delinquency, Attention Problems, and Thought Disorder, as these were the only subscales occurring with incidence of clinically significant symptoms ≥ 10%. There were no significant relationships of any FAEE with any Internalizing symptoms nor for Attention Problems. Level of concentration of ethyl myristate, ethyl palmitate, and ethyl linolenate were significantly related to severity of Externalizing problems at age 12 and to more problems with aggressive behavior at ages 10 and 12. Levels of ethyl linoleate and ethyl oleate were also related to Aggression at ages 10 and 12. Ethyl arachidonate (not shown) was also related to age 12 aggressive behavior, ($r = .165$, $p < .05$).

Greater quantities of ethyl myristate and ethyl linolenate in meconium were related to Delinquency Problems at ages 10 and 12, and ethyl myristate, ethyl linoleate, and ethyl linolenate were related to Thought Problems at age 4. There were no significant relationships to Attention Problems at any age, nor were there any FAEEs correlated with any behavior at ages 4, 6, and 9 with the exception of Thought Problems.

Table 3 presents the effects of the 5 FAEEs (ethyl myristate, ethyl palmitate, ethyl oleate, and ethyl linoleate and ethyl linolenate) on incidence of aggressive behavior and delinquent behavior at/above the clinical cutoff across all outcome ages, controlling for time varying current caregiver psychological distress and its interaction with age. There were no significant main effects, but there was a significant age by FAEE interaction for ethyl myristate and marginal trends for ethyl palmitate, ethyl oleate, and ethyl linoleate on incidence of problematic aggressive behavior, after control for caregiver distress and its interaction with age. Similar to aggression, no statistically meaningful main effects for FAEEs on delinquent behavior were noted; however, the age by FAEE interactions were significant for ethyl oleate, ethyl linoleate and ethyl linolenate after control for maternal psychological distress, with marginal trends in the remaining FAEEs. There were no gender effects, nor gender by caregiver GSI effects on any behavior (all p's> .10)

## 4. Discussion

Higher concentrations of FAEEs in meconium (ethyl myristate, ethyl palmitate, ethyl oleate, ethyl linoleate, and ethyl linolenate) were associated with higher incidence of caregiver reported clinically relevant aggressive behavior and/or delinquency at ages 10 and 12 in a sample of low socioeconomic status, urban, primarily African-American children.

The relationship of externalizing behavior problems, especially aggression and delinquency, to PAE has been well established (Mattson and Riley, 2000; Franklin et al., 2008). Tsang, et

al (Tsang et al., 2016) in a meta-analysis of 16 studies, also using the CBCL, concluded children and adolescents with FASD were at increased risk of both Internalizing and Externalizing problems compared to controls. Similarly, Khoury et al (Khoury et al., 2018), in a larger and more diverse sample of studies, found an effect size of PAE to aggressive behavior of 0.75, with more aggressive behaviors related to heavier exposure (O'Leary et al., 2010). We did not find a relationship with Internalizing behavior problems, in contrast to Tsang, et al, (Tsang et al., 2016). However, as has been noted, Internalizing behavior problems are more likely to peak in adolescence, and may be confounded by diagnostic challenges of identifying these problems in younger children (Khoury et al., 2018). It has also been suggested that PAE relationships with later Internalizing symptoms were more likely to be found in studies that include only "heavy" exposure, (Khoury et al., 2018) while our sample excluded those with known FAS.

Women in this sample who self-reported drinking were moderate to high users, averaging almost a drink a day with 63% considered to be risk drinkers based on TWEAK scores. However, the range of exposure was large, with the median number of drinks reported in the low range, and with about 40% of the sample reporting no drinking. Findings from this study are consistent with those of Minnes et al, (Minnes et al., 2010), which also found PAE to be marginally associated with increased aggression on the CBCL in the same cohort followed from 4–10 years, as measured by maternal interview at birth. Our interview was an adaptation of the time line follow-back (TLFB) interview (Sobell and Sobell, 1992; Singer, Salvator et al., 2002). Given that TLFB interviews for prenatal exposures are time consuming and difficult to staff outside of research settings, FAEE meconium analyses may serve as a valid and reliable assessment of exposure for the last two trimesters of pregnancy.

