Cognitive/Behavioral Profiles of Patients with Prenatal Alcohol Exposure

Washington State FAS Diagnostic & Prevention Network (FAS DPN)

Research Population: MRI/MRS/fMRI Study 2009 (n = 81)

Clinical Population: FASD Diagnostic Clinic 1993-present (n = 2,000)

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University of Washington 2009

The following slides were presented by Dr. Astley at the Interagency Coordinating Committee on FAS (ICCFAS) Workshop at NIAAA in Rockville MD on May 6-7, 2009.The goal was to bring together a group of experts to share information about cognitive deficits, behavioral problems, and psychopathology in individuals with prenatal alcohol exposure. Dr. Astley presented data on 2 groups of individuals with FASD: 1) A research population (n = 81) that participated in a MRI/MRS/fMRI study in 2009 and 2) 2,000 patients with prenatal alcohol exposure seen to date in the WA FAS DPN Clinics. Although each slide below is accompanied by a brief summary statement, the content of each slide is best interpreted by clinical/research professionals with expertise in neuropsychological assessment. The purpose of these slides is to illustrate how the three diagnostic classifications under the umbrella of FASD (FAS/PFAS, Static Encephalopathy/Alcohol Exposed, and Neurobehavioral Disorder/Alcohol Exposed) compare and contrast.
Publications that describe the methods and populations referenced in these slides can be found on our website. (http://depts.washington.edu/fasdpn/htmls/literature.htm)

FAS DPN **MRI, MRS, fMRI** Study Population (n = 81)

Age: 5.0 to 15.9 yrs

N	4 Study Groups	FAS Face	Brain		Alcohol
20	**FAS / PFAS**	**face**	**severe**		**alc**
24	**SE/AE** (severe ARND)		**severe**		**alc**
21	**ND/AE** (moderate ARND)			**moderate**	**alc**
16	**Control**				

Four study groups were enrolled in the MRI/MRS/fMRI study. The diagnostic criteria that define each are described in full in Astley et al., 2009 (http://depts.washington.edu/fasdpn/pdfs/FASD-Psych-MRstudy-2009.pdf). The 65 children with FASD were enrolled from the WA FAS DPN clinic sample.

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The diagnostic classifications are based on the FASD 4-Digit Diagnostic Code.
FAS / PFAS = fetal alcohol syndrome and partial FAS.
SE/AE = Static Encephalopathy / Alcohol Exposed. (comparable to severe ARND)
ND/AE = Neurodevelopmental Disorder / Alcohol exposed. (comparable to moderate ARND)
Controls were healthy peers with no prenatal alcohol exposure.
The ND/AE, SE/AE and FAS/PFAS groups reflect 3 distinct FASD clinical groups. ND/AE have moderate brain dysfunction and no FAS facial features. SE/AE have severe brain dysfunction and no FAS facial features. FAS/PFAS have severe brain dysfunction and full FAS facial features.

Washington State FAS DPN **Clinic Sample (n = 2,000)**

- Clinic opened in 1993 (16 years)
- 4-Digit Code (interdisciplinary team)
- >2000 fields of data per patient (from Diagnostic Form, New Patient Information Form, and community data)

Patient Profile			
Age	20% birth-3	60% 4-15yr	20% 16-50 yr
Gender	43% female		
Race	50% White	7% Black	11% Nat Am
Diagnosis	10% FAS	25% SE/AE	50% ND/AE
Alcohol	65% trimester 1	56% tri 2	50% tri 3
	8-12 drinks	4 days / week	
Illicit Drugs	63%		
Caregiver	20% birth mom	60% foster/adopt	

The WA State Fetal Alcohol Syndrome Diagnostic & Prevention Network (FAS DPN) is a network of FASD diagnostic clinics that all use the FASD 4-Digit Diagnostic Code and an interdisciplinary approach to FASD diagnosis. Patients span the entire age range and are typically exposed to a multitude of adverse prenatal and lifetime adverse events and exposures (e.g., 63% had prenatal exposure to illicit drugs). Only 20% of patients are still in the care of their birth mother at the time of their FASD diagnostic evaluation.

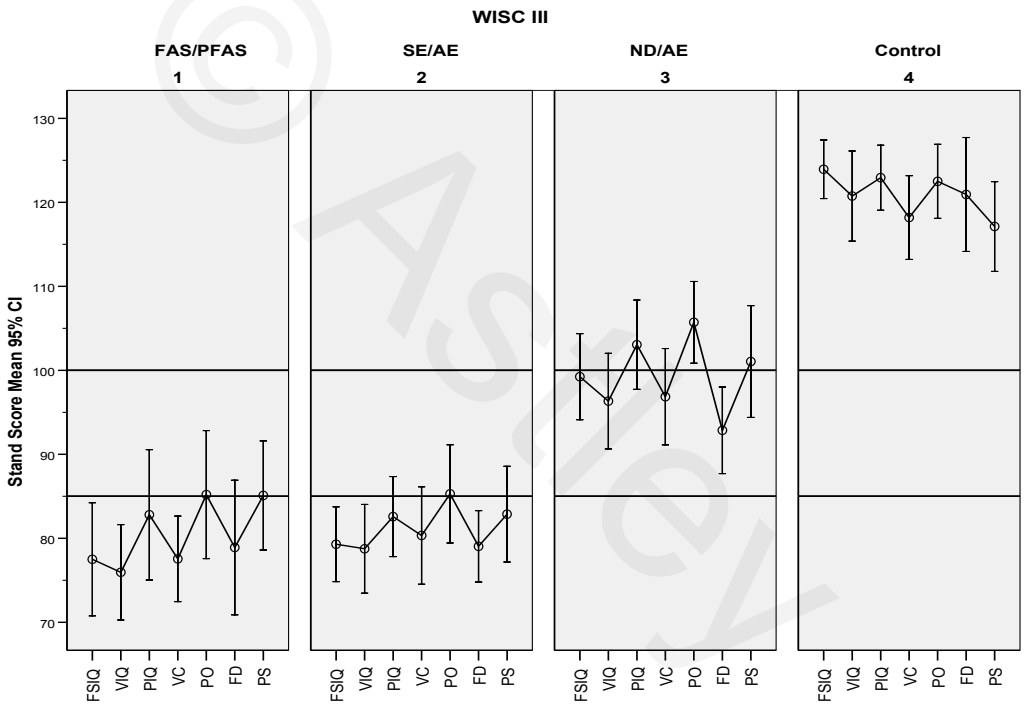
A comprehensive profile of all 1,400 WA state residents, with a confirmed prenatal alcohol exposure, evaluated for FASD at the WA FAS DPN from 1993 to 2005 is presented in Astley (2010) (http://depts.washington.edu/fasdpn/pdfs/astley-profile-2010.pdf).

FAS DPN **MRI, MRS, fMRI** Study Population (n = 81)

Psychological / Psychiatric Assessment Battery Cognition, executive function, language, memory, achievement, attention, sensory-motor, inhibitory control, adaptive and maladaptive behavior		
Neuropsychological	**Language**	**Behavioral / Parent Report**
WISC-III	**TLC**	**BRIEF**
CVLT-C	**TOLD**	**CBCL**
D-KEFS	**TOWK**	**C-DISC**
RCFT		**VABS**
WCST 128		
Key Math , WIAT		
QNST		
IVA		
VMI		

The psychological/psychiatric assessment battery for the MR study is presented above. WISC-III: Wechsler Intelligence Scale for Children; CVLT-C:Calif. Verbal Learning Test-child;D-KEFS: Delis-Kaplan Executive Function System; RCFT: Rey Complex Figure Test; WCST: Wisc Card Sort Test; QNST: Quick Neurological Screening Test; IVA: Integrated Visual Auditory Continuous Performance Test; VMI: Beery Buktenica Developmental Test of Visual-Motor Integration; WIAT: Wechsler Indiv Achieve Test; TLC: Test Lang Competence; TOLD: Test of Lang Develop; TOWK: Test of Word Knowledge; BRIEF: Behavioral Rating Inventory of Executive Function; CBCL:Child Behav Checklist; C-DISC: Computerized Diagnostic Interview Scale for Children; VABS: Vineland Adaptive Behavior Scales.

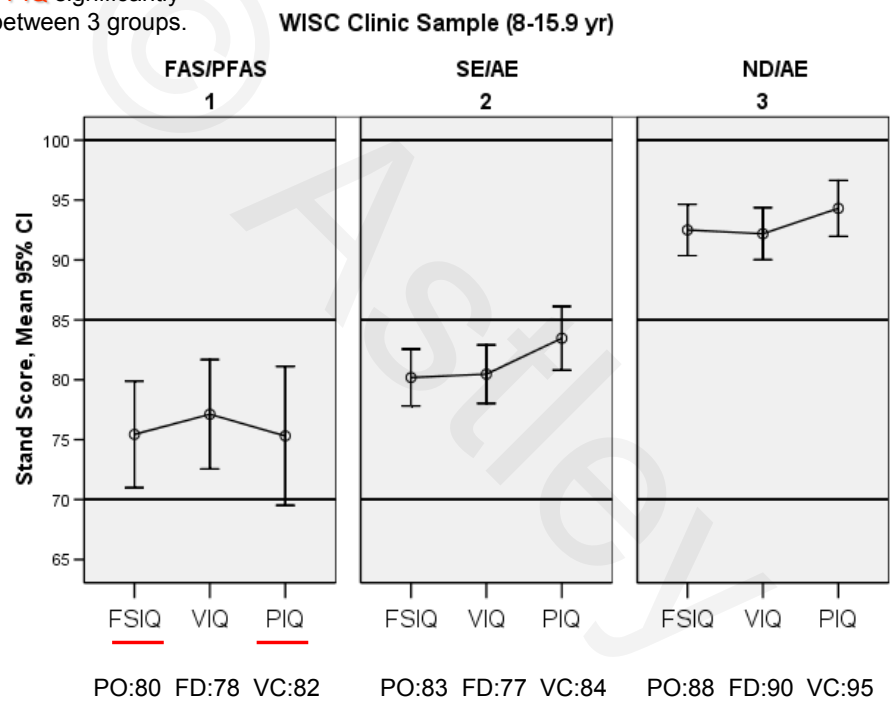
FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



In the MR study: the FAS/PFAS and SE/AE groups had comparably low WISC scores. Both groups had mean WISC scores significantly lower than the mean scores of the ND/AE group. In turn, the ND/AE group had significantly lower scores than the Control group.

FAS DPN **Clinic** Sample (n = 413)

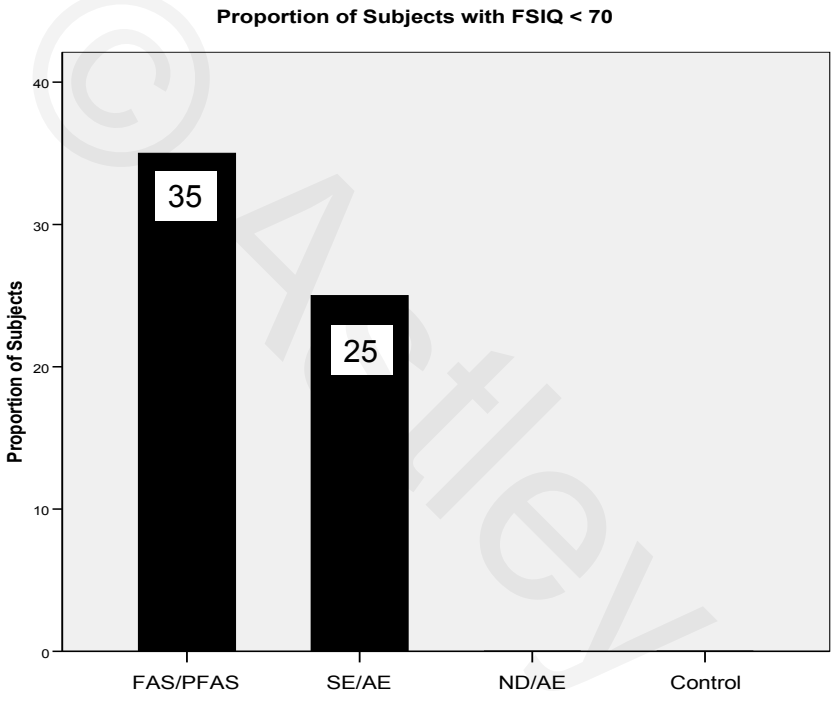
FSIQ and PIQ significantly different between 3 groups.



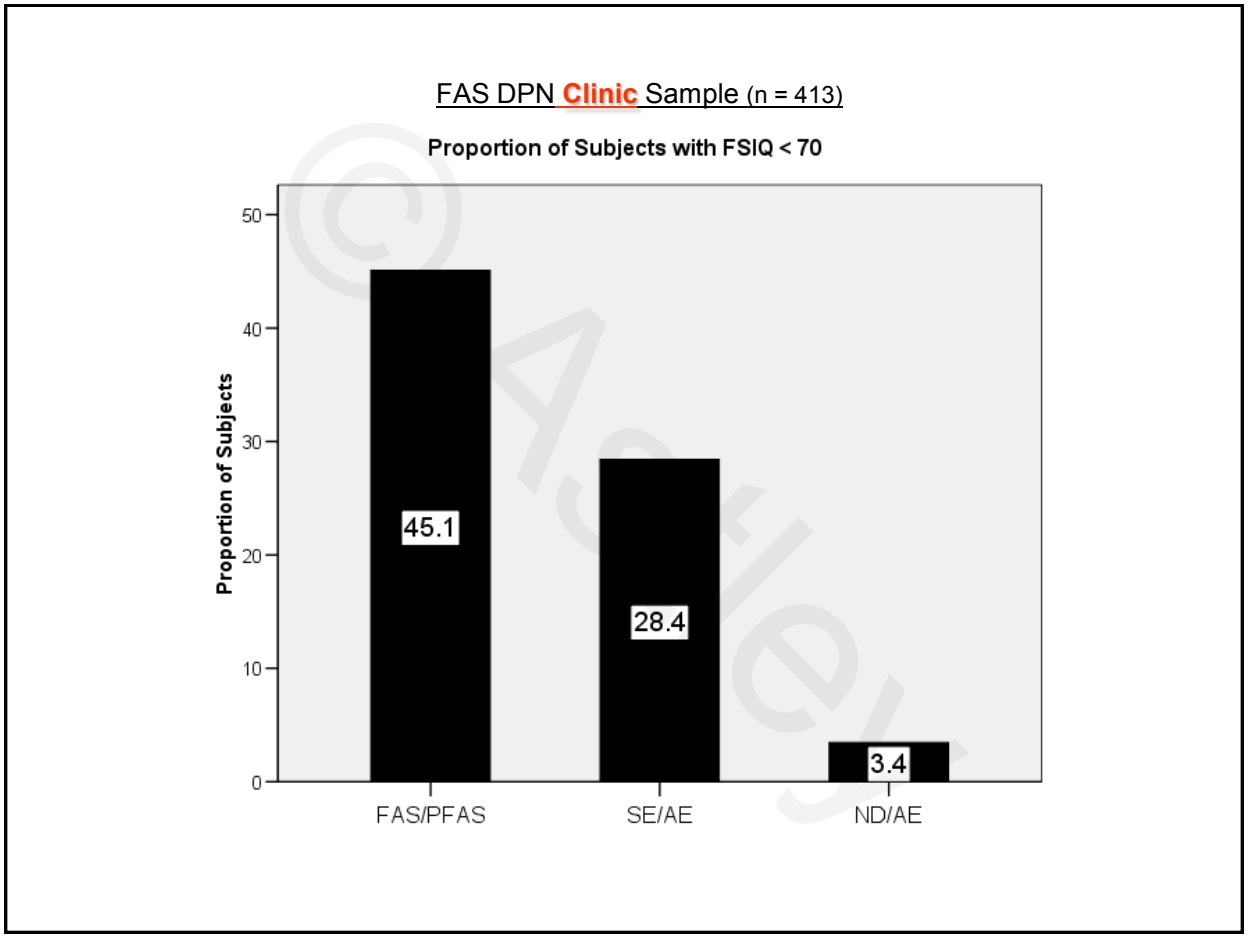
In contrast to the smaller MRI study sample (previous slide), mean FSIQ, VIQ and PIQ scores were significantly different between the FAS/PFAS group, SE/AE group, and ND/AE groups.

