A Multisite Neurobehavioral Assessment of FASD

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Sites & Collaborators

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Subjects Tested

Site	AE	Control	Contrast	Total	2-Year Goal	% of Goal
SDSU						
Old	30	26	15	71	48	148%
Young	10	15	9	34	48	71%
UMN						
Old	32	32	18	82	48	171%
Young	13	15	7	35	48	73%
Emory						
Old	13	21	7	41	48	85%
Young	16	6	7	29	48	60%
USC						
Old	15	10	--	25	32	78%
Subtotal Old	90	89	40	219	176	124%
Subtotal Young	39	36	23	98	144	68%
Total	129	125	63	317	320	**99%**

Can we accurately identify FASD/ARND?

- 60-90% of children born to alcoholic mothers do not demonstrate the classic facial features of FAS
  - These children are affected by prenatal alcohol exposure in similar ways as those children with FAS but are difficult to identify and thus do not receive adequate treatments or interventions
- Our goal is to determine which features can be used to accurately identify children affected by prenatal alcohol exposure, including those who do not have FAS

2 x 2 Design

		ADHD Dx	
		Yes	No
Alcohol Exposure	Yes	AE+	AE-
	No	ADHD	CON

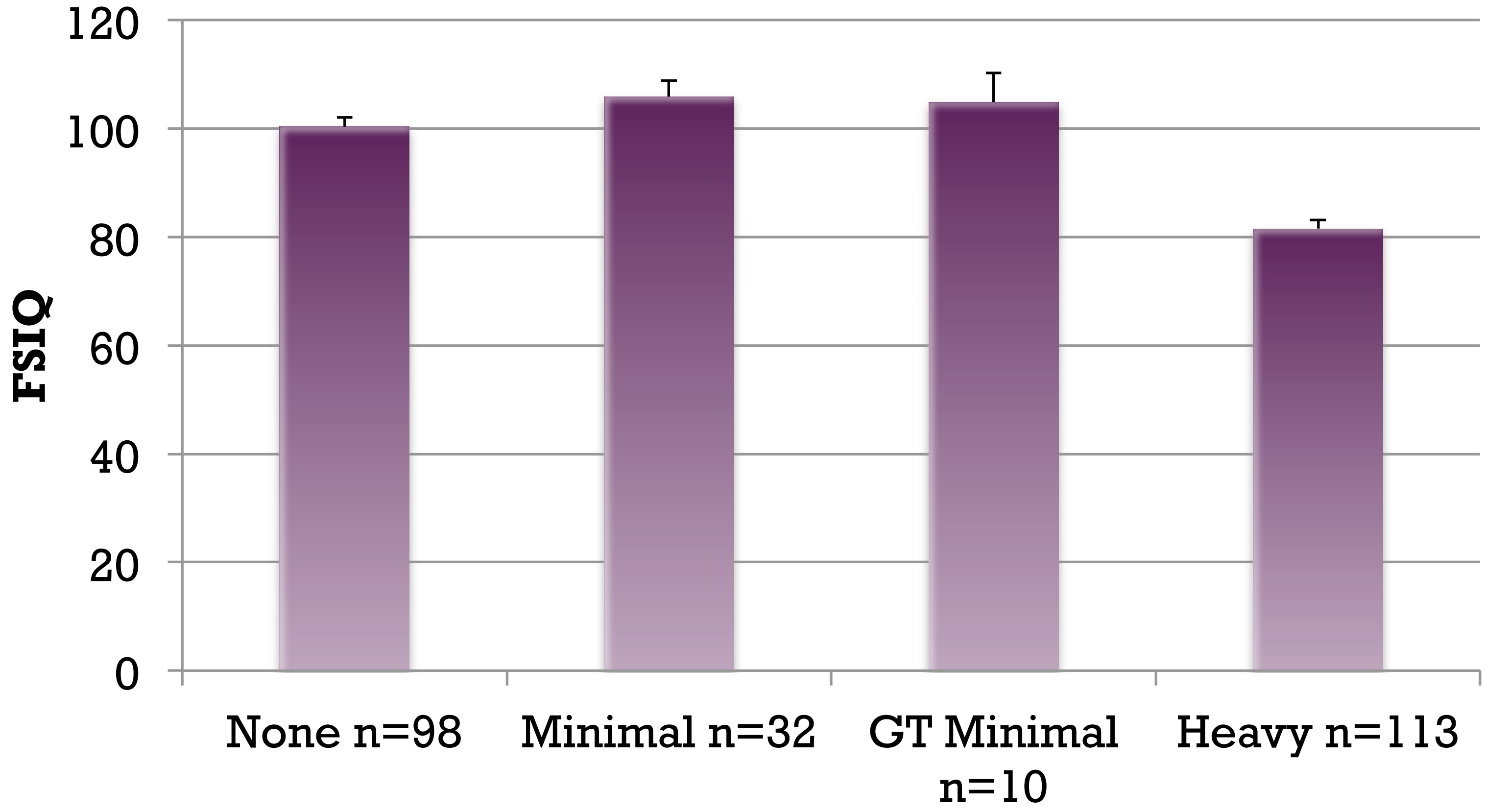
Recent Accomplishments: 2013-14

- 6 papers accepted or in press
- 2 paper under review
- 4 papers in preparation

What We Have Learned From Reviewers' Comments

- More details needed about general CIFASD methodology
- Wide age ranges an issue (corrected in CIFASD III)
- Measure of SES needed (corrected in CIFASD III)
- Alcohol exposure in the control/comparison groups less satisfying to some reviewers
  - Controls are non-exposed or "minimally" exposed (<1 drink/week on average, never more than 2 drinks on a single occasion)
  - Exploratory analyses show no IQ differences between Ss with no exposure (Mn = 100) and Ss with "minimal" exposure (Mn = 106)
- Use of "Diagnosed with ADHD" vs. "research criteria for ADHD"
- Controlling (or not) for IQ continues to be troublesome for some reviewers

FSIQ & Minimal Alcohol Exposure



+ Published Studies

ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH

Vol. **, No. *
** 2014

Effects of Prenatal Alcohol Exposure and Attention-Deficit/ Hyperactivity Disorder on Adaptive Functioning

Ashley L. Ware, Leila Glass, Nicole Crocker, Benjamin N. Deweese, Claire D. Coles, Julie A. Kable, Philip A. May, Wendy O. Kalberg, Elizabeth R. Sowell, Kenneth L. Jones, Edward P. Riley, Sarah N. Mattson, and the CIFASD

Neurotoxicology and Teratology 42 (2014) 43–50

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Correspondence of parent report and laboratory measures of inattention and hyperactivity in children with heavy prenatal alcohol exposure

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Leila Glass [a], Diana M. Graham [a], Benjamin N. Deweese [a], Kenneth Lyons Jones [b], Edward P. Riley [a], Sarah N. Mattson [a,*]

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ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH

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Effects of Prenatal Alcohol Exposure and Attention-Deficit/Hyperactivity Disorder on Adaptive Functioning

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Julie A. Kable, Philip A. May, Wendy O. Kalberg, Elizabeth R. Sowell, Kenneth L. Jones,
Edward P. Riley, Sarah N. Mattson, and the CIFASD

Background

- Prenatal alcohol exposure and idiopathic ADHD are both related to disruptions in adaptive behavior (AB).
- The combined effects of AE and ADHD on AB have not been directly examined.
- In the current study, this relation was examined in subjects from the CIFASD II dataset.

Methods

- 4 groups of children (8-16y, M=12.4) from multiple sites were tested
  - Children with histories of heavy prenatal alcohol exposure
    - With ADHD (AE+, n=82)
    - Without ADHD (AE-, n=34)
  - Children with no or minimal prenatal alcohol exposure
    - With ADHD (ADHD, n=71)
    - Without ADHD (CON, n=130)
- Caregivers completed the Vineland Adaptive Behavior Scales – second edition (VABS-II).
- Data from the communication, socialization, and daily living skills domains were analyzed using separate 2 (alcohol exposure) x 2 (ADHD) ANCOVAs.

Subject Demographics

Table 1. Demographic Data for Children with Prenatal Alcohol Exposure and ADHD (AE+), Prenatal Alcohol Exposure without ADHD (AE−), Children with ADHD (ADHD), and Control Children (CON)

Demographic variable	AE+ (*n* = 82)	AE− (*n* = 34)	ADHD (*n* = 71)	CON (*n* = 130)	Omnibus statistic	*p*-Value
CIFASD site [*N* (%)]						
Atlanta	15 (18.3)	12 (35.3)	18 (25.4)	19 (14.6)		
Los Angeles	15 (18.3)	8 (23.5)	1 (1.4)	17 (13.1)		
Northern Plains States	11 (13.4)	4 (11.8)	7 (9.9)	17 (13.1)		
Albuquerque	5 (6.1)	2 (5.9)	10 (14.1)	18 (13.8)		
San Diego	36 (43.9)	8 (23.5)	35 (49.3)	59 (45.4)		
Handedness [*N* (% Right)]	72 (87.8)	31 (91.2)	63 (88.7)	121 (93.1)	χ^2 (df = 3) = 1.98	0.577
FAS [*N* (%)]	22 (26.8)	10 (29.4)	0 (0)	0 (0)		
Sex [*N* (% Males)]	52 (63.4)	15 (44.1)	53 (74.6)	71 (54.6)	χ^2 (df = 3) = 11.91	0.008
Race [*N* (% White)][a]	52 (63.4)	13 (38.2)	46 (64.8)	91 (70.0)	χ^2 (df = 18) = 26.93	0.080
Ethnicity [*N* (% Hispanic)][b]	6 (7.3)	6 (17.6)	19 (26.8)	24 (18.5)	χ^2 (df = 6) = 13.68	0.033
Age [*M* (SD)]	12.54 (2.39)	12.66 (2.57)	11.83 (2.52)	12.51 (2.58)	F (3, 313) = 1.49	0.216
FSIQ [*M* (SD)][c]	82.42 (17.35)	88.88 (14.25)	91.80 (18.44)	110.67 (11.88)	F (3, 311) = 65.33	<0.001

ADHD, attention-deficit/hyperactivity disorder; CIFASD, Collaborative Initiative on Fetal Alcohol Spectrum Disorders; FAS, fetal alcohol syndrome; FSIQ, Full Scale IQ; NIH, National Institutes of Health.