Study limitations include the observational design as well as the use of G-C/FID to determine FAEE as the latter may increase false positives compared to other methods, and thus, underestimate FAEE effects. FAEE can also only identify alcohol exposure in the last two trimesters and may underestimate first trimester exposure. The outcome measure used, the Child Behavior Checklist 4–16, is completed by the primary caregiver, and thus influenced by the caregiver's psychological status, as demonstrated here. Moreover, a small subset of children were in adoptive, foster, or kinship care during any one or all assessments, which may also have an impact on caregiver ratings, and in developmental outcomes as we have shown in prior studies (Singer et al., 2004; Linares et al., 2006; McLaughlin et al., 2011). In this study, we controlled for caregiver psychological stress and its interactions with age and gender in data analyses to mitigate this impact. Confidence in our findings is also increased due to their consistency with our findings when maternal birth reports of prenatal alcohol exposure are used rather than FAEEs (Minnes et al., 2010) and to the larger research findings on externalizing behavior problems associated with PAE which we noted above (Tsang et al., 2016).

Strengths, however, include the longitudinal prospective design, use of both biological and interview measures of PAE and other drug exposures, exceptional follow-up retention, and exclusion of numerous confounding variables, especially other substance exposures, including cocaine, marijuana, and tobacco.

## 5. Conclusions

Our findings demonstrate that higher levels of FAEEs in meconium are related to increases in caregiver ratings of children's clinically relevant aggressive and delinquent behaviors at 10 and 12 years of age, confirming findings from prior studies of PAE. FAEE concentrations in meconium are potential biomarkers for PAE and may be useful in identifying children at risk for aggressive and delinquent behavior at school age due to prenatal alcohol exposure. Future studies should explore which thresholds of FAEE exposure are most sensitive to the association of PAE to behavioral outcomes.

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## HIGHLIGHTS

- Prenatal alcohol exposure (PAE) can result in child behavioral impairments.
- Early diagnosis of PAE for intervention is impeded by lack of valid assessments.
- Fatty acid ethyl esters (FAEE) in meconium related to behavior of children with PAE
- Higher concentrations of FAEEs predicted higher aggressive/delinquent behavior.
- FAEEs in meconium may be markers for aggressive/delinquent behavior related to PAE.

**Table 1.**

Demographic, Medical, and Psychological Characteristics of Mothers and Infants at Birth (*N*=194)

| | *n* (%)/Mean ± SD | Median (10% - 90%) |
|---|---|---|
| *Biological maternal* | | |
| African American | 155 (79.9) | |
| Low socioeconomic status | 194 (100) | |
| Married | 25 (12.9) | |
| Age at birth | 27.28 ± 5.25 | 26 (21 – 35) |
| Years of education | 11.77 ± 1.50 | 12 (10 – 14) |
| Number of prenatal visits | 7.41 ± 4.94 | 8 (1 – 14) |
| Parity | 2.82 ± 1.68 | 3 (1 – 5) |
| Global Severity Index | 0.67 ± 0.69 | 0.45 (0.08 – 1.51) |
| PPVT-R Standard Score | 76.76 ± 13.35 | 77 (60 – 93) |
| WAIS-R Block Design | 7.06 ± 2.10 | 7 (5 – 9) |
| WAIS-R Picture Completion | 6.90 ± 2.32 | 6 (5 – 10) |
| Measures of drinking during pregnancy(*n*=114)[a] | | |
| Number of drinks on drinking day | 2.14 ± 2.79 | 1.5 (0.25 – 4.5) |
| Number of drinking days per week | 1.37 ± 1.49 | 0.75 (0.06 – 3.5) |
| Number of drinks per week | 6.51 ± 11.95 | 1.98 (0.06 – 18) |
| More than usual number of drinks | 5.74 ± 8.83 | 3 (0 – 14) |
| Risk drinking (TWEAK ≥ 2) | 72 (63) | |
| Other substance use during pregnancy[a] | | |
| Cigarettes/day (*n* = 118) | 12.15 ± 10.71 | 10.5 (1.25 – 20) |
| Marijuana joints/week (*n* = 47) | 2.88 ± 4.23 | 1.1 (0.13 – 7) |
| Cocaine units/week (*n* = 89) | 24.23 ± 51.34 | 5 (0.38 – 70) |
| *Child* | | |
| Male | 86 (44.3) | |
| Gestational age (weeks) | 38.4 ± 2.9 | 39 (35 – 41) |
| Prematurity (< 37 wks gestational age) | 41 (21.1) | |
| Hobel Neonatal Risk score | 5.8 ± 15.2 | 0 (0 – 15) |
| Birth weight (grams) | 2994 ± 674 | 3130 (2050 – 3710) |
| Birth length (cm) | 48.8 ± 3.9 | 49.0 (44.4 – 53.0) |
| Head circumference (cm) | 33.1 ± 2.4 | 33.0 (30.2 – 35.5) |
| FAEE Levels | | |
| Ethyl Myristate | 715.14 ± 2334.97 | 50.15 (0.00 – 1620.51) |
| Ethyl Myristate | 1206.09 ± 3333.89 | 151.57 (32.85 – 2727.45) |
| Ethyl Oleate | 14797.15 ± 46714.97 | 304.03 (54.60 – 35334.00) |
| Ethyl Linoleate | 22850.92 ± 75878.14 | 249.27 (0.00 – 56301.43) |
| Ethyl Linolenate | 5819.61 ± 18122.41 | 136.15 (0.00 – 18732.70) |