It is important to note that not all patients in the FAS DPN clinical sample receive the same battery of psychological tests. Tests will vary by patient age and area of concern. Note that the sample size varies for each psychological assessment.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)

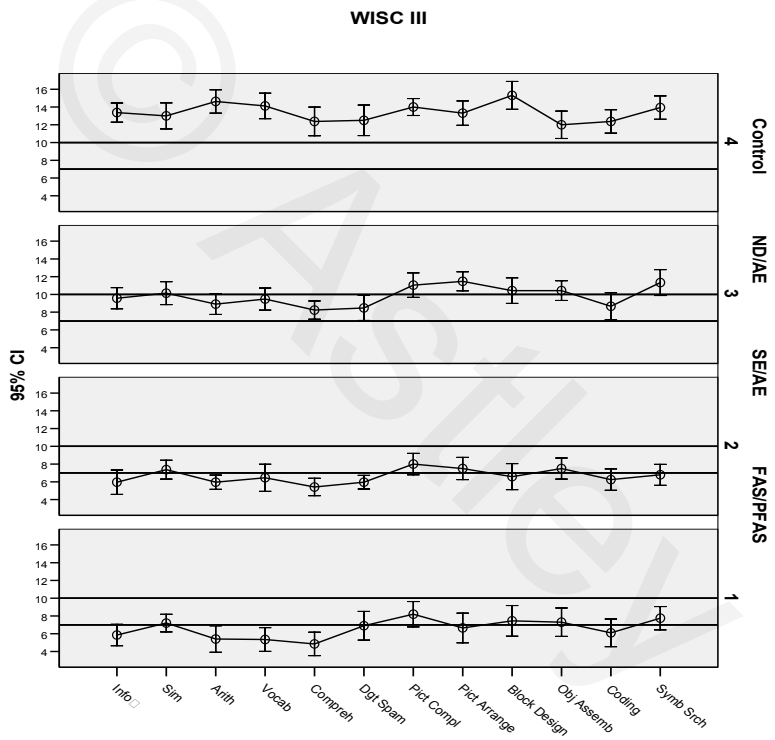


Among the children in the MR study, only 35% and 25% of children in the FAS/PFAS and SE/AE groups, respectively, had WISC III FSIQ < 70. No children in the ND/AE or control groups had FSIQ scores < 70.



Among the 413 children with FSIQ scores in the clinical population, the proportion of patients with FSIQ <70 decreased significantly as the severity of the FASD diagnostic classification decreased from FAS/PFAS to SE/AE to ND/AE.

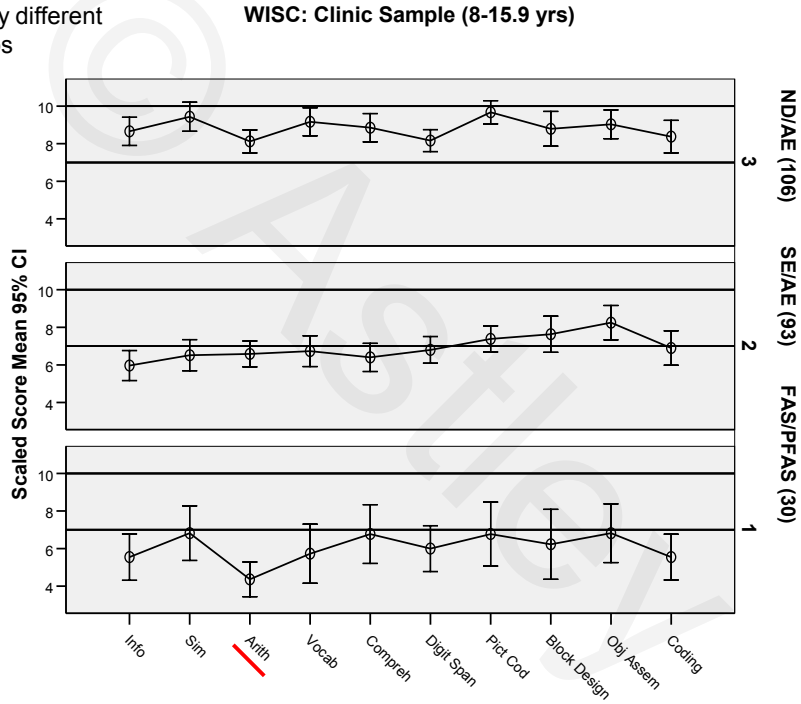
FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



Among the MR study sample, the mean scaled scores of the WISC III subtests are presented. Normal development is reflected by a mean scale score = 10. The horizontal lines drawn on the graphs reflect the mean (scaled score = 10) and -1 SD (scaled score = 7).

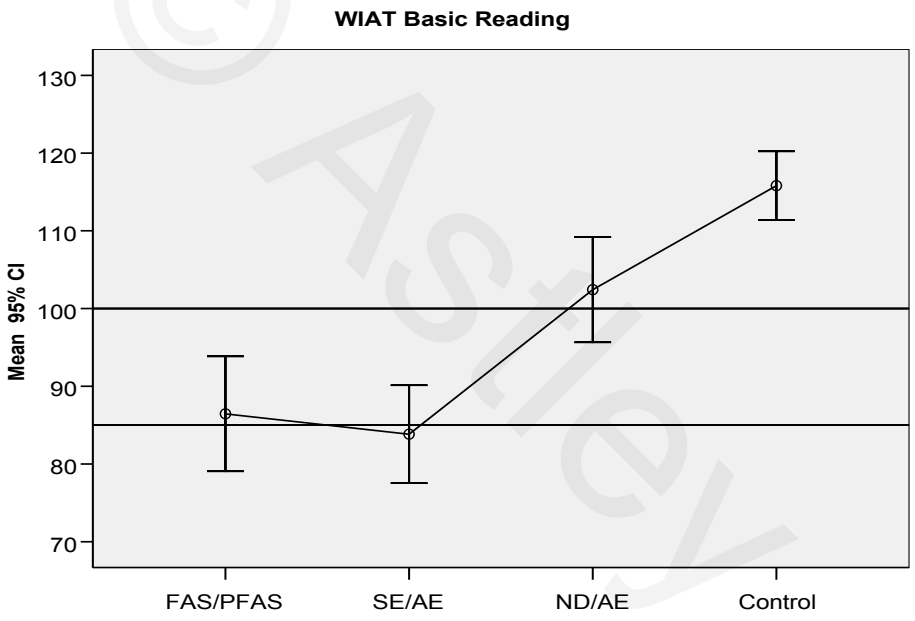
FAS DPN **Clinic** Sample (n = 229)

Arith significantly different between 3 groups



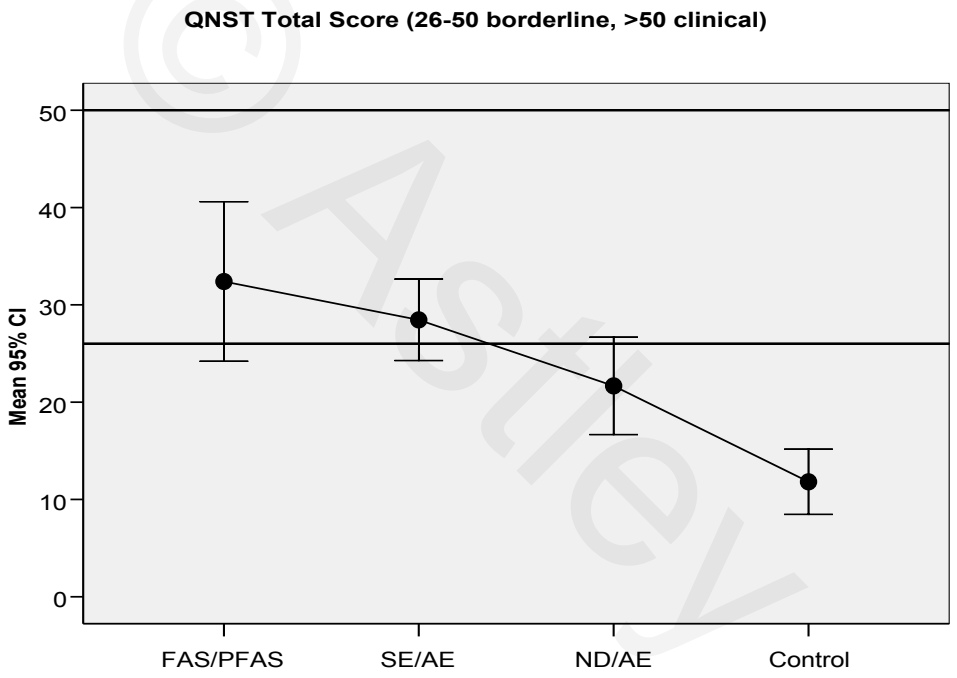
Among the Clinic Sample of 229 patients with WISC subtest scores, the FAS/PFAS and SE/AE groups had comparably low performance with one exception. The FAS/PFAS group had significantly lower performance on the Arithmetic subtest relative to the SE/AE group. Both the FAS/PFAS and SE/AE groups had significantly lower performance on the WISC subtests relative to the ND/AE group.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



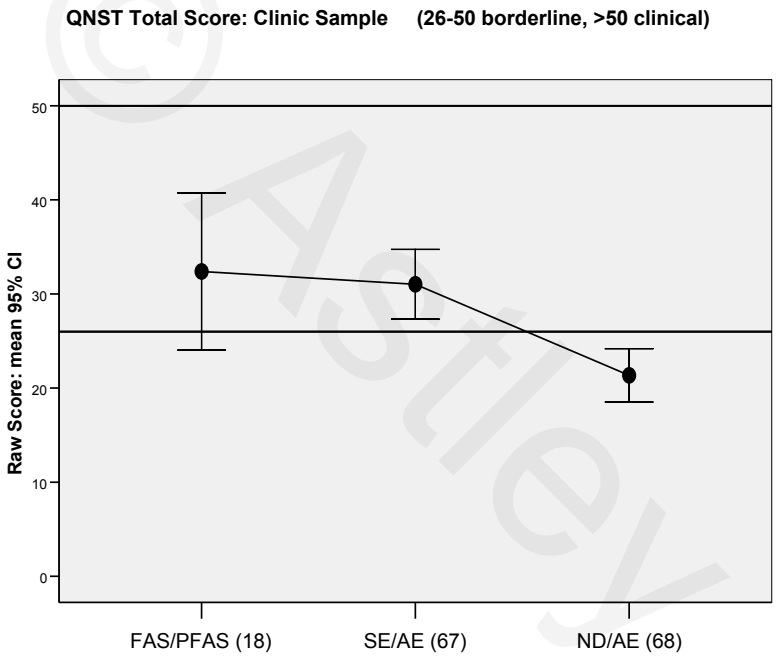
Among the MR study sample, the FAS/PFAS and SE/AE groups had significantly lower performance on the WIAT Basic Reading subtest than the ND/AE and Control groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



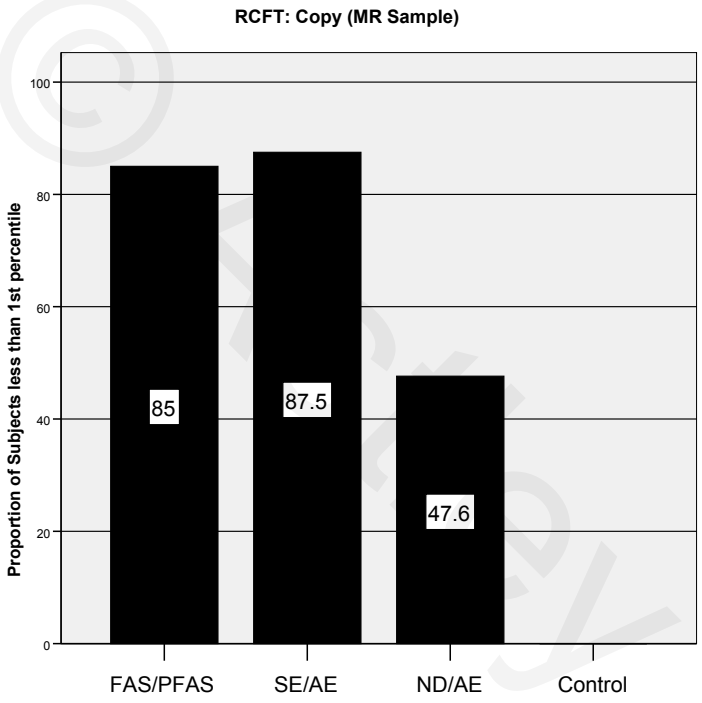
Among the MR study sample, the mean total raw score for the Quick Neurological Screening Test decreased significantly as the severity of the FASD diagnostic classification decreased from FAS/ PFAS to SE/AE to ND/AE to Controls. The higher the score, the greater the neurological abnormality. A total raw score between 26 and 50 is in the clinical borderline range.

FAS DPN Clinic Sample (n = 153)



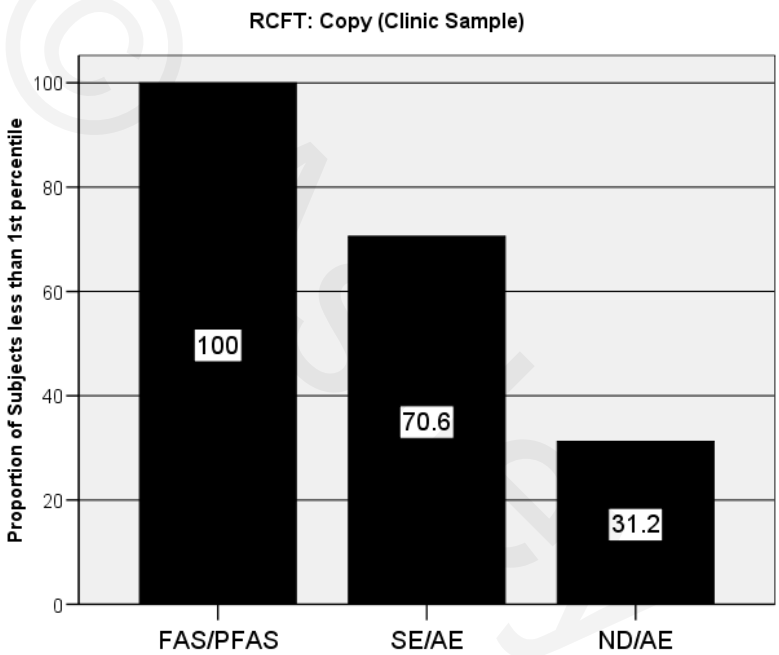
Among the 153 patients with FASD from the Clinical sample, the mean total raw score for the QNST was in the clinical borderline range for the FAS/PFAS and SE/AE groups. These two groups had significantly higher scores than the ND/AE group. A higher score reflects great neurological abnormality.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



Among the MR study sample, over 85% of the FAS/PFAS and SE/AE groups performed below the 1st percentile on the Copy subtest of the Rey Complex Figure Test. Forty-seven percent of the ND/AE group performed below the 1st percentile. No children in the Control group performed below the 1st percentile.