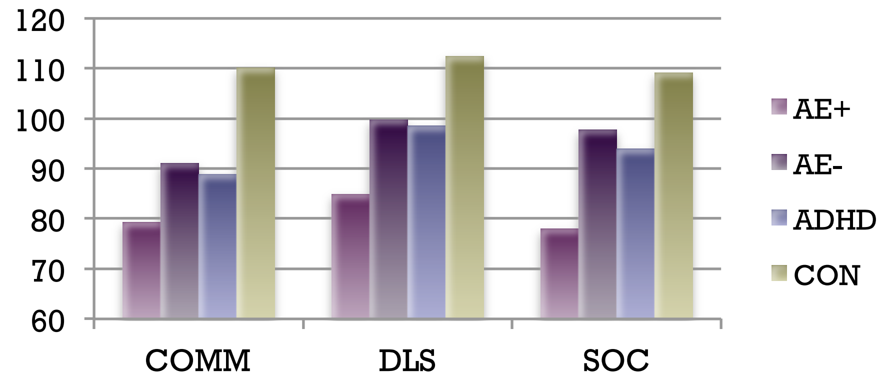
[a]Race was analyzed using NIH-designated categories: American Indian/Alaska Native, Asian, Black or African American, White, More than one Race, Other, Unknown/Not Specified.

[b]Ethnicity was missing for 7 subjects.

[c]FSIQ was missing for 2 subjects.

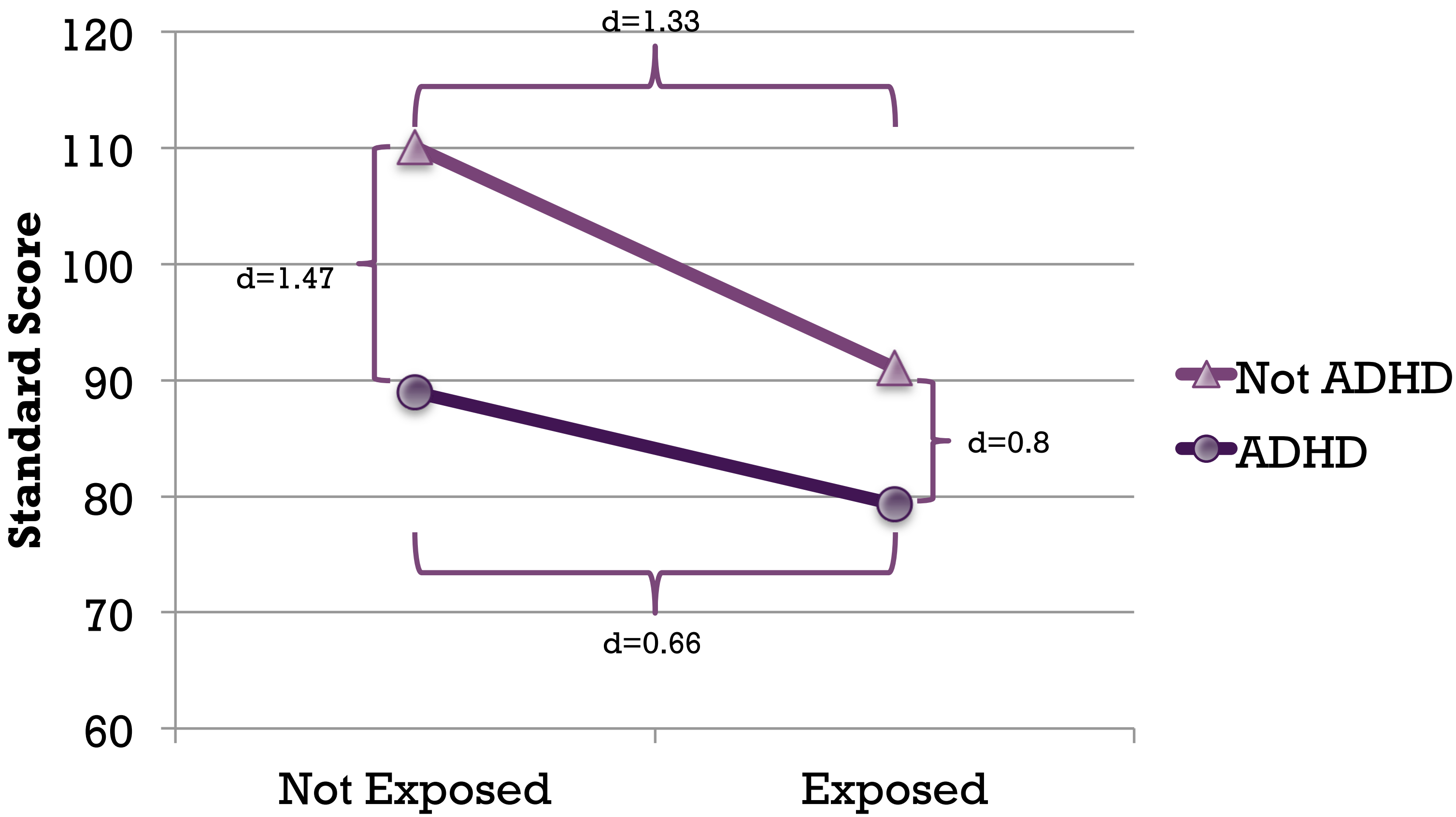
Results

- The main effects of AE were significant for all domains (exposed < non-exposed)
- The main effects of ADHD were significant for all domains (ADHD < non-ADHD)
- The AE x ADHD interaction was significant for the Communication Domain



Domain	ME of AE	ME of ADHD	AE x ADHD
Communication	$p<.001$	$p<.001$	$p=.007$
Daily Living Skills	$p<.001$	$p<.001$	$p=.964$
Socialization	$p<.001$	$p<.001$	$p=.279$

Communication Domain: AE x ADHD Interaction



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Conclusions/Implications

- As in previous studies, AE and ADHD relate to deficits in adaptive behavior.
- However, these effects are not uniform (at least in Communication)
  - ADHD effects children with minimal or no prenatal exposure more than children with prenatal exposure.
  - Prenatal alcohol exposure affects children without ADHD more than children with ADHD.
- The strongest impairment in communication (and to a lesser extent in the other domains) is seen in children with both prenatal alcohol exposure and ADHD.

Neurotoxicology and Teratology 42 (2014) 43–50

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Correspondence of parent report and laboratory measures of inattention and hyperactivity in children with heavy prenatal alcohol exposure

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Background

- The identification of inattention and hyperactivity relies primarily upon parent/guardian evaluations. Clinical research and practice support a multi-method approach to validating behavioral problems in school.
- There is a high rate of comorbid ADHD and reports of inattention and hyperactivity in children with prenatal alcohol exposure.
- In the current study, we examined whether parent-reported symptoms of hyperactivity and inattention were substantiated by objective laboratory measures.

Methods

- 3 groups of children (8-16y) were assessed:
  - Children with histories of heavy prenatal alcohol exposure (**AE**, n=44)
  - Children with no or minimal prenatal alcohol exposure
    - with ADHD (**ADHD**, n=16)
    - without ADHD (**CON**, n=22)

	Lab Measure	**Parent Measure**
Inattention	CPT Omission	DBD-Inattention
Hyperactivity	ACT Median Activity	DBD-Hyperactivity

CPT = NES3 Continuous Performance Task Omission Errors

ACT = Motionlogger Wristwatch Actigraph – Median Activity

DBD = Disruptive Behavior Disorder Scale

Subject Demographics

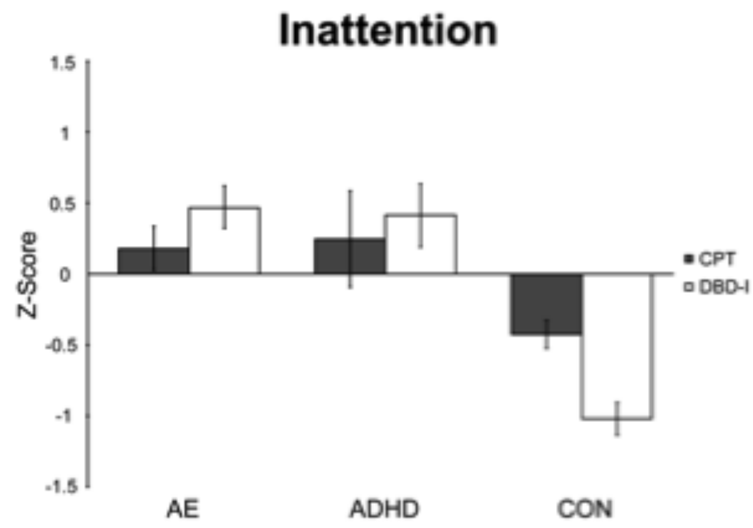
Table 1
Demographic information for the alcohol-exposed (AE), attention-deficit/hyperactivity disorder (ADHD) and control (CON) groups.

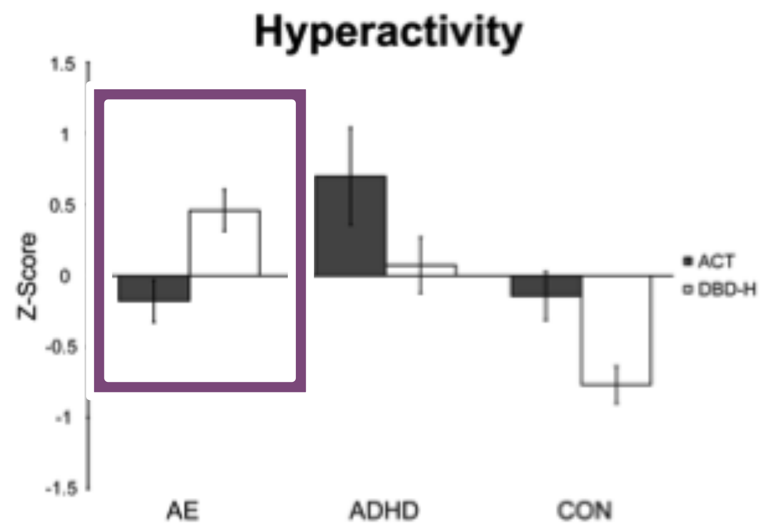
Variable	AE (*n* = 44)	ADHD (n = 16)	CON (n = 22)
Handedness [*n* (% right)]	37 (84.1)	15 (93.8)	21 (95.5)
Sex [*n* (% female)]	15 (34.1)	4 (25.0)	11 (50.0)
Race [*n* (% White)]	28 (63.6)	11 (68.8)	17 (77.3)
Ethnicity [*n* (% Hispanic)]	5 (11.4)	2 (12.5)	5 (22.7)
Age [*M* (SD)]	12.3 (3.52)	12.2 (3.43)	11.9 (2.71)
SES [*M* (SD)]	46.8 (12.60)	51.7 (9.96)	49.5 (11.52)
IQ [*M* (SD)][a]	96.4 (16.25)	101.4 (19.31)	109.6 (12.08)
FAS diagnosis [*n* (% FAS)]	9 (20.5)	0 (0.0)	0 (0.0)
ADHD diagnosis [*n* (% ADHD)]	34 (77.3)	16 (100.0)	0 (0.0)
Inattentive	13 (38.2)	10 (62.5)	0 (0.0)
Hyperactive–impulsive	0 (0.0)	0 (0.0)	0 (0.0)
Combined	21 (61.8)	6 (37.5)	0 (0.0)

[a] IQ estimate based on Leiter-R BRIEF-IQ score. Significant group differences were found on this measure with AE < ADHD and CON, $p < .05$.