| | ***n* (%)/Mean ± SD** | **Median (10% - 90%)** |
|---|---|---|
| Ethyl Arachidonate | 1022.11 ± 2804.85 | 187.69 (0.00 – 2299.17) |

[a]Based on users (*n*) only

[1]PPVT-R - Peabody Picture Vocabulary Test – Revised

[2]WAIS-R - Wechsler Adult Intelligence Scale-Revised

[3]TWEAK - T—Tolerance, W—Worried, E—Eye-opener, A—Amnesia, K—K/Cut Down

**Table 2.**

Correlations between FAEE and CBCL Externalizing and Internalizing T scores and Categorical scores for Aggression, Delinquency, Attention, and Thought Problem Subscales at each Follow-up Visit

| | T-score | | Categorical (> 10% frequency) | | | |
|---|---|---|---|---|---|---|
| **Age (Years)** | **Internalizing** | **Externalizing** | **Aggression** | **Delinquency** | **Attention** | **Thought Problem** |
| ***log (ethyl myristate)*** | | | | | | |
| 4 | 0.065 | 0.0178 | −0.0714 | −0.1033 | 0.017 | 0.1619* |
| 6 | 0.0854 | 0.0789 | −0.0531 | 0.0556 | 0.1207 | 0.079 |
| 9 | 0.0597 | 0.069 | 0.0711 | 0.0623 | −0.0212 | 0.0726 |
| 10 | 0.0642 | 0.1011 | 0.1695* | 0.1656* | 0.1391 | 0.0266 |
| 11 | 0.1464 | 0.0816 | 0.0971 | 0.0956 | 0.024 | 0.0125 |
| 12 | 0.1109 | 0.1628* | 0.2154* | 0.1551* | 0.1083 | 0.0561 |
| ***log (ethyl palmitate)*** | | | | | | |
| 4 | 0.0404 | −0.0214 | −0.0646 | −0.1127 | 0.0278 | 0.1391 |
| 6 | 0.0553 | 0.073 | −0.0499 | 0.0554 | 0.1297 | 0.07 |
| 9 | −0.0096 | 0.0478 | 0.0094 | 0.0204 | −0.0277 | 0.0172 |
| 10 | −0.0275 | 0.0811 | 0.1520* | 0.1326 | 0.1133 | 0.0248 |
| 11 | 0.1157 | 0.1047 | 0.0881 | 0.1386 | 0.022 | 0.0004 |
| 12 | 0.0306 | 0.1589* | 0.1858* | 0.0993 | 0.0828 | 0.0804 |
| ***log (ethyl oleate)*** | | | | | | |
| 4 | 0.0155 | −0.0058 | −0.0649 | −0.1282 | 0.0215 | 0.1447 |
| 6 | 0.0217 | 0.0824 | −0.0283 | 0.1047 | 0.0725 | 0.0635 |
| 9 | 0.0402 | 0.0878 | 0.0350 | 0.0962 | 0.0143 | 0.0746 |
| 10 | 0.021 | 0.0972 | 0.1831* | 0.1696* | 0.1161 | 0.0253 |
| 11 | 0.1067 | 0.084 | 0.0862 | 0.1421 | 0.0404 | 0.0072 |
| 12 | 0.0522 | 0.1441 | 0.1598* | 0.1005 | 0.0775 | 0.0713 |
| ***log (ethyl linoleate)*** | | | | | | |
| 4 | 0.0409 | 0.0284 | −0.0446 | −0.1205 | 0.0259 | 0.1679* |
| 6 | 0.0568 | 0.0839 | −0.0360 | 0.1045 | 0.0696 | 0.0672 |
| 9 | 0.054 | 0.0721 | 0.0516 | 0.0973 | 0.0086 | 0.0816 |
| 10 | 0.038 | 0.0938 | 0.1800* | 0.1574* | 0.1293 | 0.0345 |
| 11 | 0.1087 | 0.066 | 0.0788 | 0.116 | 0.0315 | 0.0139 |
| 12 | 0.0917 | 0.1357 | 0.1756* | 0.1151 | 0.0884 | 0.0831 |
| ***log (ethyl linolenate)*** | | | | | | |
| 4 | 0.0366 | 0.032 | −0.0451 | −0.1124 | 0.0653 | 0.1818* |
| 6 | 0.0876 | 0.1033 | −0.0530 | 0.1143 | 0.0896 | 0.0832 |
| 9 | 0.0577 | 0.0894 | 0.0750 | 0.1074 | 0.0139 | 0.096 |
| 10 | 0.057 | 0.1177 | 0.1703* | 0.1762* | 0.1358 | 0.014 |
| 11 | 0.1424 | 0.0916 | 0.1026 | 0.1381 | 0.0323 | 0.0256 |
| 12 | 0.095 | 0.1591* | 0.1887* | 0.1747* | 0.0552 | 0.0654 |