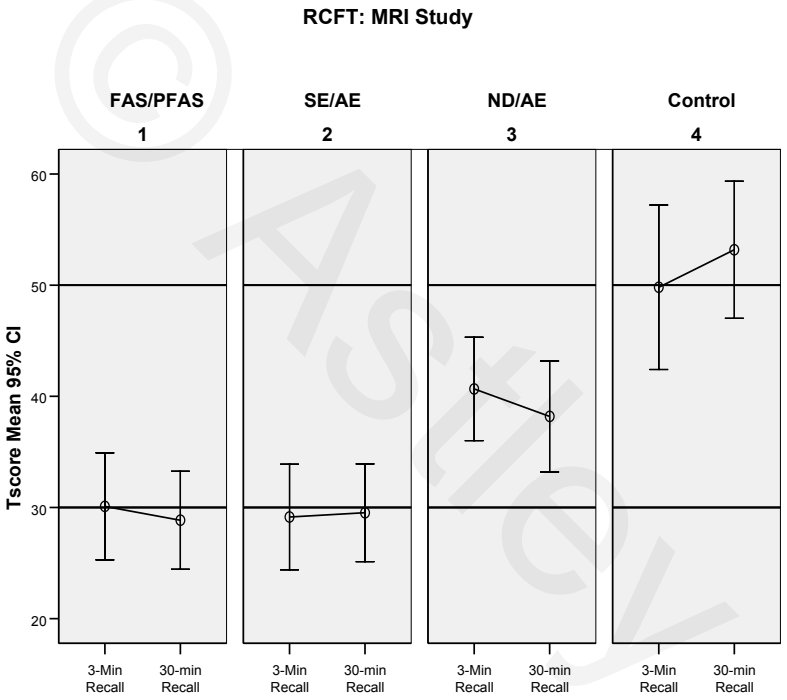
FAS DPN Clinic Sample (10 FAS/PFAS, 34 SE/AE, 32 ND/AE)



3 groups significantly different

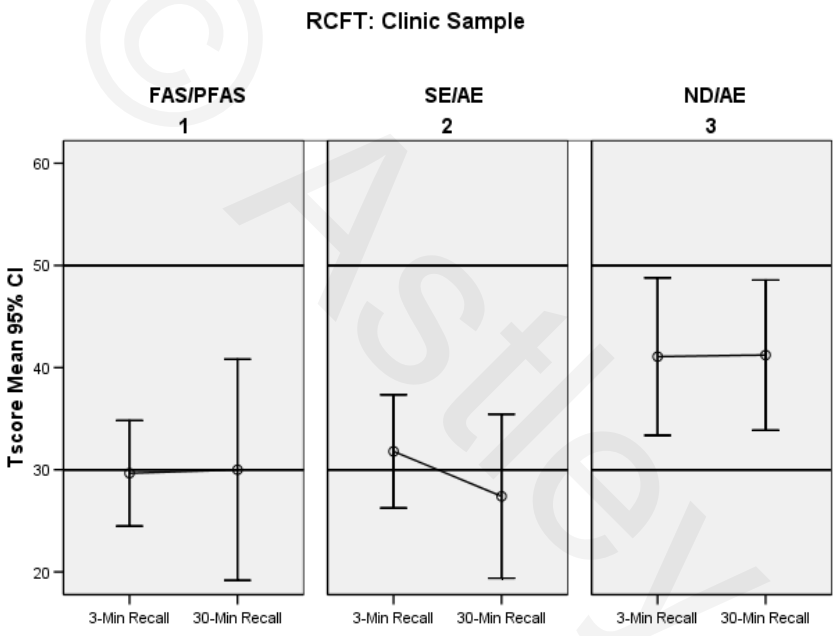
Among the 76 patients with FASD from the Clinical sample who were administered the Rey Complex Figure Test, the proportion of patients who performed below the 1st percentile on the Copy subtest increased significantly with increasing severity of FASD diagnostic classification.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



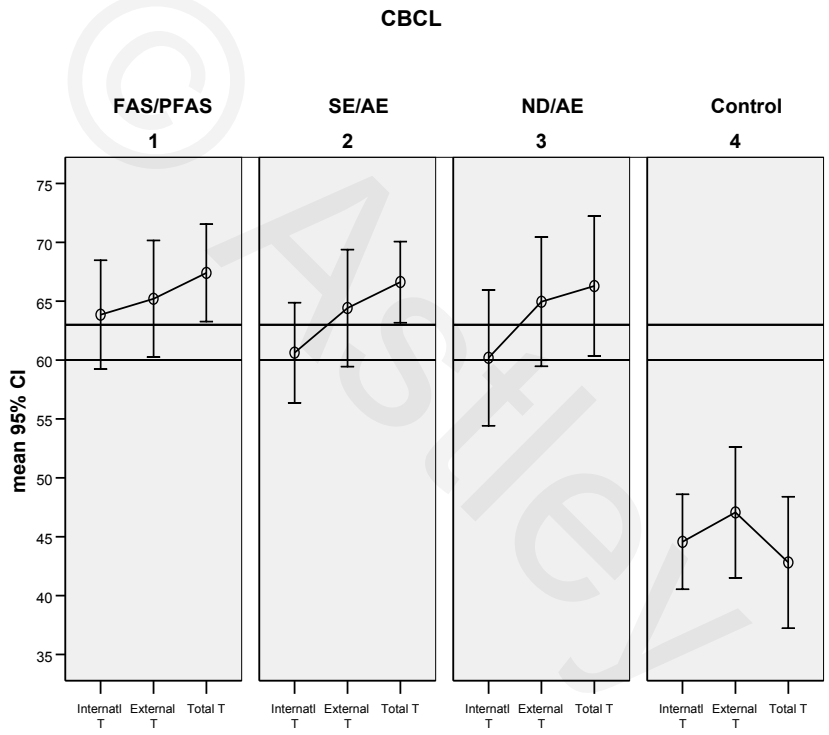
Among the MR study sample, the FAS/PFAS and SE/AE groups performed comparably low on the 3-minute and 30-minute recall subtests of the RCFT. The ND/AE group performed better than the FAS/PFAS and SE/AE groups, but worse than the Control group.

FAS DPN Clinic Sample (10 FAS/PFAS, 34 SE/AE, 32 ND/AE)



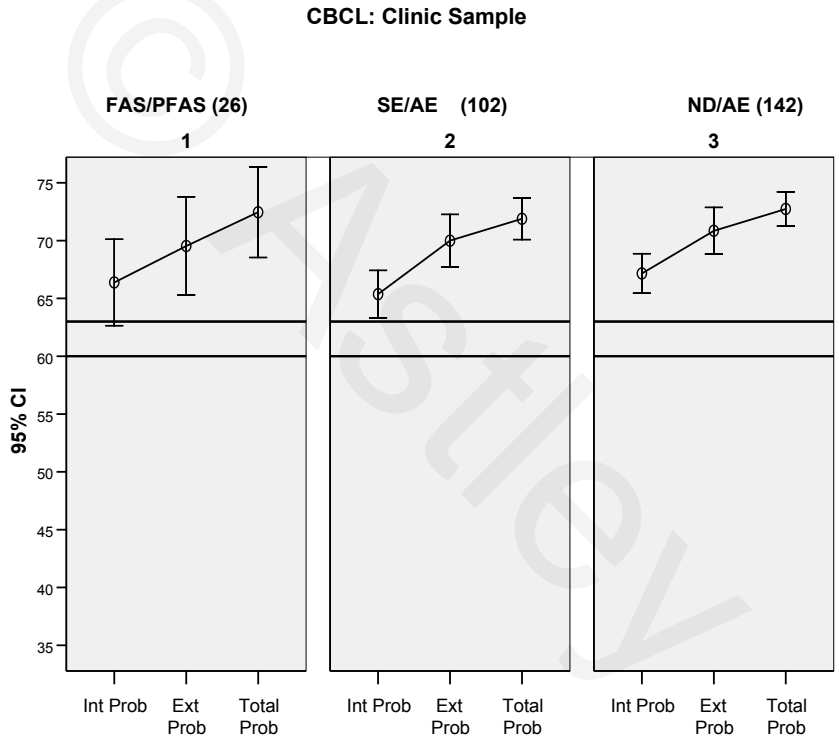
Among the 76 patients with FASD from the Clinic sample, the FAS/PFAS and SE/AE groups performed comparably low. The performance of the ND/AE group was slightly higher. Normal performance is reflected by a T score = 50. A T score of 30 is 2 SDs below the mean.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



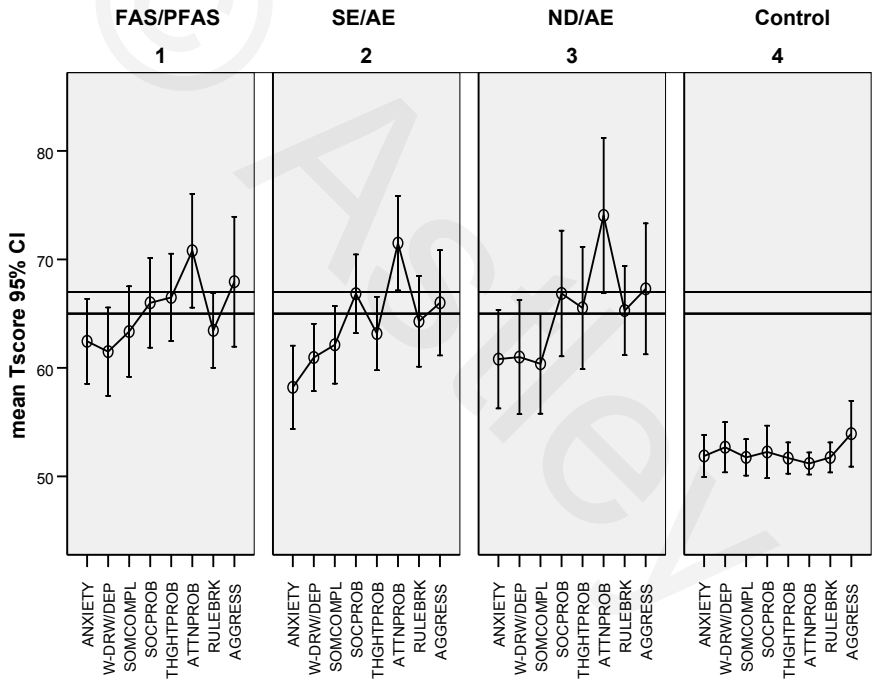
Among the MR study sample, caregiver report of child behavior on the Child Behavior Checklist was in the clinical range for the Internal, External, and Total Problem scales across the three FASD study groups. T-scores > 63 are in the clinical range. Scores between 60 and 63 are in the borderline clinical range. Unlike many measures of neuropsychological performance, behavioral problems appear to be comparably elevated across all three FASD study groups.

FAS DPN Clinic Sample (n=270)



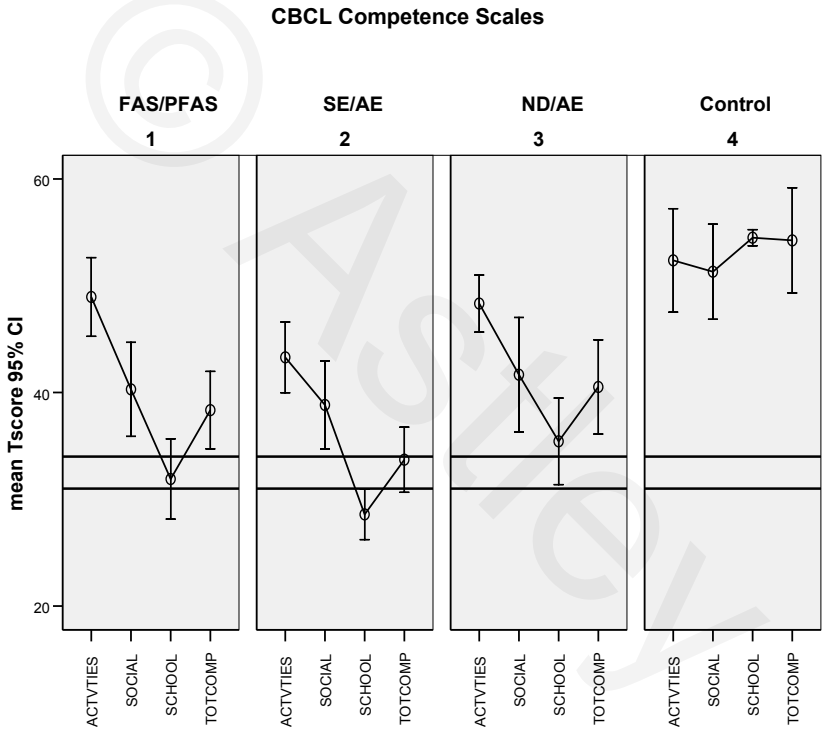
The CBCL profiles observed among the 270 children with FASD from the Clinic sample were similar to the profiles observed among the 65 children with FASD from the MR study. All 3 groups had Problem scores in the clinical range (T score > 63).