Results

- No significant Group (AE, CON, ADHD) x Type (Parent, Lab) x Domain (Hyperactivity, Inattention).
- **Inattention** – significant Group x Type interaction. Significant main effect of Group for both Parent and Lab measures (AE, ADHD > CON, AE = ADHD)
- **Hyperactivity** – significant Group x Type interaction. Significant main effect of Group for Parent (AE, ADHD > CON; ADHD = AE) and Lab (AE = CON; ADHD > AE, CON)





Positive scores = higher activity, increased omission errors and higher symptom counts

Results

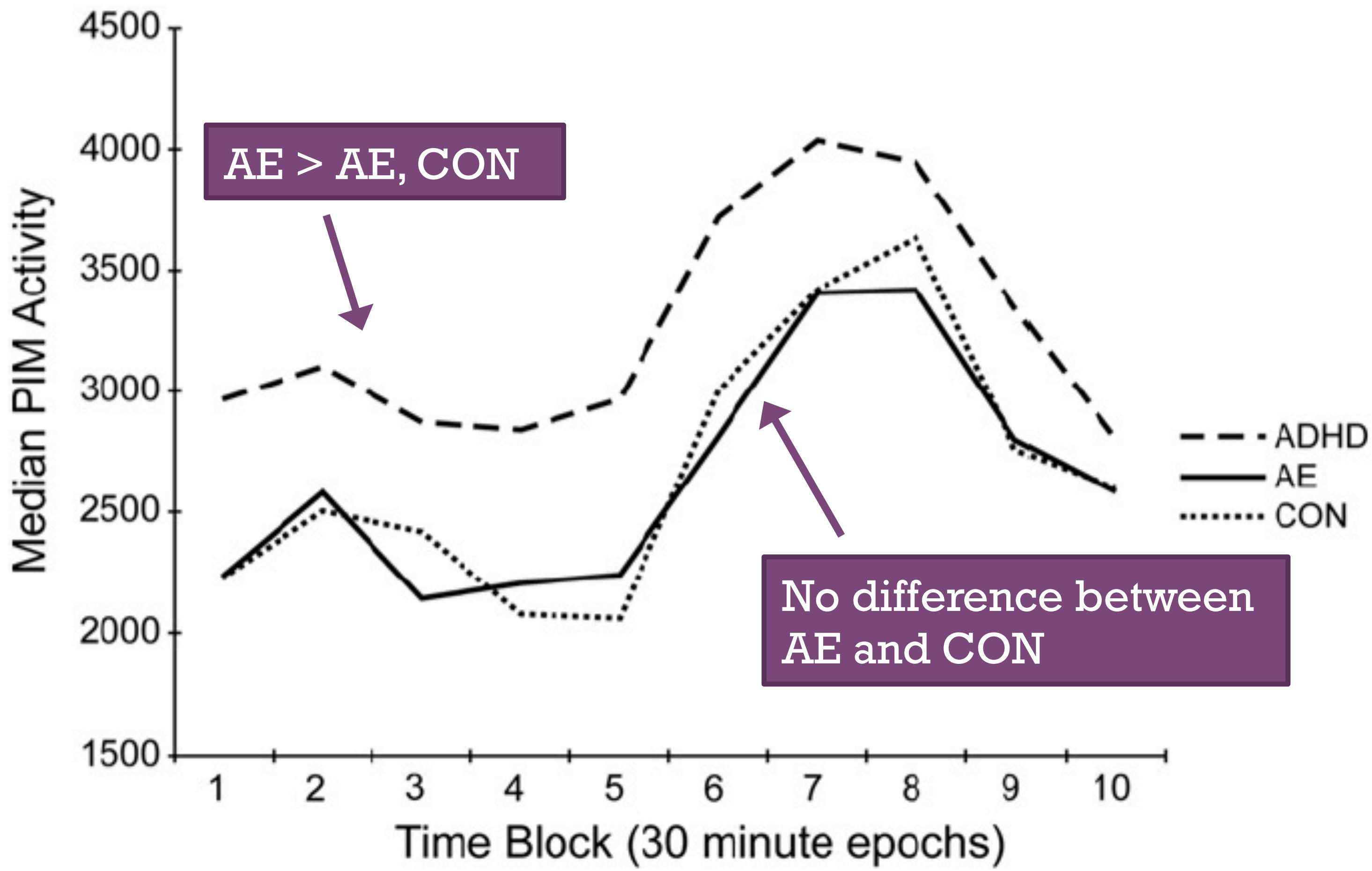


Fig. 2. Median activity level as measured by actigraphy (laboratory measure of activity) over a 5-hour period across groups: children with prenatal alcohol exposure (AE), attention-deficit/hyperactivity disorder (ADHD), and controls (CON). Each time block is a 30-minute period.

Conclusions/Implications

- The clinical groups (AE, ADHD) had higher parent reports of inattention and hyperactivity.
- For inattention, the laboratory measure validated the parent-report in both AE and ADHD.
- The laboratory measure substantiated the presence of hyperactivity in children with ADHD, but not in children with prenatal alcohol exposure.
- Children with prenatal alcohol exposure, despite the majority meeting criteria for ADHD, did not differ from controls on the objective measure of hyperactivity.

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Papers Under Review

THE CLINICAL UTILTY AND SPECIFICITY OF PARENT REPORT OF EXECUTIVE FUNCTION AMONG CHILDREN WITH PRENATAL ALCOHOL EXPOSURE

Tanya T. Nguyen; Leila Glass; Claire D. Coles; Julie A. Kable; Philip A. May; Wendy O. Kalberg; Elizabeth R. Sowell; Kenneth Lyons Jones; Edward P. Riley; Sarah N. Mattson, and the CIFASD

DISCRIMINATING BEHAVIORAL SUBGROUPS AMONG CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE

Diana M. Graham; Benjamin N. Deweese; Scott C. Roesch; Claire D. Coles; Julie A. Kable; Philip A. May; Wendy O. Kalberg; Elizabeth R. Sowell; Kenneth Lyons Jones; Edward P. Riley; Sarah N. Mattson, and the CIFASD

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THE CLINICAL UTILTY AND SPECIFICITY OF PARENT REPORT OF EXECUTIVE FUNCTION AMONG CHILDREN WITH PRENATAL ALCOHOL EXPOSURE

Tanya T. Nguyen; Leila Glass; Claire D. Coles; Julie A. Kable; Philip A. May; Wendy O. Kalberg; Elizabeth R. Sowell; Kenneth Lyons Jones; Edward P. Riley; Sarah N. Mattson, and the CIFASD

Status: Being Revised after Reviewer Comments

Background

- Both prenatal alcohol exposure and ADHD result in behavioral issues related to poor executive function abilities.

- The Behavior Rating Inventory of Executive Function (BRIEF) is a parent rating scale designed to assess behavioral problems associated with executive dysfunction in children in real-world settings. However, it's relationship to neuropsychological measures of executive function have not yet been assessed in this population.

- The current study aimed to
  - characterize the EF deficits in children with FASD using a multi-method approach
  - examine the association between the BRIEF and neuropsychological measures
  - determine if a unique score profile on the BRIEF can identify children with FASD with and without ADHD, compared to children with ADHD and controls.

Methods

- *N* = 373 children ages 8-16 years
  - Alcohol-exposed children with ADHD (**AE+**, *n* = 79)
  - Alcohol-exposed children without ADHD (**AE-**, *n* = 36)
  - Non-exposed children with ADHD (**ADHD**, *n* = 90)
  - Non-exposed children without ADHD (**CON**, *n* = 168)
- Children completed a standardized neuropsychological test battery focused on executive function. Caregivers completed the BRIEF.
- Neuropsychological and BRIEF data were analyzed using 2 (exposure) x 2 (ADHD) MANOVA.
- The relationship between neuropsychological and BRIEF variables were examined using within-group Pearson correlations.
- Data were analyzed using 3 discriminant function analyses
  - AE- & CON; AE+ & ADHD; AE+ & AE-