**Table 3.**

Effects of FAEEs, Age, and Caregiver Distress on CBCL aggressive behavior and Delinquent behavior ≥ borderline/clinical cut-off (T score ≥ 65)

| | | Aggressive behavior | | Delinquent behavior | |
|---|---|---|---|---|---|
| | *df* | $\chi^2$ | *p* | $\chi^2$ | *p* |
| **Log ethyl myristate** | 1 | 0.35 | 0.55 | 1.29 | 0.26 |
| Age | 5 | 7.51 | 0.19 | 5.31 | 0.38 |
| **Log ethyl myristate* Age** | 5 | 10.97 | 0.052 | 10.24 | 0.07 |
| Current caregiver GSI | 1 | 13.05 | 0.0003 | 8.66 | 0.003 |
| Current caregiver GSI * Age | 5 | 10.06 | 0.07 | 8.44 | 0.13 |
| **Log ethyl palmitate** | 1 | 0.19 | 0.66 | 1.34 | 0.25 |
| Age | 5 | 6.79 | 0.24 | 4.32 | 0.50 |
| **Log ethyl palmitate* Age** | 5 | 9.8 | 0.08 | 10.24 | 0.07 |
| Current caregiver GSI | 1 | 12.48 | 0.0004 | ^ 8..0 | 0.004 |
| Current caregiver GSI * Age | 5 | 9.98 | 0.08 | 8.48 | 0.13 |
| Log ethyl oleate | 1 | 0.32 | 0.57 | 1.61 | 0.20 |
| Age | 5 | 6.11 | 0.29 | 4.63 | 0.46 |
| **Log ethyl oleate* Age** | 5 | 10.28 | 0.06 | 13.22 | 0.02 |
| Current caregiver GSI | 1 | 12.95 | 0.0003 | 8.75 | 0.003 |
| Current caregiver GSI * Age | 5 | 9.82 | 0.08 | 8.76 | 0.12 |
| **Log ethyl linoleate** | 1 | 1.43 | 0.23 | 1.57 | 0.21 |
| Age | 5 | 5.26 | 0.38 | 5.93 | 0.31 |
| **Log ethyl linoleate* Age** | 5 | 9.34 | 0.09 | 12.56 | 0.03 |
| Current caregiver GSI | 1 | 1.06 | 0.30 | 8.97 | 0.003 |
| Current caregiver GSI * Age | 1 | 0.02 | 0.89 | 8.61 | 0.13 |
| **Log ethyl linolenate** | 1 | 0.62 | 0.43 | 2.08 | 0.15 |
| Age | 5 | 6.80 | 0.24 | 6.38 | 0.27 |
| **Log ethyl linolenate* Age** | 5 | 8.56 | 0.13 | 11.21 | 0.047 |
| Curre.t cai'giver 3SI | 1 | 12.77 | 0.0004 | 8.83 | 0.003 |
| Current caregiver GSI * Age | 1 | 9.72 | 0.08 | 8.54 | 0.13 |

CBCL=Child Behavior Checklist; GSI= Global Severity Index