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



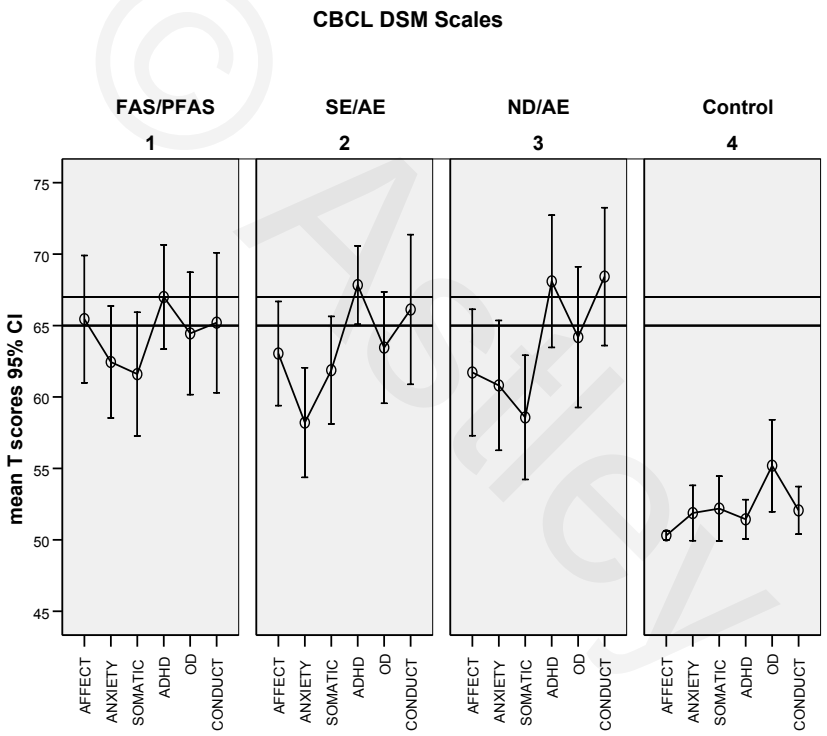
Among the MR study sample, the profiles across the three FASD groups are comparable and elevated relative to the Control group. T scores > 69 are in the clinical range. T scores between 65 and 69 are in the borderline clinical range.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



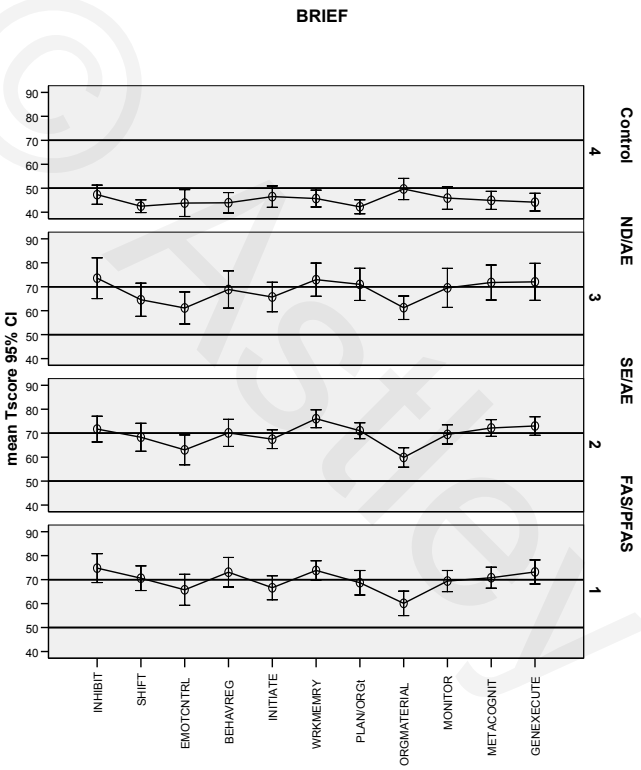
Among the MR study sample, T scores on the CBCL Competence Scales were comparably low across the three FASD groups relative to the Control Group. T scores below 31 (the lowest horizontal line) are in the clinical range.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



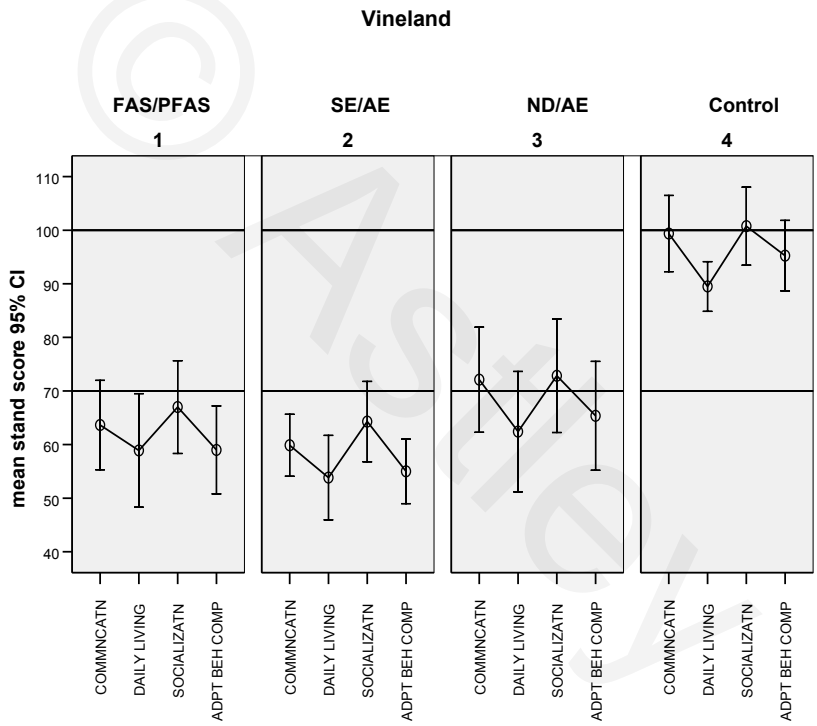
Among the MR study sample, the T scores on the CBCL DSM scales are comparably elevated into the clinical borderline range relative to the control group.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



In the MR study sample, caregiver report on the Behavioral Inventory of Executive Function is comparably elevated into the clinical range across all three FASD study groups relative to the Control

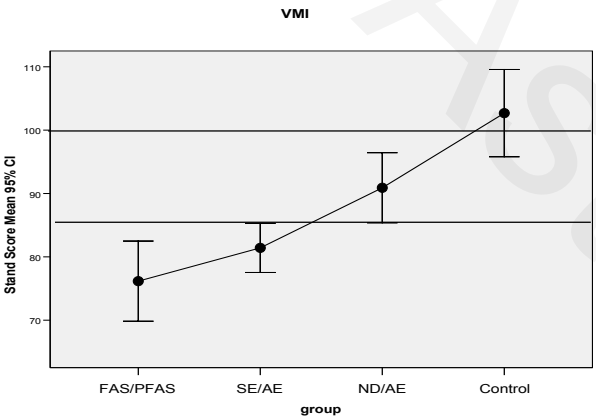
FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



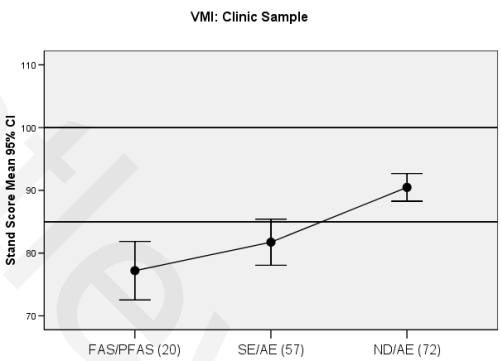
Among the MR study sample, caregiver report on the Vineland Adaptive Behavior Scales is in the clinical range across all three FASD study groups relative to the Controls.

FAS DPN **MRI** and **Clinic** Samples

MRI Sample (n = 65)

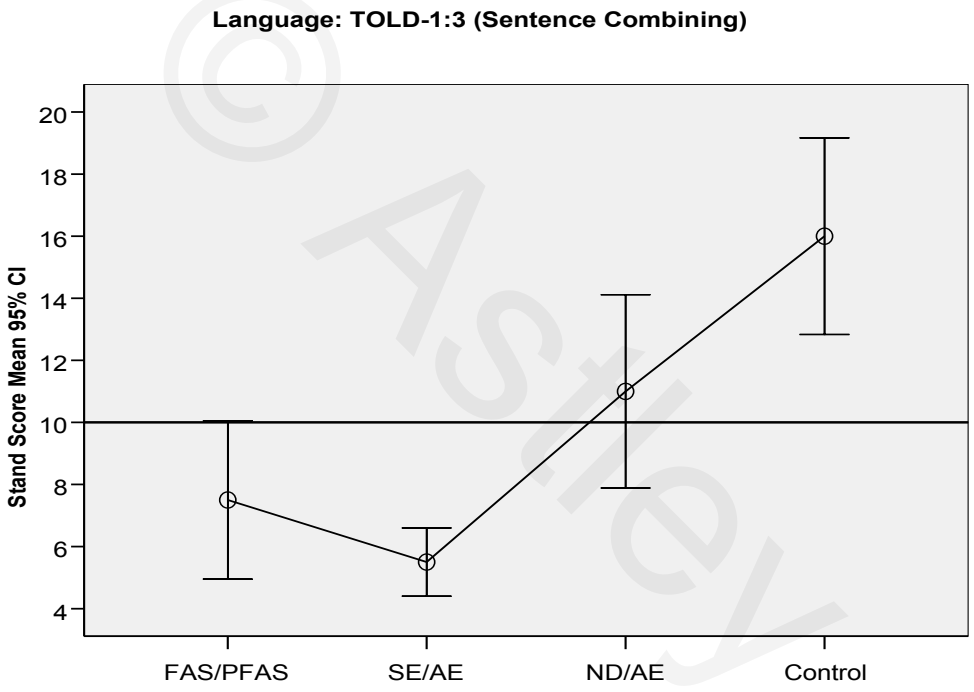


Clinic Sample (n = 149)



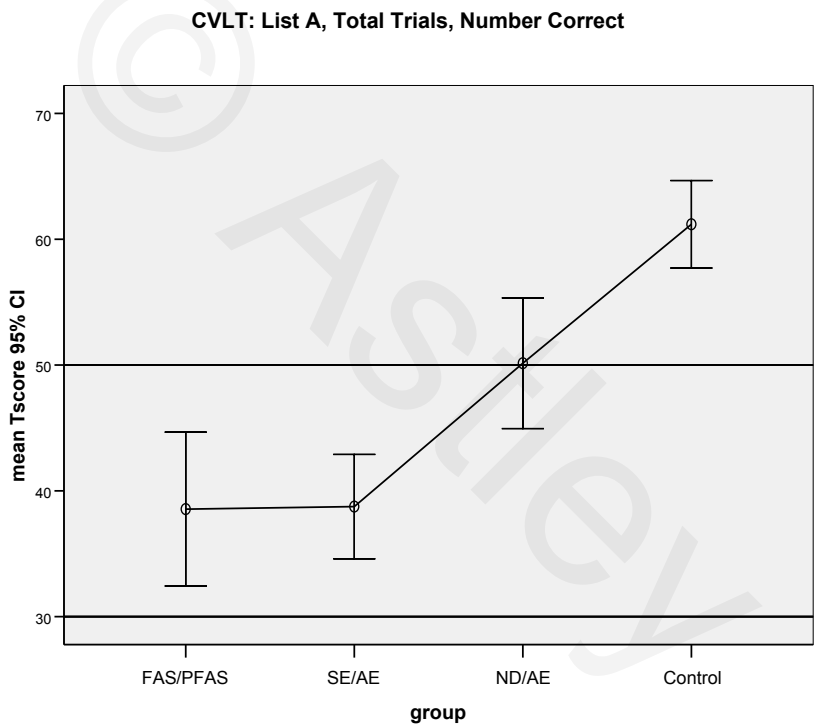
Performance on the Visual Motor Integration task improved as the severity of the FASD diagnostic classification decreased. Mean standard scores on the Visual Motor Integration test were comparable between the MR and Clinic samples. Normal performance is reflected by a mean standard score = 100 (15 SD). The lower horizontal line reflects 1 SD below the mean.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



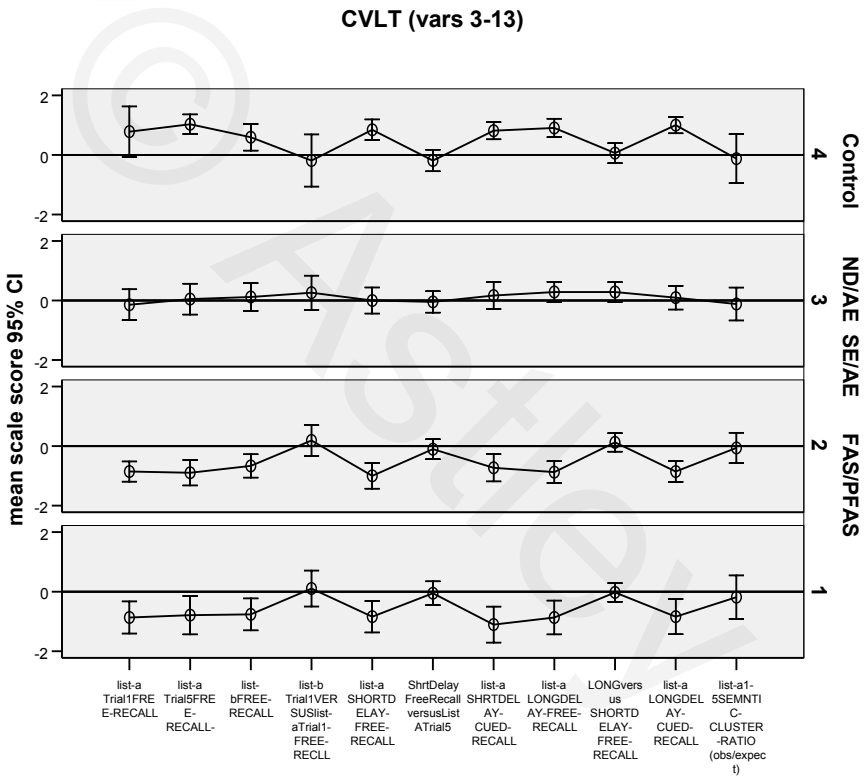
Among the MR study sample, performance on the Test of Language Development was comparably low among the FAS/PFAS and SE/AE groups. The ND/AE group performed at a level intermediate between the Control and (FAS/PFAS, SE/AE) groups. Normal performance is reflected by a mean scaled score of 10 (3 SD).