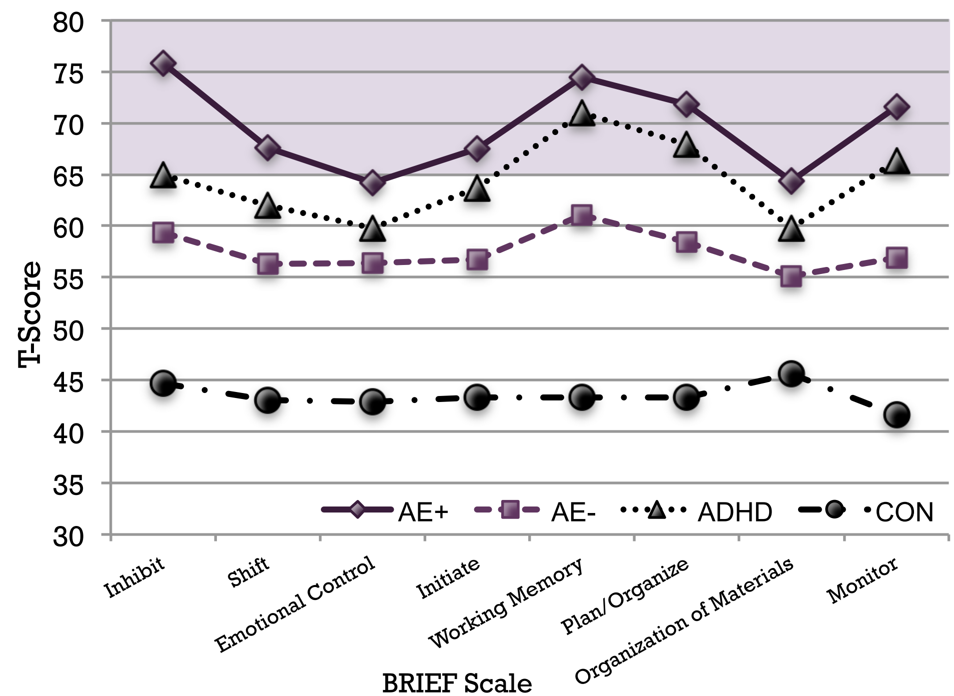
Subject Demographics

Variable	AE+ (n = 79)	AE- (n = 36)	ADHD (n = 90)	CON (n = 168)
CIFASD Site [n (%)]				
Atlanta	15 (19.0)	14 (38.9)	19 (21.1)	32 (19.0)
Los Angeles	14 (17.7)	8 (22.2)	2 (2.2)	17 (10.1)
Northern Plains	10 (12.6)	7 (19.4)	13 (14.4)	25 (14.9)
Albuquerque	7 (8.9)	0 (0.0)	17 (18.9)	30 (17.9)
San Diego	33 (41.8)	7 (19.4)	39 (43.3)	64 (38.1)
Sex [n (% Females)]	29 (36.7)	20 (80.6)	23 (35.6)	75 (44.6)
Age in years [M (SD)]	12.6 (2.4)	12.9 (2.8)	11.5 (2.7)	12.4 (2.5)
Handedness [n (% Right)]	68 (86.1)	32 (88.9)	80 (88.9)	157 (93.5)
Race [n (%White)]	27 (34.2)	21 (58.3)	24 (26.7)	44 (26.2)
Ethnicity [n (% Hispanic)]	6 (7.6)	4 (11.1)	22 (24.4)	37 (22.0)
FSIQ [M (SD)]	80.3 (17.1)	85.3 (14.5)	91.6 (18.9)	104.3 (16.8)
FAS Diagnosis [n (%)]	23 (29.1)	11 (30.6)	0 (0)	0 (0)

Results

- Interactions between AE and ADHD were found on nearly all BRIEF scales.
  - Pairwise comparison revealed significant differences between all groups on all scales (AE +>ADHD> AE-> CON)

- Main effects of AE and ADHD were found on neuropsychological performance.
  - No difference between AE+ and AE-



Results

- Very few significant weak correlations between BRIEF scales and neuropsychological performance.

- BRIEF scales could successfully discriminate groups of children
  - Overall classification accuracy greater than 72% for each analysis
  - Group classification rates ranging from 70-94%.

BRIEF Scale	AE- & CON	AE+ & ADHD	AE+ & AE-
Inhibit	-.112	**.815***	**.429***
Shift	.077	.123	.182
Emotional Control	**.300***	-.260	-.211
Initiate	-.149	-.125	**-.344***
Working Memory	**.858***	-.065	-.012
Plan/Organize	.036	**.335***	**.466***
Organization of Materials	-.146	**.382***	.105
Monitor	.189	.118	**.531***

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Conclusions/Implications

- Findings are consistent with prior studies showing an exacerbated effect of multiple risk factors in the AE+ group, resulting in more severe deficits in parent-reported behavior but not in neuropsychological performance.
- While the BRIEF may not measure executive function in the traditional neuropsychological sense of the construct, it captures valuable information about children's behavior and is sensitive to the effects of prenatal alcohol exposure and ADHD.
- The BRIEF may be a useful screening tool for prenatal alcohol exposure, particularly in settings where neuropsychological assessment may not be immediately available (e.g., school settings, doctor's offices).
  - Measure should be used only as a complement to, rather than replace, traditional neuropsychological tests to assess cognitive function.

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DISCRIMINATING BEHAVIORAL SUBGROUPS AMONG CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE

Diana M. Graham; Benjamin N. Deweese; Scott C. Roesch; Claire D. Coles; Julie A. Kable; Philip A. May; Wendy O. Kalberg; Elizabeth R. Sowell; Kenneth Lyons Jones; Edward P. Riley; Sarah N. Mattson, and the CIFASD

Status: Being Revised after Reviewer Comments

+ Background

- Inaccurate clinical identification
  - Lack of physical dysmorphology in absence of FAS
  - Overlap with other developmental disorders
  - Within-group heterogeneity
- Variability in prenatal alcohol exposure is a hallmark feature of teratogens (Riley & Vorhees, 1986)
- A single profile may lead to inaccurate identification
- In this study we examined within-group behavioral heterogeneity and its relation to cognition (i.e., EF)

Methods

- Subjects
  - Alcohol-Exposed (AE; n = 136)
  - Controls with minimal or no exposure (CON; n = 141)
- Data Analyzed using Latent Profile Analyses (LPA)
  - AE vs. CON
  - Within AE
- Follow-up ANOVA comparing EF performance of AE profiles

CBCL Syndrome Scales (Parent)	
Rule-Breaking Bx	Anxious/ Depressed
Aggressive Bx	Somatic Complaints
Thought Problems	Withdrawn/ Depressed
Attention Problems	Social Problems

D-KEFS Measures (Child)	
Trail Making	Verbal Fluency
Design Fluency	Color-Word Interference
20 Questions	Tower