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)

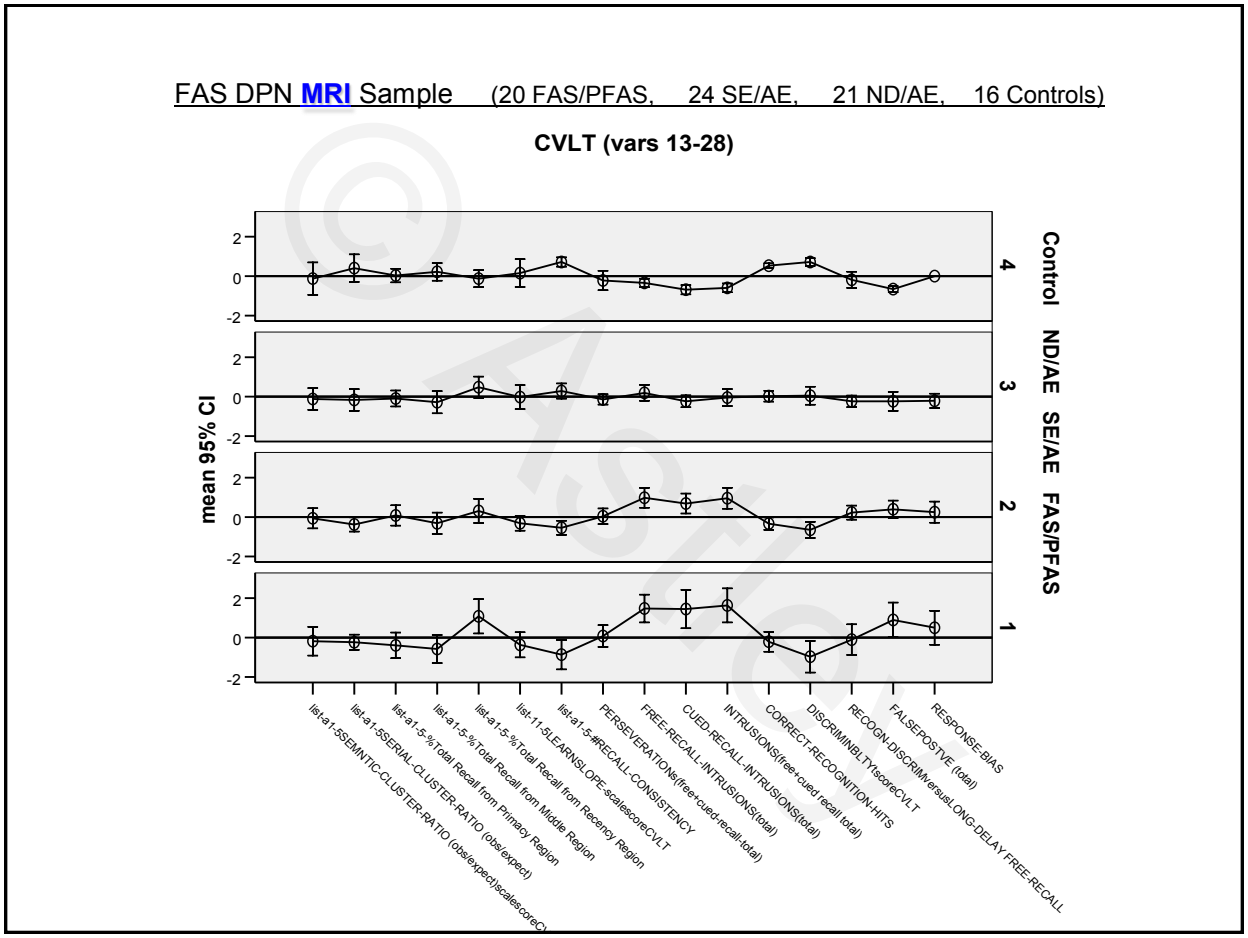


Among the MR study sample, performance on this CVLT subtest was comparably low among the FAS/PFAS and SE/AE groups. Performance by the ND/AE group was intermediate between the Control and (FAS/PFAS and SE/AE) groups. Normal performance is reflected by a T score = 50 (10 SD).

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)

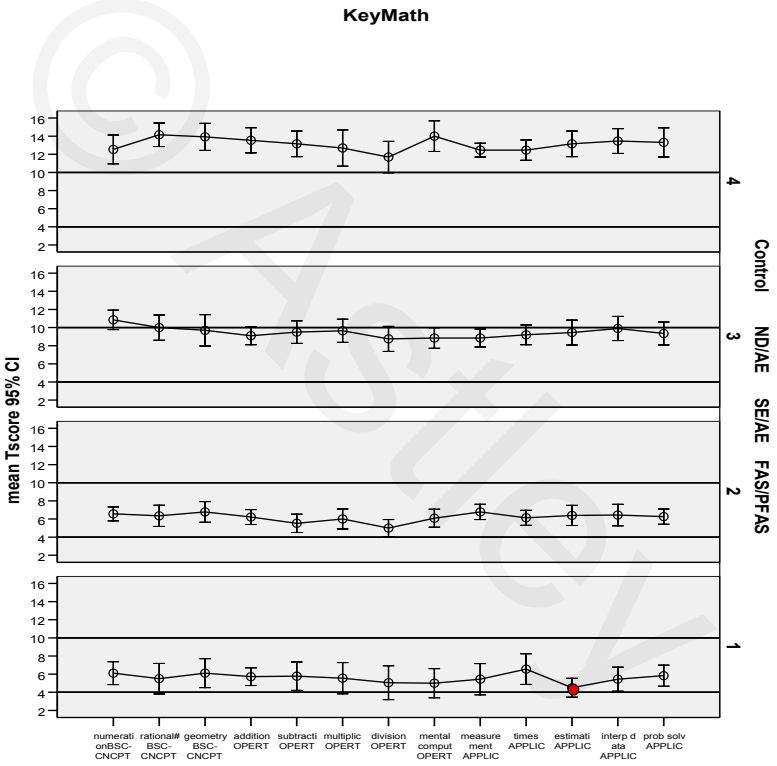


Among the MR study sample, performance on these CVLT subtests was comparably low among the FAS/PFAS and SE/AE groups. Performance by the ND/AE group was intermediate between the Control and (FAS/PFAS and SE/AE) groups.



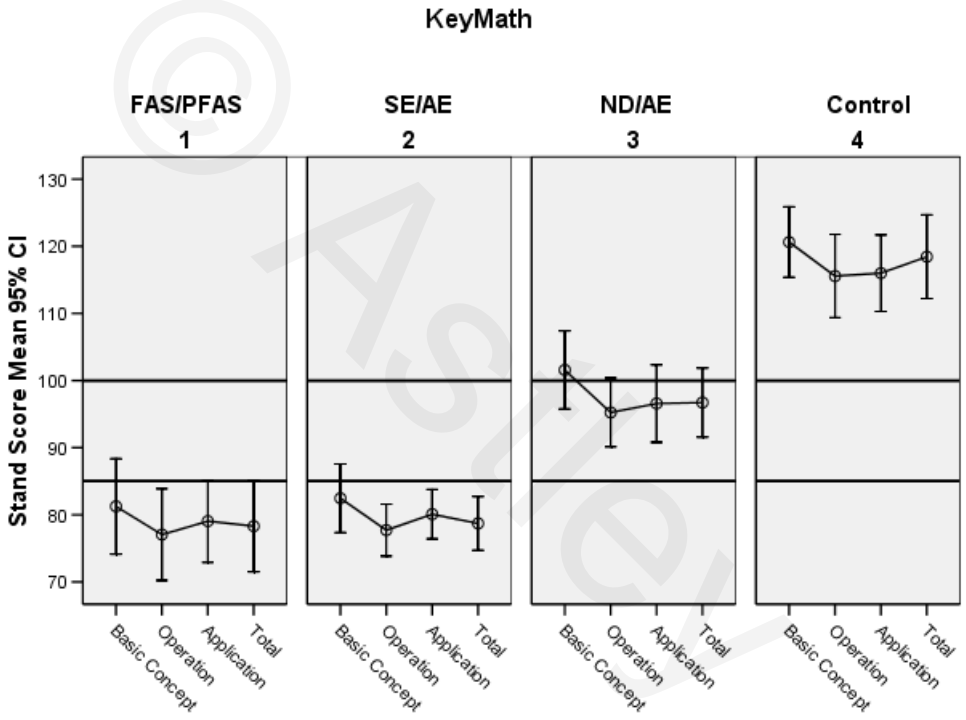
Among the MR study sample, the profile of performance across these CVLT tasks varied by FASD diagnostic classification.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



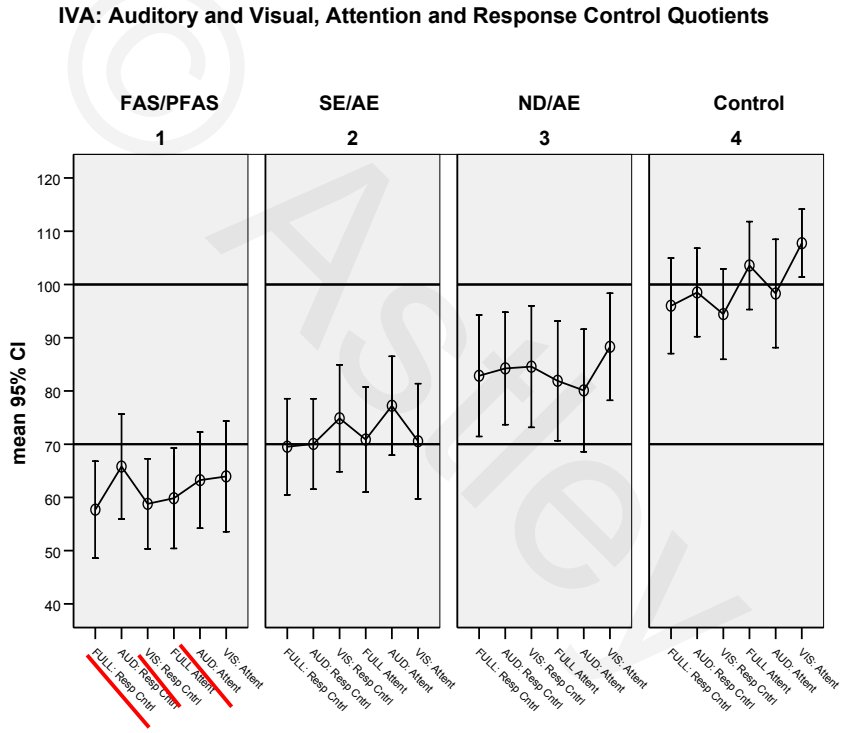
Among the MR study sample, performance on these KeyMath subtests were comparably low among the FAS/PFAS and SE/AE groups with one exception. The FAS/PFAS group performed significantly lower than the SE/AE group on the Estimation subtest. Performance by the ND/AE group was intermediate between the Control and (FAS/PFAS, SE/AE) groups. The top horizontal line reflects normal performance (scaled score = 10). The bottom horizontal line reflects 2 SDs below the mean.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



Among the MR study sample, performance by the FAS/PFAS and SE/AE groups were comparably low. Performance by the ND/AE group was intermediate between the Control and (FAS/PFAS, SE/AE) groups. Normal performance is reflected by a mean standard score = 100 (15 SD).

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



Among the MR study sample, performance on the IVA improved significantly with decreasing severity of FASD diagnostic classification. Performance on the Full Response Control, Visual Response Control, and Auditory Attention subtests were significantly lower in the FAS/PFAS group relative to the SE/AE group. Normal performance is reflected by a mean standard score = 100. The horizontal line at 70 reflects 2 SDs below the mean.

FAS DPN MR Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)

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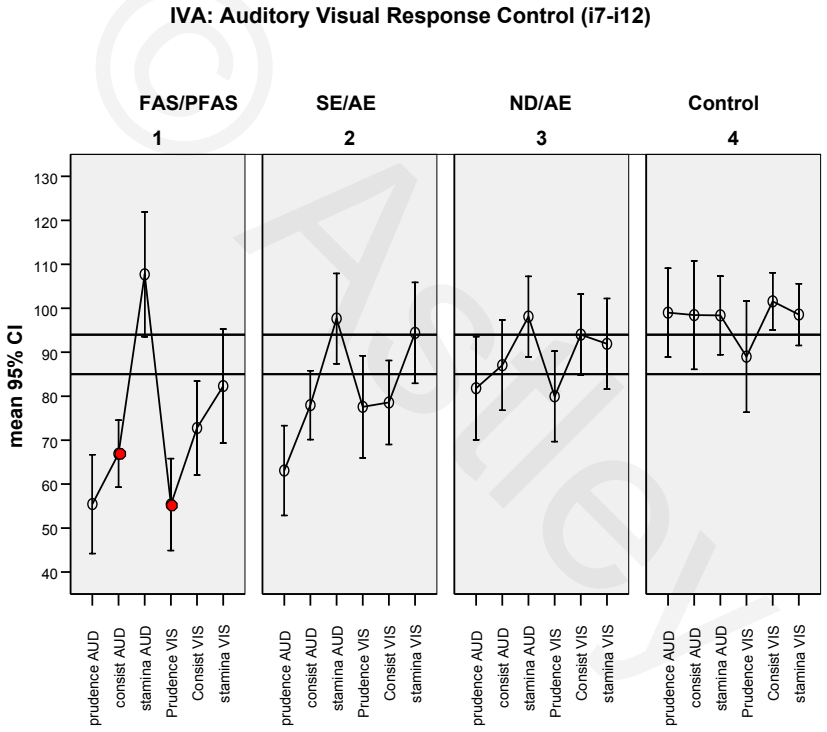
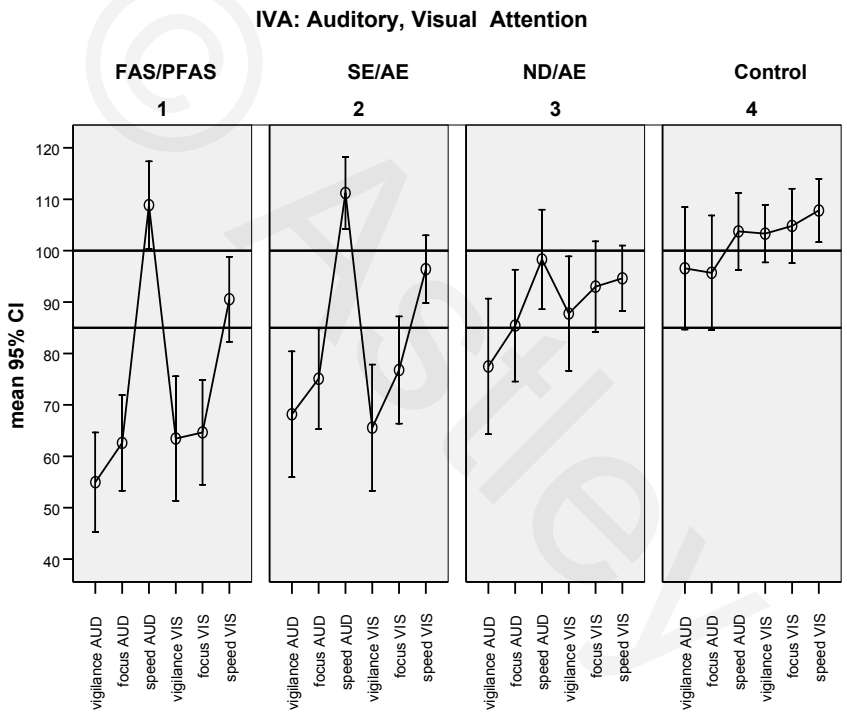


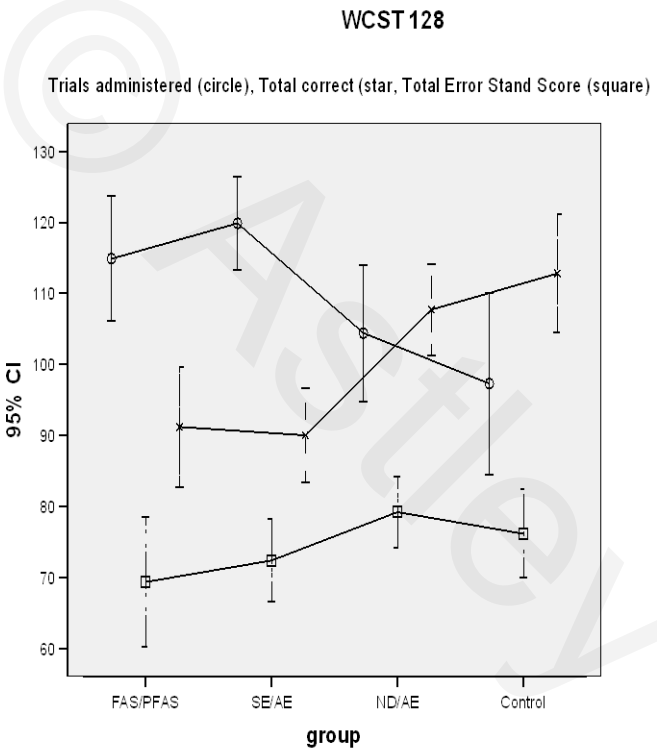
Standardized scores for the Integrated Visual Auditory continuous performance test among the MR study sample. The two red markers reflect mean scores that are significantly lower in the FAS/PFAS group relative to the SE/AE group.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