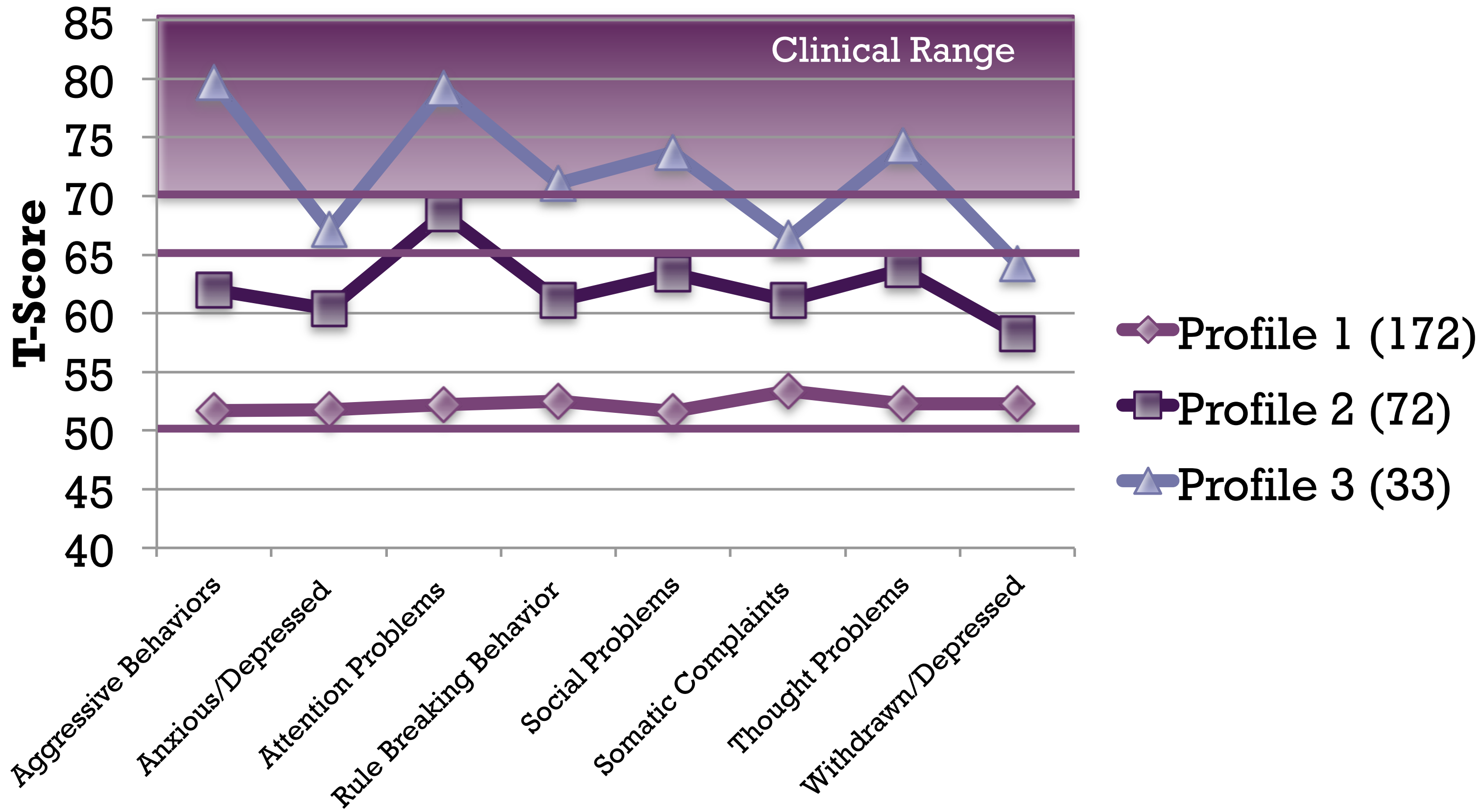
+

Subject Demographics

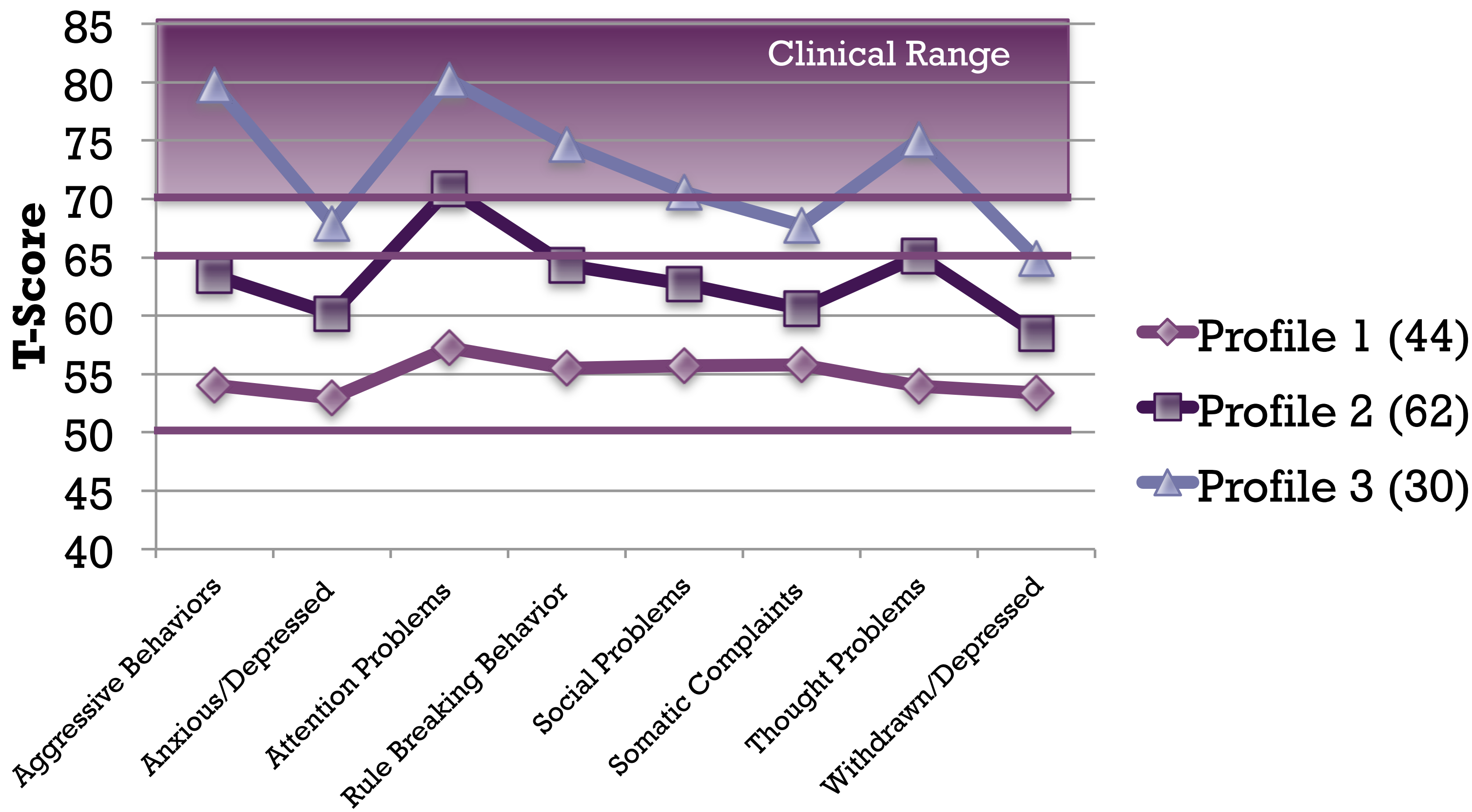
Variable	AE (*n* = 136)	CON (*n* = 141)
CIFASD Site [n (%)]		
Atlanta	30 (22.1)	19 (13.5)
Los Angeles	25 (18.4)	18 (12.8)
Northern Plains	19 (14.0)	20 (14.2)
Albuquerque	12 (8.8)	25 (17.7)
San Diego	50 (36.8)	59 (41.8)
Sex [*n* (% Females)]	59 (43.4)	62 (44.0)
Age in years [*M* (SD)]	12.5 (2.36)	12.4 (2.58)
Handedness [*n* (% Right)]	120 (88.2)	132 (93.6)
Race [*n* (%White)]*	71 (52.2)	100 (70.9)
Ethnicity [*n* (% Hispanic)]	19 (14.0)	30 (21.3)
FSIQ [*M* (SD)]*	83.3 (16.51)	109.7 (11.96)
FAS [*n* (% Diagnosed)]	37 (27.2)	0 (0)
ADHD [*n* (% Clinical Level)]	83 (61.0)	0 (0)

* Indicates significant at the $p < .05$ level

Alcohol-Exposed & Control Subjects



Alcohol-Exposed Subjects Only

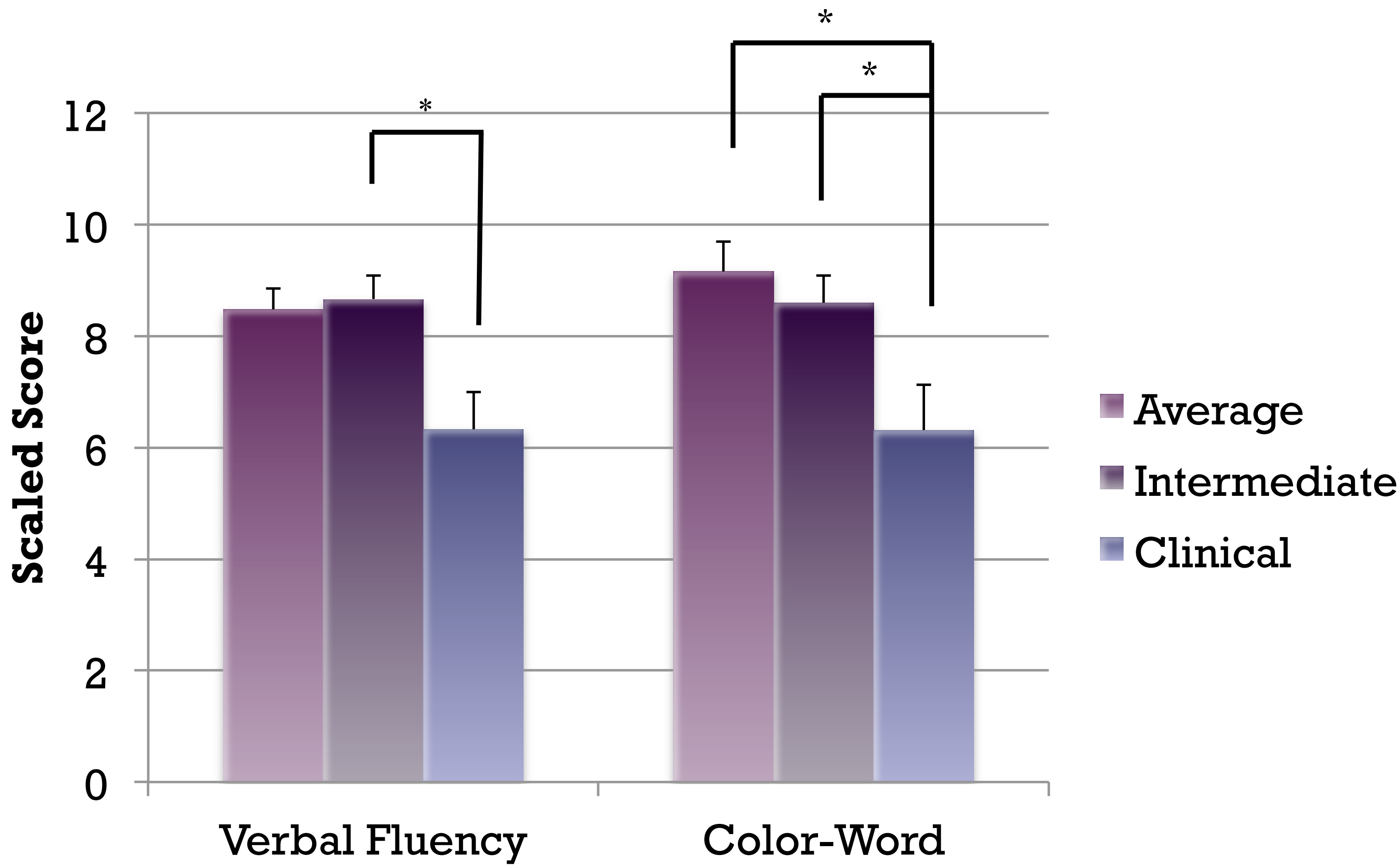


Results: Subgroup Demographic Information

Variable \ Profile	LPA (AE vs. CON) Average (*n* = 172)	Intermediate (*n* = 72)	Clinical (*n* = 33)	LPA (AE Only) Average (*n* = 44)	Intermediate (*n* = 62)	Clinical (*n* = 30)
Site [*n* (%)]						
San Diego	68 (39.5)	29 (40.3)	12 (36.4)	14 (31.8)	25 (40.3)	11 (36.7)
Atlanta	28 (16.3)	15 (20.8)	6 (18.2)	11 (25.0)	13 (21.0)	6 (20.0)
Los Angeles	25 (14.5)	11 (15.3)	7 (21.2)	10 (22.7)	8 (12.9)	7 (23.3)
Albuquerque	26 (15.1)	7 (9.7)	4 (12.1)	3 (6.8)	6 (9.7)	3 (10.0)
Plains States	25 (14.5)	10 (13.9)	4 (12.1)	6 (13.6)	10 (16.1)	3 (10.0)
Sex [*n* (%) Females]	**78 (45.3)**	**35 (48.6)**	**8 (24.2)**	22 (50.0)	29 (46.8)	8 (26.7)
Race [*n* (%) White]	110 (64.0)	40 (55.6)	21 (63.6)	19 (43.2)	32 (50.0)	20 (70.0)
Ethnicity [*n* (%) Hispanic]	39 (22.7)	8 (11.1)	2 (6.1)	11 (25.0)	7 (9.7)	1 (6.7)
Handedness [*n* (%) Right]	**162 (94.2)**	**62 (86.1)**	**28 (84.8)**	43 (97.7)	52 (82.8)	25 (83.3)
Age [*M* (SD)]	12.5 (2.57)	12.3 (2.29)	13.0 (2.35)	12.5 (2.45)	12.4 (2.35)	12.8 (2.29)
FSIQ [*M* (SD)]	**104.6 (15.99)**	**86.6 (16.89)**	**77.6 (18.82)**	87.4 (14.60)	82.7 (15.98)	78.2 (19.14)
Alcohol-Exposed [*n* (%)]	41 (23.8)	62 (86.1)	33 (100.0)	12 (27.3)	18 (29.0)	7 (23.3)
ADHD [*n* (%) Clinical Level]	**9 (5.2)**	**46 (63.9)**	**28 (84.8)**	**10 (22.7)**	**48 (77.4)**	**25 (83.3)**
FAS [*n* (%) Diagnosed]	12 (7.0)	16 (22.2)	7 (21.2)	12 (27.3)	18 (29.0)	7 (23.3)

* Indicates significant at the $p < .05$ level

+ Results: Severity of Behavior Relates to EF



Conclusions/Implications

- Results confirmed behavior problems in alcohol-exposed children and indicated that the degree of effect is not uniform
- Behavioral profiles were characterized by differences in severity rather than in types of behavioral problems.
- Severity of behavior problems relate to difference in executive function
  - Children with intermediate to severe behavior problems have greater EF impairment (i.e., verbal fluency, inhibition, cognitive flexibility)

Specific Aim 1

- **Use existing data to develop a tiered or hierarchical approach to identification of affected cases.** This aim will determine the measures, from all four clinical domains of CIFASD (neurobehavior, dysmorphology, 3D facial imaging, and brain imaging) that could be used clinically to identify alcohol-affected children.

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CONSTRUCTING A CLASSIFICATION MODEL FOR CHILDREN WITH PRENATAL ALCOHOL EXPOSURE

Diana M. Graham and Sarah N. Mattson

Status: Data Analysis/Trouble Shooting Phase

Background

- Our goal is to develop a very small set of variables that can be used to accurately and efficiently identify children affected by prenatal alcohol exposure
- We originally planned to conduct CART (classification and regression tree) analyses but these were abandoned because they were not flexible enough to build a specific predictive model
- We are currently focusing on discriminant function analyses (DFA)

Methods

- Measures from CIFASD II
  - Non-overlapping variables (significant for either presence of alcohol exposure OR presence of ADHD) were selected
    - 17 neuropsychological variables from the D-KEFS and CANTAB
    - 34 behavioral variables from the CBCL and DBD (primarily item data)
- Subjects groups for comparison
  - AE+ADHD vs. ADHD
  - AE-ADHD vs. CON
- Analyses
  - Discriminant Function Analyses (DFA)

Subject Demographics

Variable	AE+ADHD (*n* = 62)	AE-ADHD (*n* = 28)	ADHD (*n* = 94)	CON (*n* = 144)
Site [*n* (%)]				
Albuquerque	7 (11.3)	1 (3.6)	17 (18.1)	26 (18.1)
Atlanta	10 (16.1)	10 (35.7)	19 (20.2)	19 13.2)
Los Angeles	14 (22.6)	8 (28.6)	3 (3.2)	18 (12.5)
Plains States	4 (6.5)	2 (7.1)	12 (12.8)	18 (12.5)
San Diego	27 (43.5)	7 (25.0)	43 (45.7)	63 43.8)
Age [*M* (SD)]*	12.43 (2.21)	12.71 (2.62)	11.46 (2.63)	12.47 (2.56)
FSIQ [*M* (SD)]*	82.49 (18.31)	89.04 (14.78)	92.44 (18.13)	109.67 (11.90)
Sex [*n* (% Female)]	23 (37.1)	13 (46.4)	22 (23.4)	65 (45.1)
Race [*n* (% White)]*	37 (59.7)	7 (12.1)	41 (43.6)	78 (54.2)
Ethnicity [*n* (% Hispanic)]	8 (12.9)	3 (10.7)	16 (17.0)	26 (18.1)
Handedness [*n* (% Right)]	53 (85.5)	27 (96.4)	84 (89.4)	134 (93.1)
ADHD [*n* (% Diagnosed)]	62 (100)	0 (0)	94 (100)	0 (0)
FAS [*n* (% Diagnosed)]	0 (0)	0 (0)	0 (0)	0 (0)

* Significant at a rate of $p < .05$

Preliminary Results

AE-ADHD vs. CON

Classification Results[a]

		AE– vs CON	Predicted Group Membership AE–	CON	Total
Original	Count	AE–	11	3	14
		CON	10	46	56
		Ungrouped cases	40	18	58
	%	AE–	78.6	21.4	100.0
		CON	17.9	82.1	100.0
		Ungrouped cases	69.0	31.0	100.0

a. 81.4% of original grouped cases correctly classified.

- Discriminant function coefficients ranged from .34 - .94 (absolute values)
- Overall classification rate of 81.4%
  - WISC Similarities Standard Score
  - Philtrum Length Percentile

AE+ADHD vs. ADHD

Classification Results[a]

		AE+ vs CON	Predicted Group Membership AE+	CON	Total
Original	Count	AE+	16	2	18
		CON	3	41	44
		Ungrouped cases	22	12	34
	%	AE+	88.9	11.1	100.0
		CON	6.8	93.2	100.0
		Ungrouped cases	64.7	35.3	100.0

a. 91.9% of original grouped cases correctly classified.

- Discriminant function coefficients ranged from .34 – 1.45 (absolute values)
- Overall classification rate of 91.9%
  - 8 Items from CBCL
  - Number of incorrect errors on Spatial Working Memory task (CANTAB) – 8 boxes condition
  - Total number of double errors in Spatial Working Memory task (CANTAB)

Specific Aims 2-4

- **Test the specificity and sensitivity of the model developed in Aim 1 in children ages 10-16.** A battery of standardized neurobehavioral tests will be administered to subjects in three subject groups (alcohol-exposed, AE; non-exposed Controls; and non-exposed clinically-referred Contrast subjects) at four sites. Sensitivity (AE vs. Control) and specificity (AE vs. Contrast) will both be tested. Data will be combined with data from other CIFASD projects.

- **Test the utility of the model in younger children, ages 5-7.** A similar battery of age-appropriate standardized neuropsychological tests will be administered to young children in the same three subject groups at three of the four sites. Sensitivity and specificity will be tested as in Aim 2.

- **Targeted assessment of memory function.** In Phase I and II, our test batteries focused heavily on executive function, which proved to be an important domain in our preliminary neurobehavioral profile. Past studies and some preliminary data suggest that memory is another important domain and further study, including tests of both sensitivity and specificity, is warranted.

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Effects of Age and Sex on Behavioral and Neuropsychological Functioning in FASD

Amy L. Panczakiewicz, Leila Glass,…, Sarah Mattson, & the CIFASD

Status: Abstract Submitted to RSA 2014

Background

- The effects of age and sex on the neurobehavioral profile of FASD are relatively understudied.
- Understanding how these factors contribute to cognitive and behavioral deficits seen in FASD may improve diagnostic accuracy and lead to better screening tools and ultimately improved intervention focused at high-risk subgroups.
- In the current study, we examined the interaction between age, sex, and alcohol exposure on neuropsychological outcomes.

Methods

- 253 children (5y-16y, M = 11.48) were tested and separated into 4 groups
  - Exposure: Alcohol-exposed vs. controls with minimal or no prenatal alcohol exposure
  - Age: 5-7y vs. 10-16y

	Young	Old
AE	37	89
CON	38	89

- Children completed the California Verbal Learning Test (CVLT-C).

- Caregivers completed the Vineland Adaptive Behavior Scales (VABS-II).

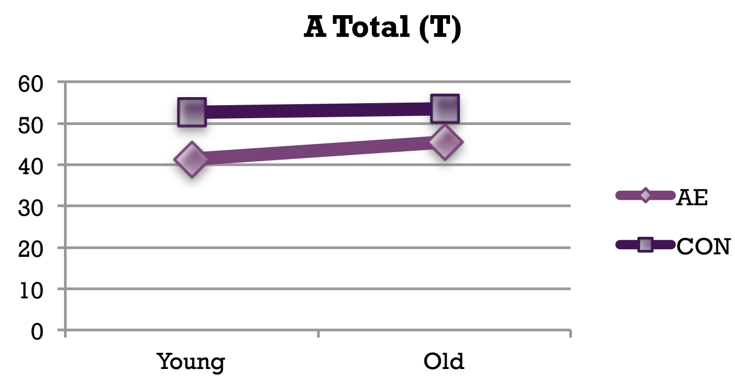
- Neurobehavioral data were analyzed using a 2 (Exposure) x 2 (Sex) x 2 (Age) design.

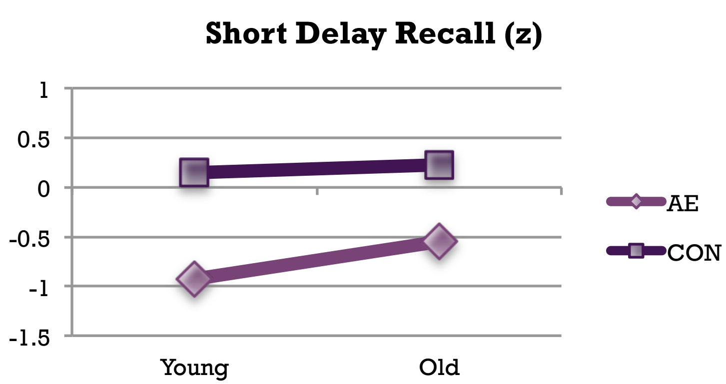
Subject Demographics

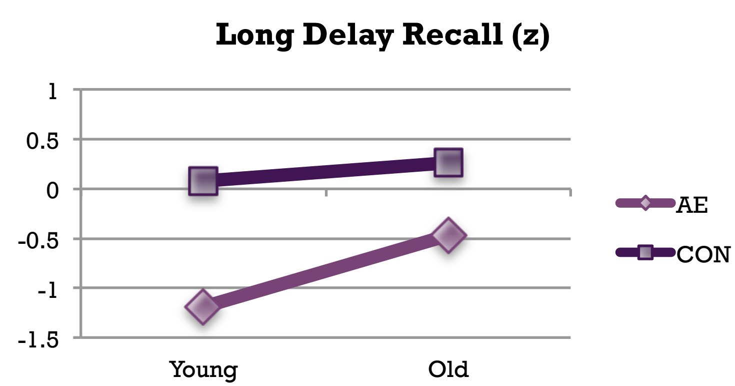
Variable	Young (5-7)		Old (10-16)	
	AE (n = 37)	CON (n = 38)	AE (n = 89)	CON (n = 89)
CIFASD Site [n (%)]				
Atlanta	17 (45.9)	7 (18.4)	13 (14.6)	23 (25.8)
Los Angeles	0 (0.0)	1 (2.6)	15 (16.9)	10 (11.2)
Northern Plains	11 (29.7)	15 (39.5)	31 (34.8)	29 (32.6)
San Diego	9 (24.3)	15 (39.5)	30 (33.7)	27 (30.3)
Sex [n (% female)]	18 (48.6)	20 (52.6)	38 (42.7)	41 (46.1)
Age [M (SD)]	6.9 (.9)	6.6 (.9)	13.1 (2.1)	13.9 (2.1)
Handedness [n (% right)]	29 (78.4)	37 (97.4)	78 (87.6)	79 (88.8)
Race [n (%White)]	14 (37.8)	27 (71.1)	52 (58.4)	46 (51.7)
Ethnicity [n (% Hispanic)]	5 (13.5)	5 (13.2)	15 (16.9)	16 (18.0)
FSIQ [M (SD)]	85.1 (13.8)	104.0 (13.4)	88.8 (12.2)	13.9 (16.6)
FAS diagnosis [n (%)]	6 (16.2)	0 (0)	17 (22.7)	0 (0)