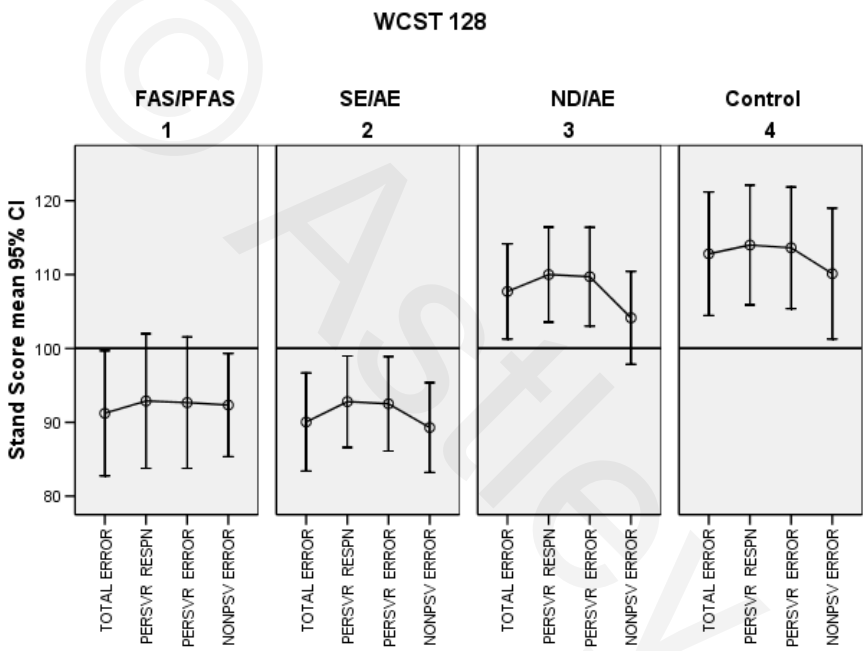
Among the MR sample, performance on these IVA subtests among the FAS/PFAS and SE/AE groups are comparably low. Performance in the ND/AE group is intermediate between the Control and (FAS/PFAS, SE/AE) groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



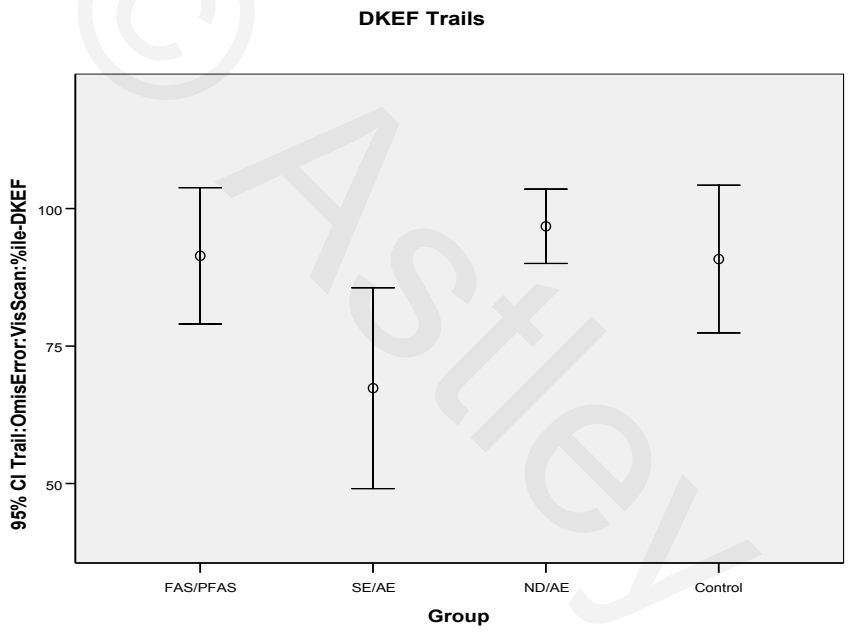
Mean standardized scores on the Wisconsin Card Sort Test across the MR study groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



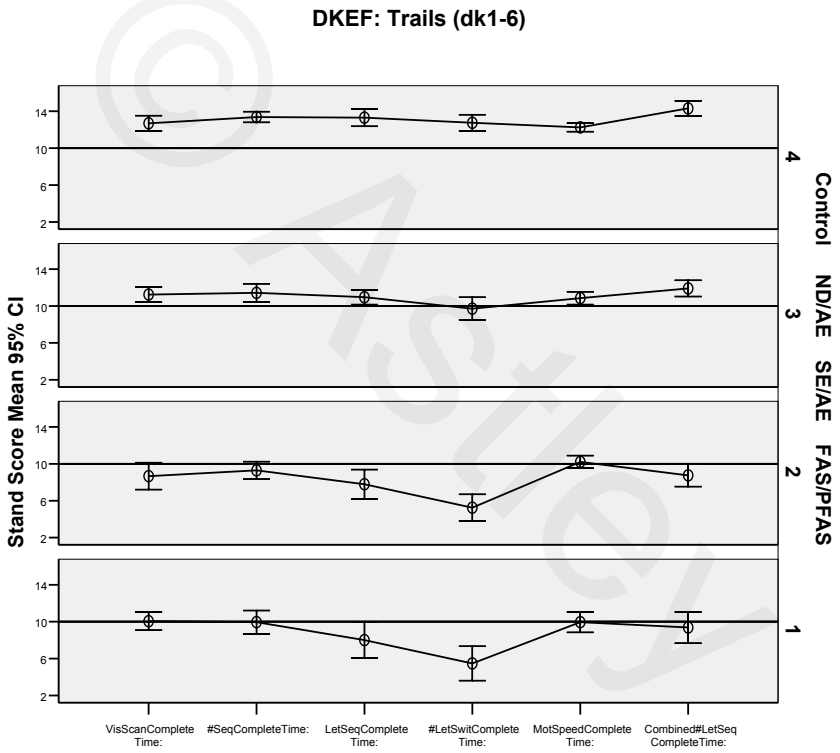
Among the MR study sample, performance on these Wisconsin Card Sort Test tasks were comparably low among the FAS/PFAS and SE/AE groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



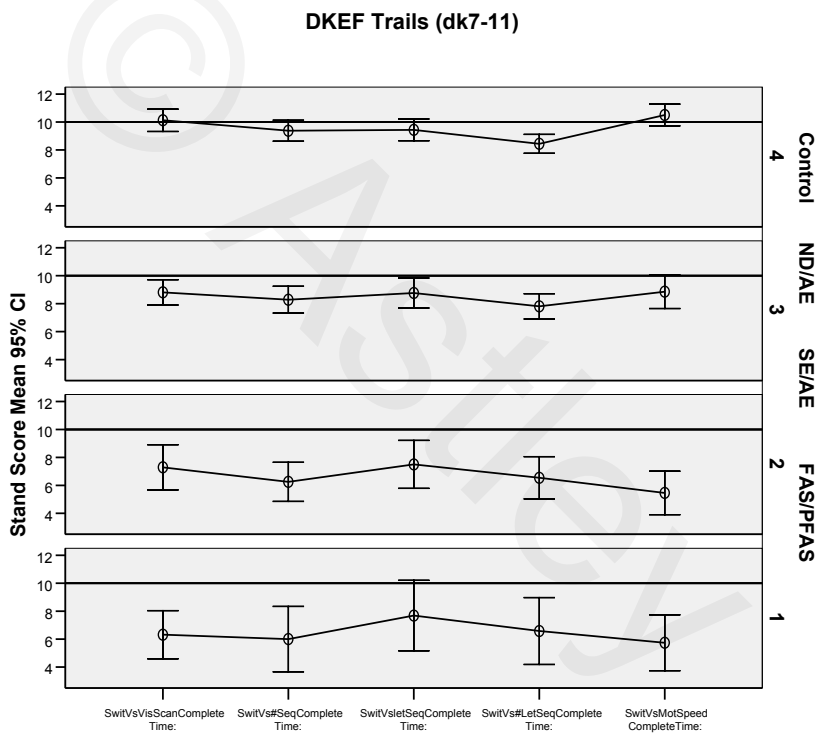
Delis-Kaplan Executive Function System: Trails Subtest: Visual Scanning Omission Errors percentile scores across the MR FASD study groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



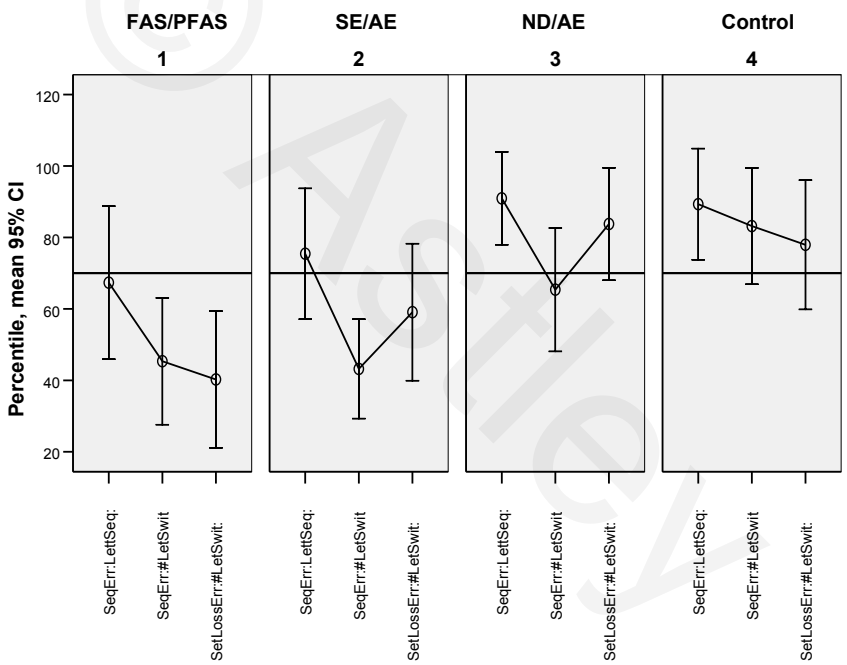
Delis-Kaplan Executive Function Systems: Trails Subtest; Scaled Scores for Completion Times across the MR FASD study groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)

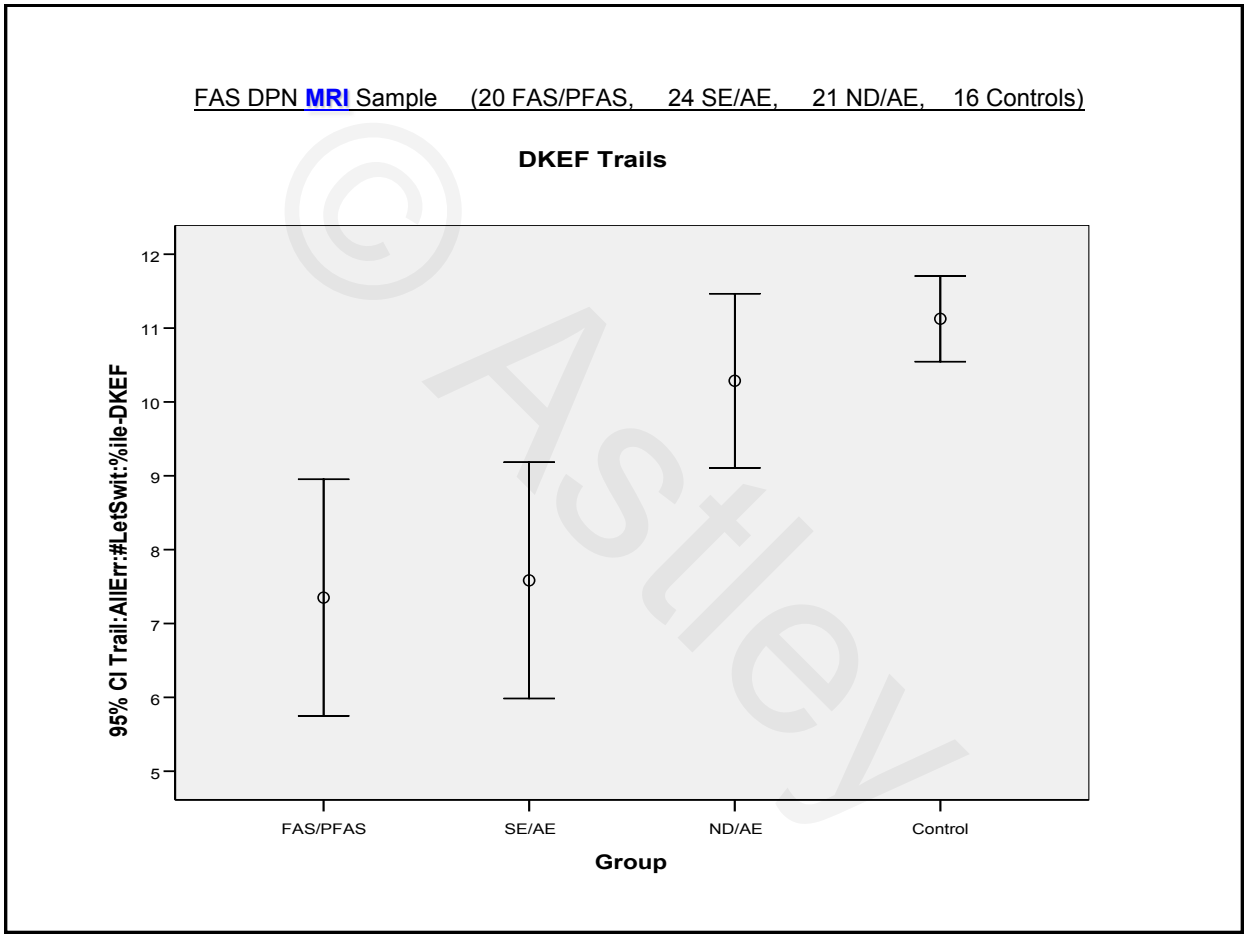


Delis-Kaplan Executive Function Systems: Trails Subtest; Scaled Scores for Completion Times across the MR FASD study groups.

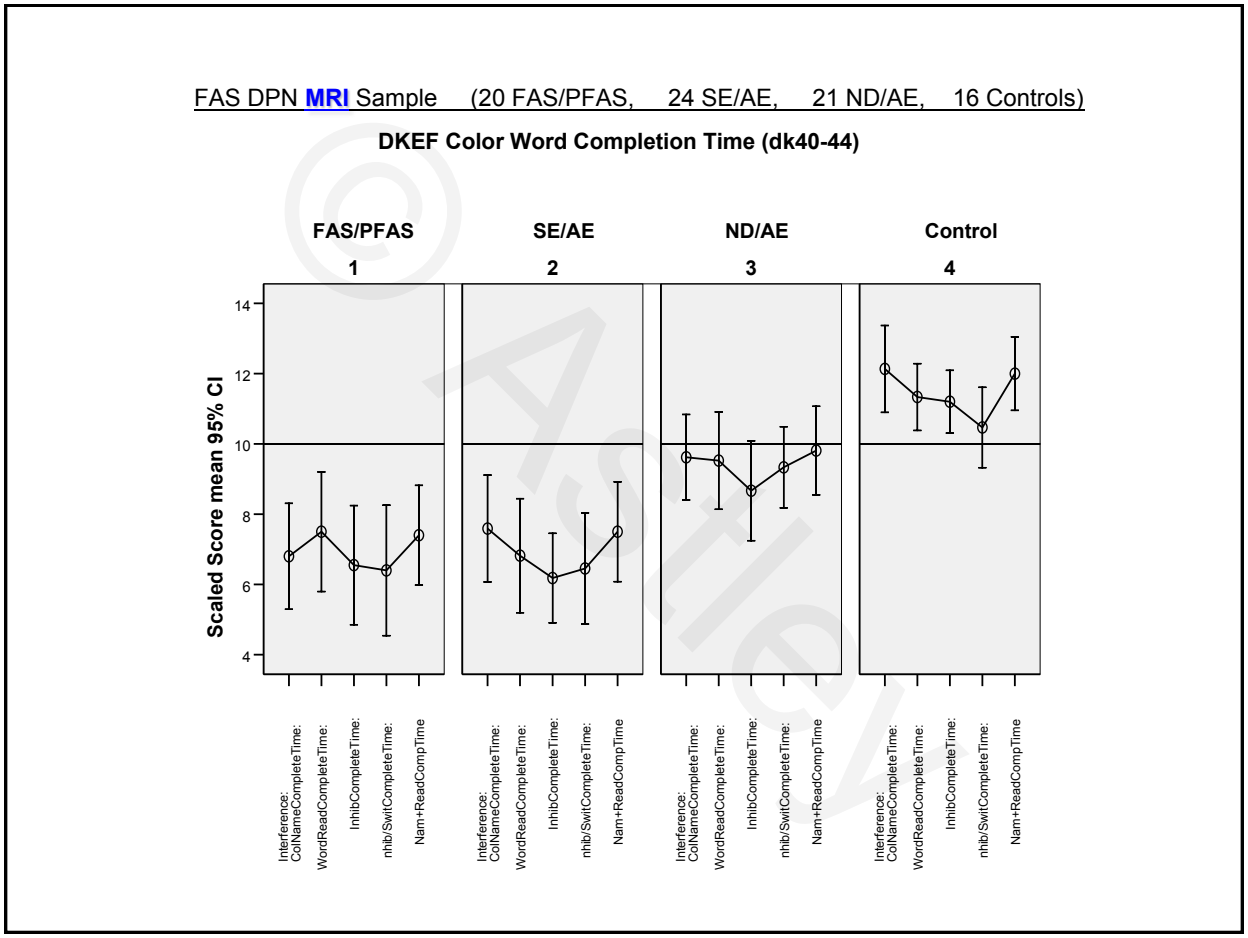
FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



Delis-Kaplan Executive Function Systems: Trails Subtest; Percentile Scores across the MR FASD study groups.

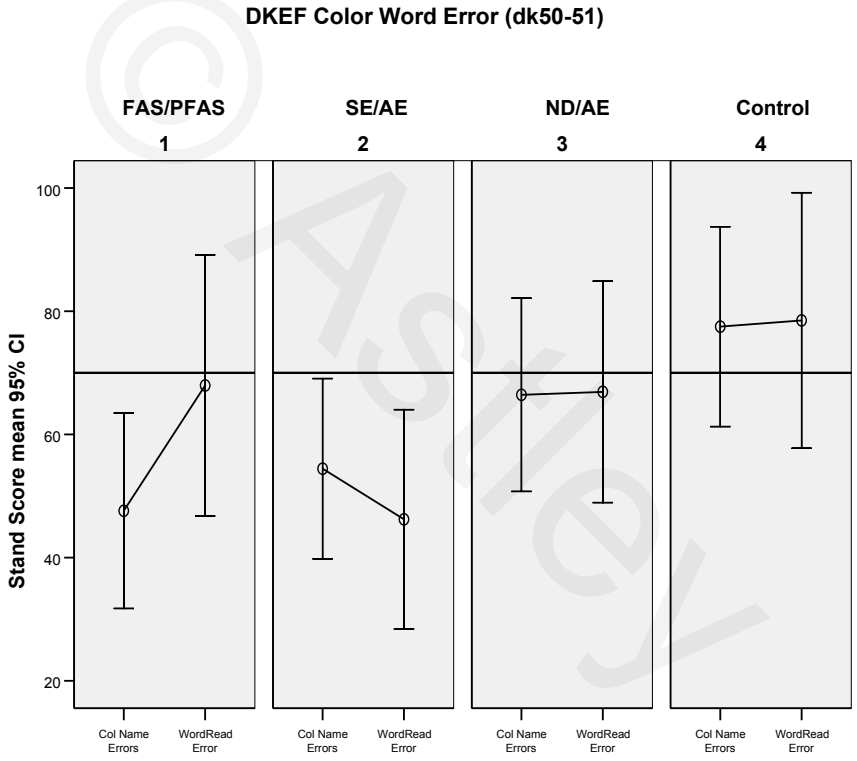


Delis-Kaplan Executive Function Systems: Trails Subtest; All Errors; Number Letter Switching.



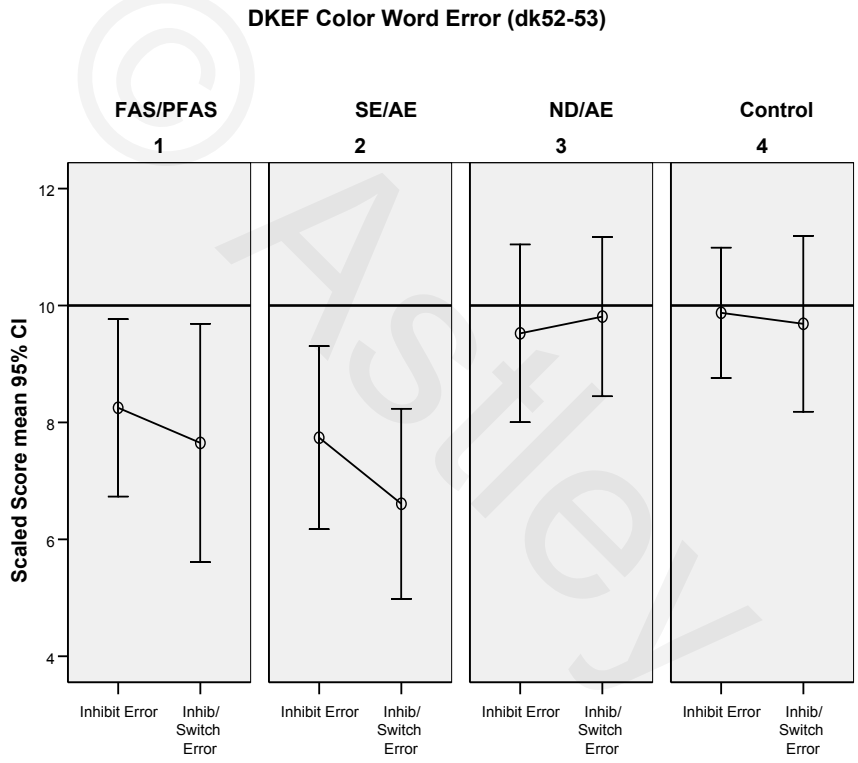
Delis-Kaplan Executive Function Systems: Color Word Subtest; Scaled Scores for Completion Times across the MR FASD study groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



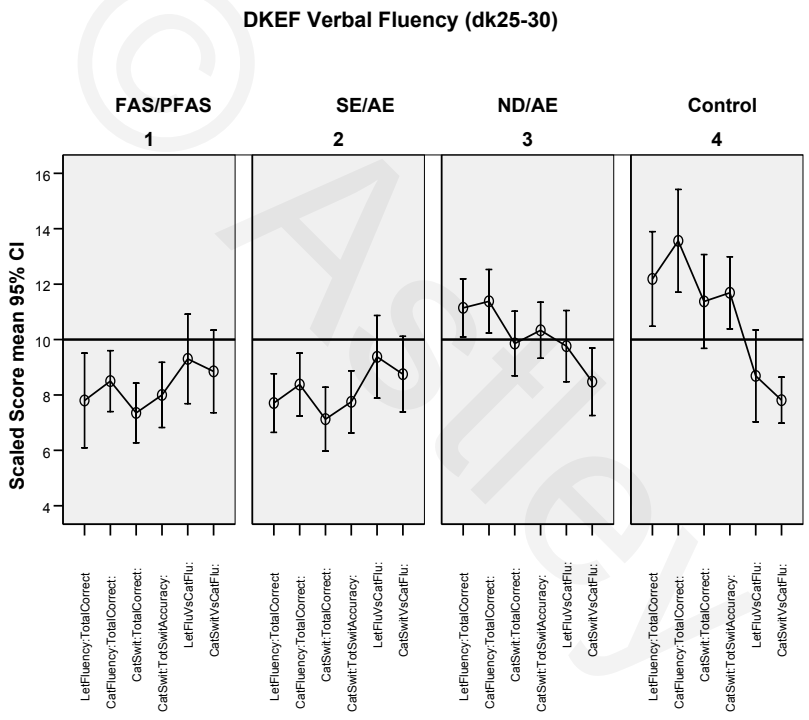
Delis-Kaplan Executive Function Systems: Color Word Subtest; Standardized Scores for Errors across the MR FASD study groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



Delis-Kaplan Executive Function Systems: Color Word Subtest; Standardized Scores for Errors across the MR FASD study groups.

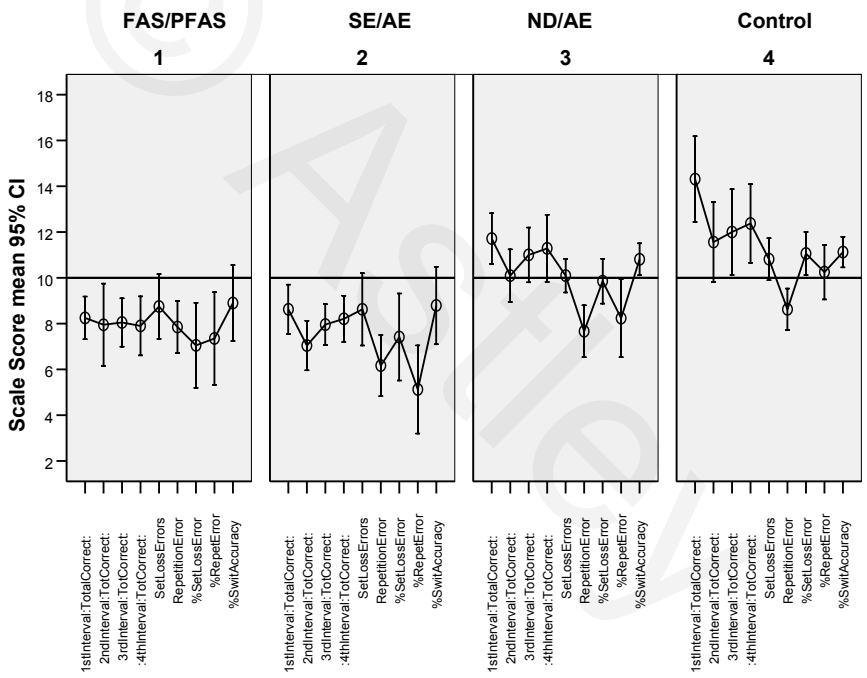
FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



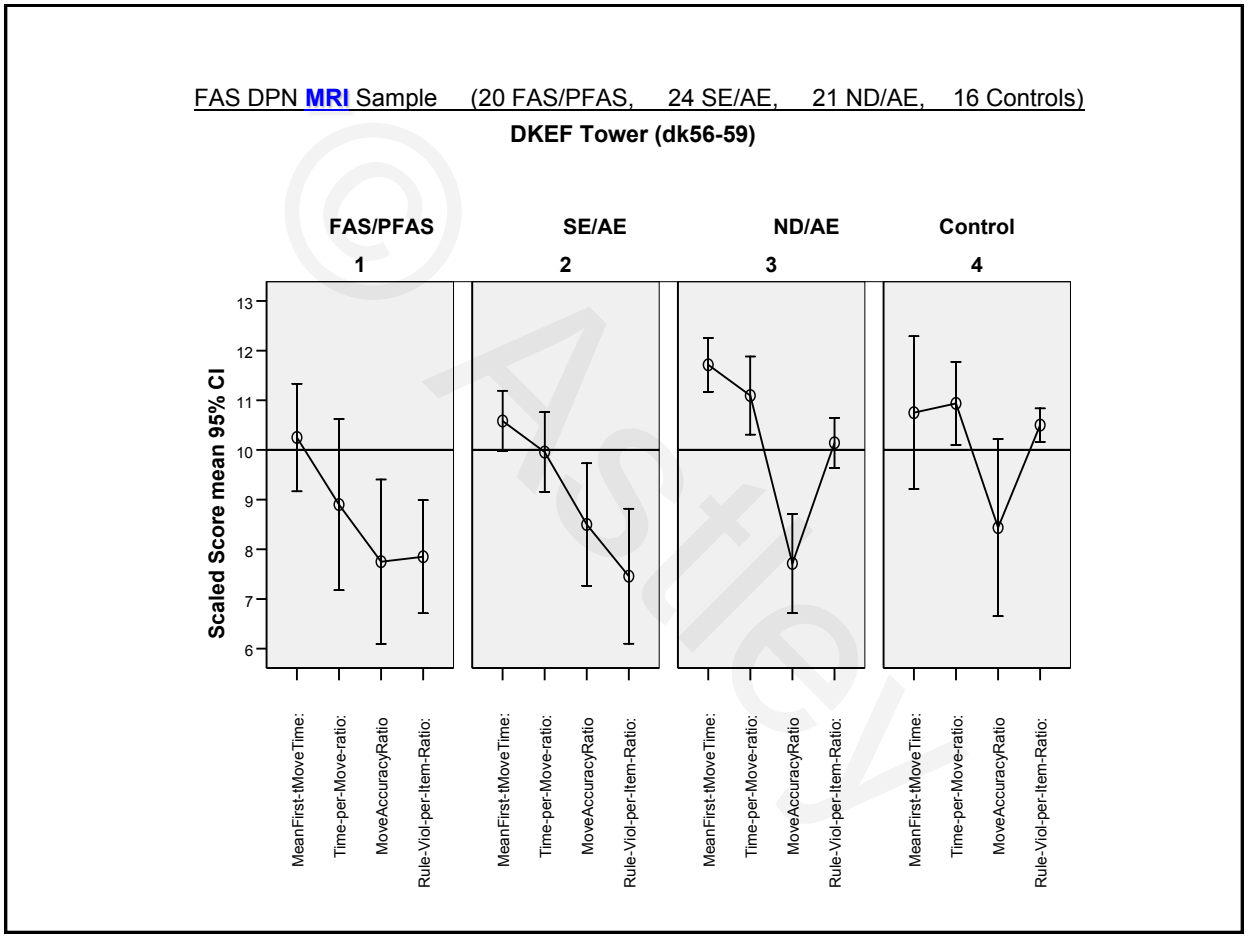
Delis-Kaplan Executive Function Systems: Verbal Fluency Subtest; Standardized Scores across the MR FASD study groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)