Results: Verbal Learning & Memory

- Main effects of group and age on all CVLT-C variables
- No effects of sex
- No interactions

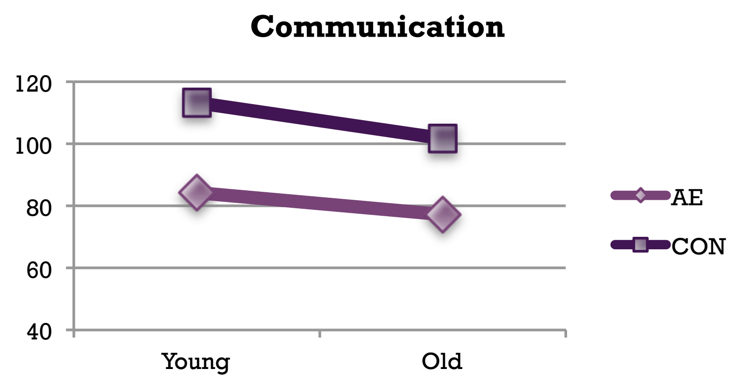


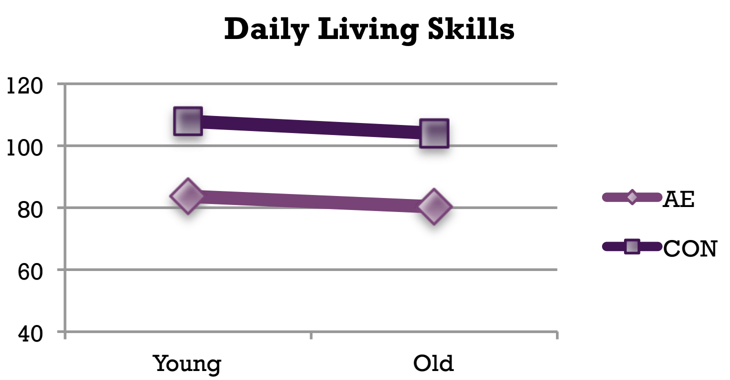


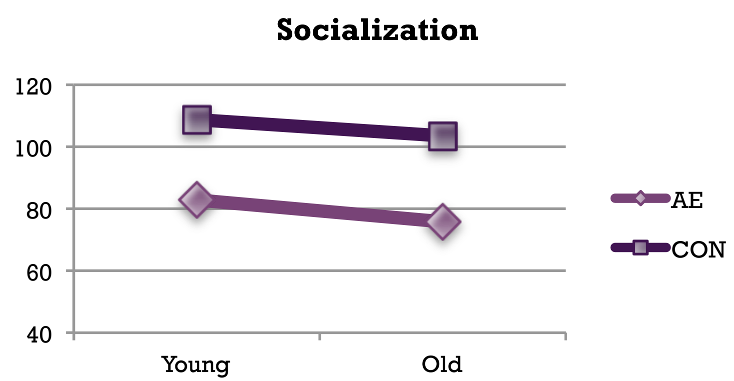


Results: Adaptive Behavior

- Main effects of group and age on all VABS-II variables
- No effects of sex
- No interactions







Conclusions/Implications

- Consistent with previous studies, alcohol exposure was associated with neuropsychological and behavioral impairments.
- Age
  - Overall, older children in both groups performed *worse* on behavior ratings but *better* on memory scores, even when corrected for age.
  - The lack of interaction between age and group may suggest that while performance changes with age, the degree of change is not related to prenatal alcohol exposure.
- Sex
  - No differences between boys and girls were observed in either domain.

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DISRUPTIVE BEHAVIORS INCREASE WITH AGE IN CHILDREN PRENATAL ALCOHOL EXPOSURE

Patrick Goh, …, Sarah N. Mattson, and the CIFASD

Status: Conceptualization/Data Analysis Phase

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Background

- Prenatal alcohol exposure (AE) and ADHD have been known to be associated with juvenile delinquency
- Children with both AE and ADHD display a higher rate of disruptive behaviors compared to children with ADHD at certain ages
- It is unknown at what age these group differences begin to occur
- In the current study, this relation was examined in subjects from the CIFASD II dataset.

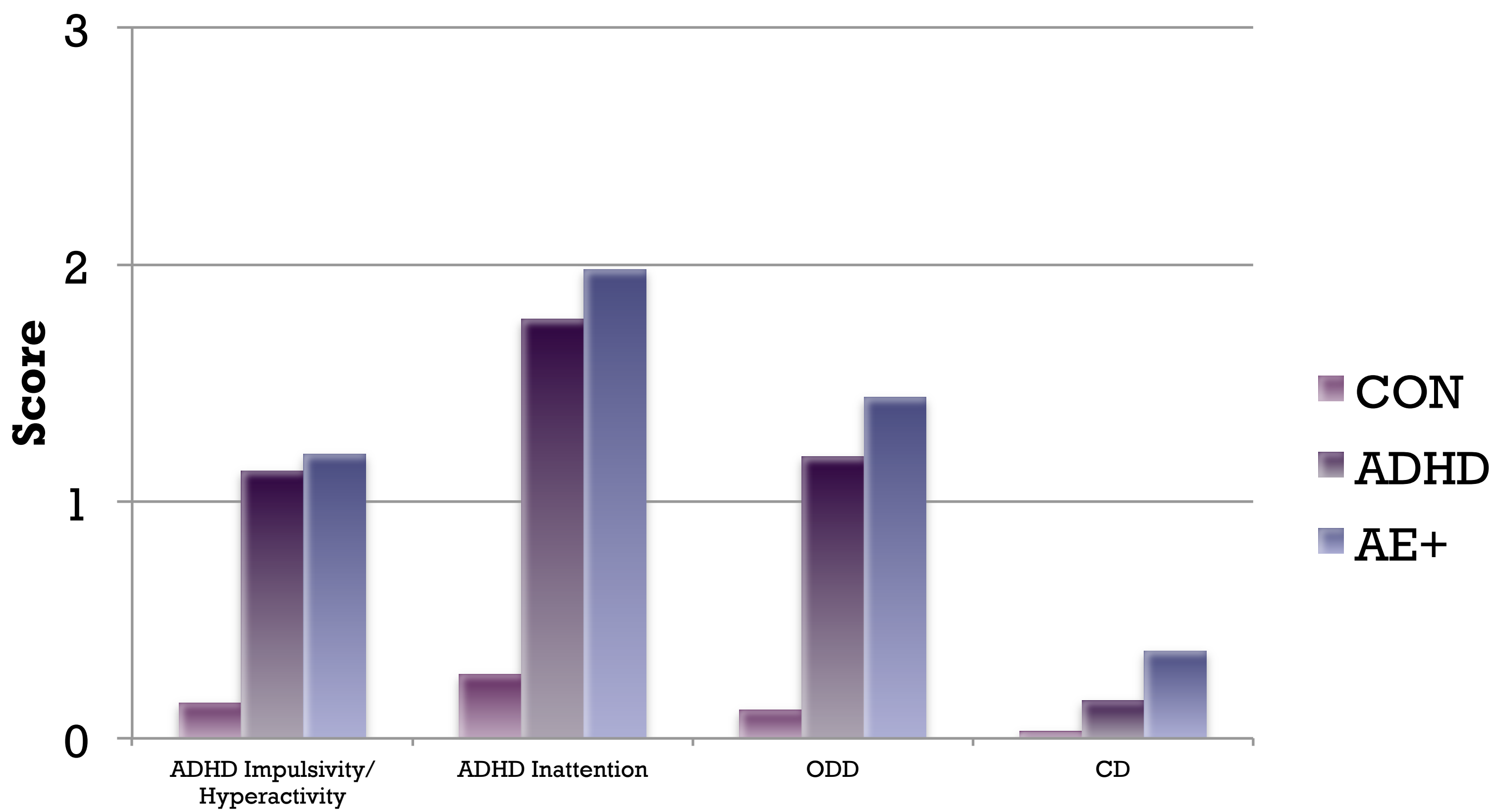
Methods

- 3 groups of children (8-16y, M=12.06) from multiple sites were tested
  - Children with histories of heavy prenatal alcohol exposure and attention deficit/hyperactivity disorder (AE+, n=84)
  - Nonexposed children with attention-deficit/hyperactivity disorder (ADHD, n=90)
  - Nonexposed controls without alcohol exposure or ADHD (CON, n=137)
- Caregivers completed the Disruptive Behavior Disorder Rating Scale (DBD)
- DBD factor scores were analyzed using 3 (Group) x 3 (Age) ANOVA
  - ADHD Impulsivity/Hyperactivity, ADHD Inattention, ODD, CD
  - Age groups: 8-10, 11-13, 14-16

Subject Demographics

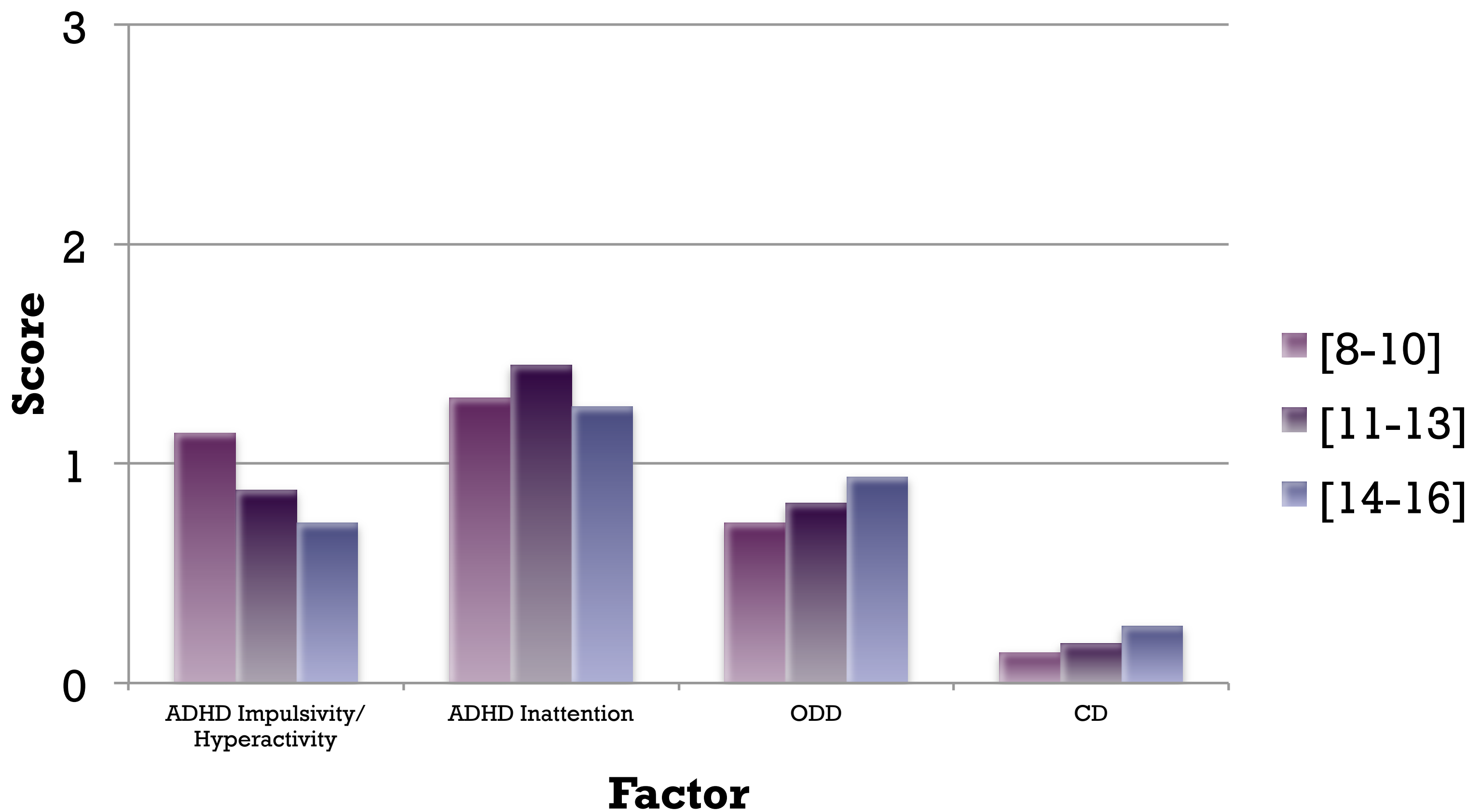
Variable	AE+ (n = 84)	ADHD (n = 90)	CON (n = 137)
CIFASD Site [n (%)]			
Atlanta	17 (20.2)	18 (20.0)	18 (13.1)
Los Angeles	17 (20.2)	2 (2.2)	18 (13.1)
Northern Plains	9 (10.7)	13 (14.4)	20 (14.6)
Albuquerque	7 (8.3)	15 (16.7)	24 (17.5)
San Diego	34 (40.5)	42 (46.7)	57 (41.6)
Sex [n (% Females)]	32 (38.1)	21 (23.3)	64 (46.7)
Age in years [M (SD)]	12.5 (2.2)	11.1 (2.3)	12.3 (2.4)
Handedness [n (% Right)]	70 (83.3)	80 (88.9)	128 (93.4)
Race [n (%White)]	50 (59.5)	61 (67.8)	94 (68.6)
Ethnicity [n (% Hispanic)]	6 (7.1)	21 (23.3)	30 (21.9)
FSIQ [M (SD)]	81.4 (17.2)	92.6 (18.1)	109.5 (11.6)
FAS Diagnosis [n (%)]	22 (26.2)	0 (0)	0 (0)

Results: Group Main Effects



Across Age, AE+ and ADHD groups display significantly higher rates of disruptive behaviors than CON on all DBD measures

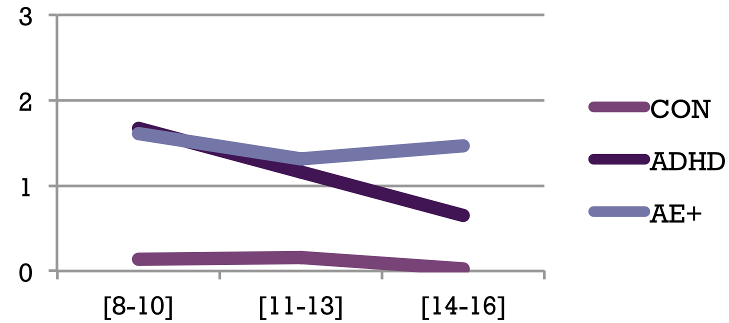
Results: Age Main Effects



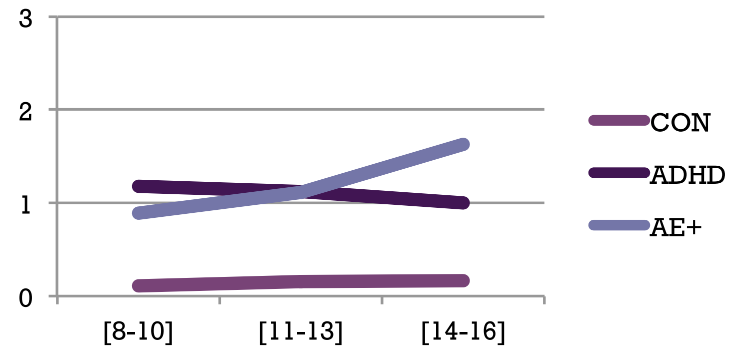
Across Group, significant main effect of age in ADHD Impulsivity/ Hyperactivity and CD factor scores

Results: Significant Age x Group Interactions

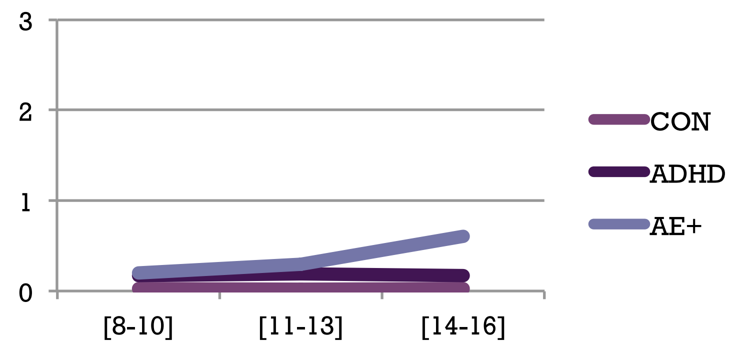
- ADHD impulsivity/ hyperactivity factor scores



- ODD factor scores



- CD factor scores



Conclusions/Implications

- The differences in rate of delinquent acts between AE+ and ADHD groups changes as age increases
  - Ages 8-10: no significant differences are found in rates of ODD, CD, and ADHD impulsivity/hyperactivity type delinquent acts between groups.
  - Around age 14 (ODD & CD behaviors) and age 11 (ADHD Impulsivity/Hyperactivity behaviors), the AE+ group begins to display higher rates of delinquent behaviors compared to the ADHD group.
- AE+ and ADHD groups differed on 3 DBD factors at older ages, suggesting these items may be useful in differential diagnosis.
  - Exposed children in the oldest age group (14-16) have higher rates of H/I, ODD, and CD behaviors than non-exposed children with ADHD.

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Validating DSM-5 Criteria for ND-PAE

Leila Glass, …, Julie Kable, …, Sarah Mattson & the CIFASD

Status: Conceptualization/Data Analysis Phase

Background

- Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE) appears in the DSM 5 Appendix
- Ongoing efforts to determine the clinical relevance, proper interpretation, and sensitivity and specificity of the criteria
- No specific guidelines available to define criteria in a easily replicable manner (i.e., measures, cut-offs, number of scores impaired in a single domain)
- In the current study we are operationalizing criteria and determining base-rates using CIFASD II data

Methods

- Impairment as 1 SD below the mean balances sensitivity and specificity
- Consider base rates of impaired scores – two scores within a domain is less likely than two impaired scores across two domains
- Clinical judgment and theoretical reasoning to justify measures used and clinical significance

Criteria

- Criteria B (1+)
  - 1. Global Intellectual Impairment
  - 2. Impairment in Executive Function
  - 3. Impairment in Learning
  - 4. Impairment in Memory
  - 5. Impairment in Visual-Spatial Reasoning
- Criteria C (1+)
  - 1. Impairment in Mood /Behavioral Regulation
  - 2. Attention Deficit
  - 3. Impairment in Impulse Control
- Criteria D (2+, including 1 or 2)
  - 1.Communication Deficit
  - 2. Social Impairment
  - 3. Impairment in Daily Living Skills
  - 4. Motor Impairment

3		1		
Impairment in Impulse Control		Communication Deficit		
CBCL Rule-Breaking Subscale	NEPSY Inhibition Subtest	VABS Communication Composite	CELF expressive language Scale	CELF receptive language Scale

Status

- Determining appropriate variables, cutoffs, and interpretations for criteria
- Will run CIFASD subjects through automated criteria to determine classification accuracy, sensitivity, and specificity

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Ultimately aim to assist in the interpretation and implementation of ND-PAE criteria in clinical settings to improve identification of affected children, differential diagnosis, and patient care

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Other Preliminary Results

- Examining comorbidity in FASD and differences in neurobehavior related to comorbidity
  - In entire CIFASD II sample, rates of ADHD, ODD, or CD are higher in the AE Ss than in the non-exposed (NE) subjects even though we recruited for ADHD
    - In the sample of Ss with ADHD (both AE and NE), rates of CD are higher in the AE (21%) than NE (5%) Ss.
    - Rates of ODD are similar between groups (54% AE, 46% NE)
  - IQ scores vary by comorbidity