DKEF Verbal Fluency Conditions123 (dk31-39)

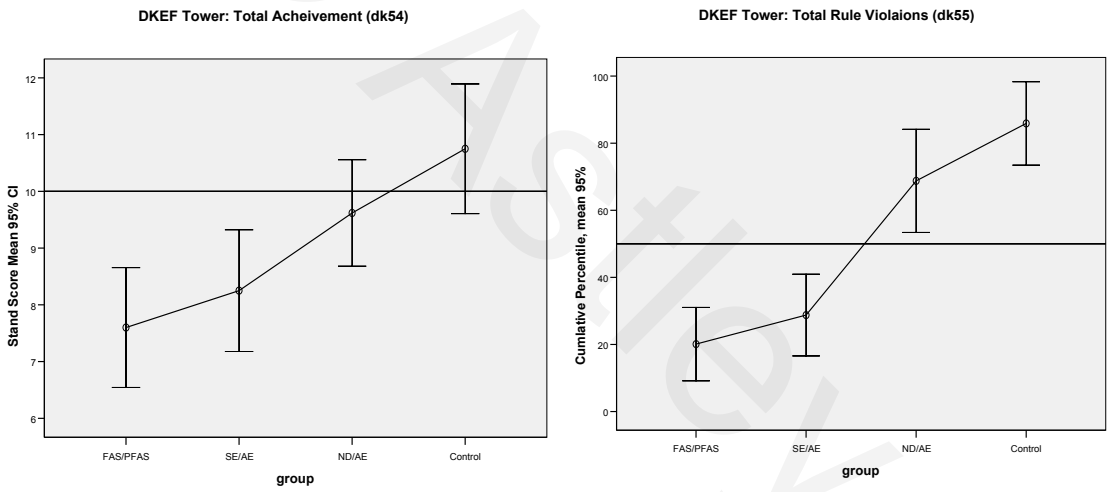


Delis-Kaplan Executive Function Systems: Verbal Fluency Subtest; Scaled Scores across the MR FASD study groups.



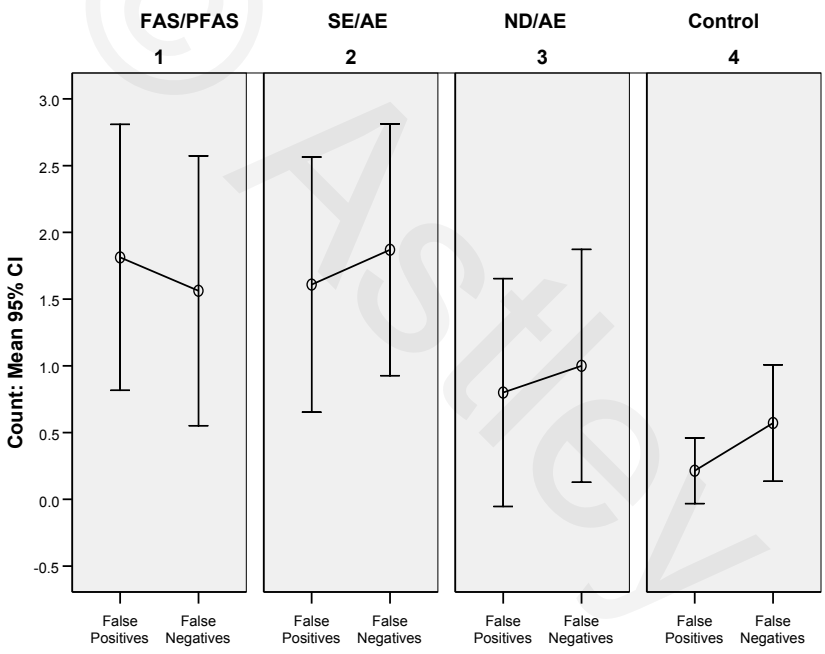
Delis-Kaplan Executive Function Systems: Tower Subtest; Scores across the MR FASD study groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



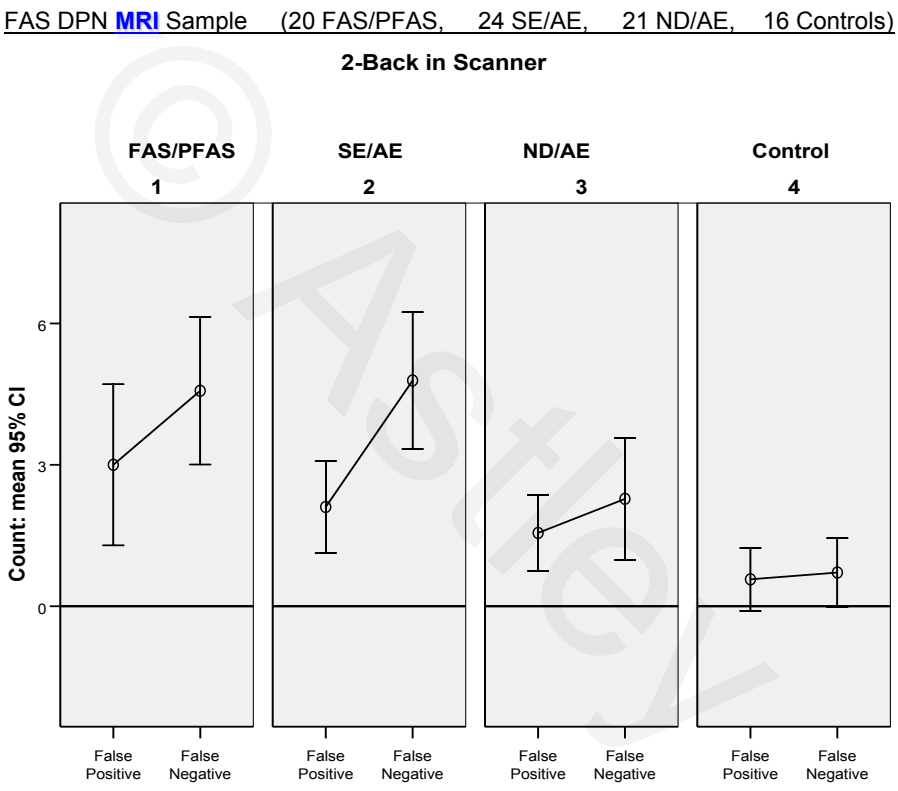
Delis-Kaplan Executive Function Systems: Tower Subtest; Total Acheivement and Total Rule Violations across the MR FASD study groups.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



Please see Astley et al., (2009) (http://depts.washington.edu/fasdpn/pdfs/FASD-fMRI-2009.pdf) for a full description of the fMRI study outcomes. Study subjects were administered an N-back working memory task while in the MR scanner. The task involved viewing a series of images (faces), one at a time, and deciding whether the present image matched the image presented N images back. The images were 4 male and 4 female faces.

In this 1-back task, the mean number of false-positive and false-negative responses was elevated in the FAS/PFAS and SE/AE groups relative to the ND/AE group.



Please see Astley et al., (2009) (http://depts.washington.edu/fasdpn/pdfs/FASD-fMRI-2009.pdf) for a full description of the fMRI study outcomes. Study subjects were administered an N-back working memory task while in the MR scanner. The task involved viewing a series of images (faces), one at a time, and deciding whether the present image matched the image presented N images back. The images were 4 male and 4 female faces.

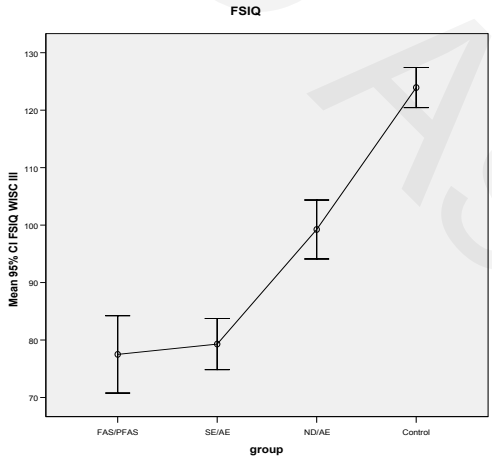
In this 2-back task, the mean number of false-positive and false-negative responses was elevated in the FAS/PFAS and SE/AE groups relative to the ND/AE group.

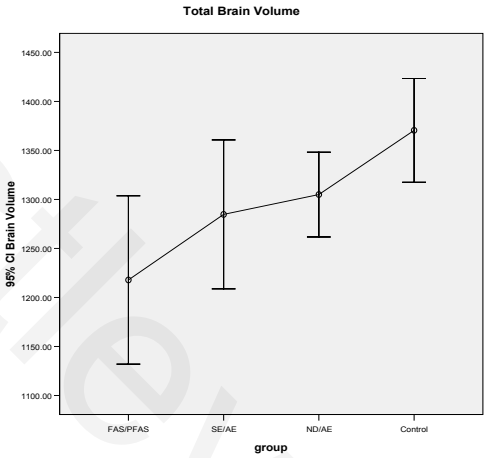
FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)

FAS DPN MR Study: Psychiatric Conditions (C-DISC)				
Proportion of Subjects with the Condition				
Condition	FAS/PFAS	SE/AE	ND/AE	Control
	N=20	N=24	N=21	N=16
AD/HD	63	71	67	0
ODD	47	58	52	13
CD	37	21	48	0
Generalized Anxiety	21	8	5	0
Separation Anxiety	16	8	14	0
OCD	11	4	14	0
PTSD	11	4	0	0
Social Phobia	11	4	10	0
Maj Depress / Dysthymic	5	8	5	0
Mania / Hypomania	5	0	0	0
Schizophrenia	5	0	0	0
Panic	0	0	5	0

Among the MR study sample, the prevalence of psychiatric conditions identified by the Computerized Diagnostic Interview Schedule for Children was comparably high among the three FASD study groups.

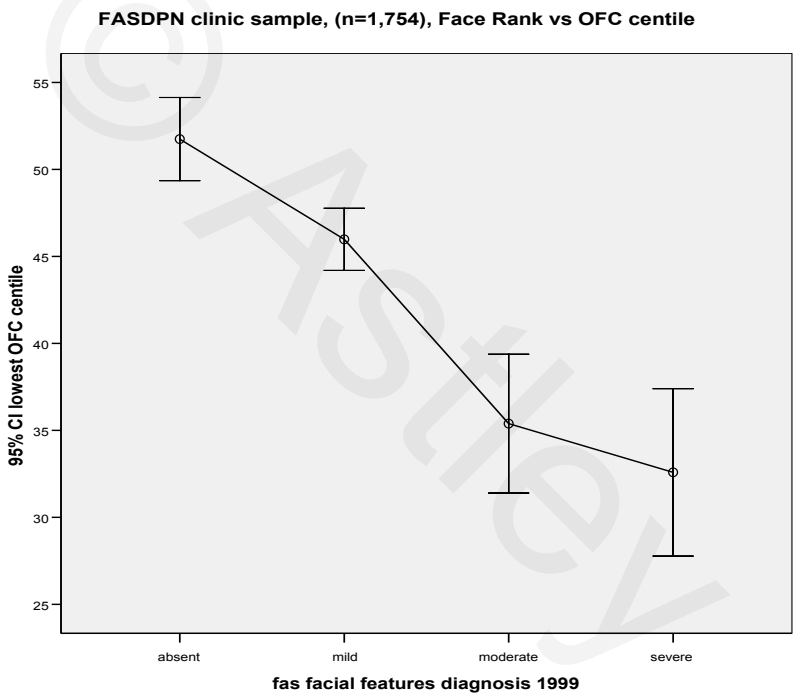
FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)





Please see Astley et al., (2009) (http://depts.washington.edu/fasdpn/pdfs/astley-mri.pdf) for a full description of the MRI outcomes. The two graphs above illustrate how the three FASD clinical subgroups derived by the 4-Digit Diagnostic Code (ND/AE, SE/AE, and FAS/PFAS) are distinct from one another in both brain function and brain structure. They reflect three increasingly more impaired clinical groups.

FAS DPN Clinic Sample (n = 1,754)



Among the 1,754 patients in the FAS DPN clinical sample, a very strong correlation exists between mean head circumference (OFC) and the magnitude of expression of the FAS Facial phenotype (as defined by the FASD 4-Digit Code). The more severe the expression of the FAS facial phenotype, the smaller the OFC.

FAS DPN **MRI** and **Clinic** Samples

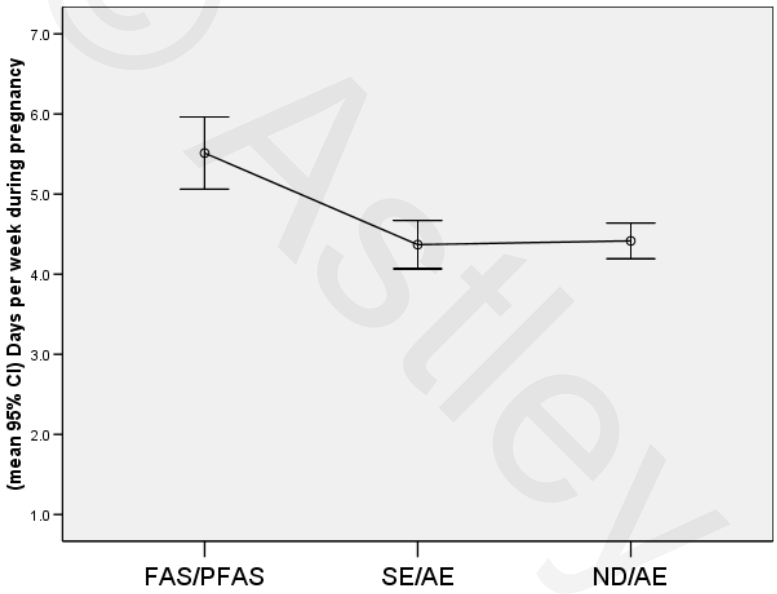
Significant Differences between FAS/PFAS and SE/AE

	FAS/PFAS	SE/AE
FAS Face	Yes	No
Alcohol: More days/week	6 days / week	4 days / week
Alcohol: All 3 trimesters	77%	59%
Smaller OFC	30th percentile	43rd percentile
Microcephalic	49% of subjects	27% of subjects
Frontal lobe	Disproportionately smaller	
Choline: Frontal/Parietal	Significantly lower	
WISC PIQ	76	82
WISC Arith	4	6
WISC mazes	2.8	6.5
Key Math estimation	5	6.4
VMI	77	89
RCFT Copy (raw)	11	18
IVA Full Response Quot.	58	70

It is often stated in the FASD published literature that CNS structural/behavioral abnormalities are comparable between individuals with FAS and ARND. The data from the WA FAS DPN clinical and research populations demonstrate that the CNS structural/behavioral abnormalities present in individuals with FAS are distinct from individuals with severe ARND (SE/AE) and moderate ARND (ND/AE).

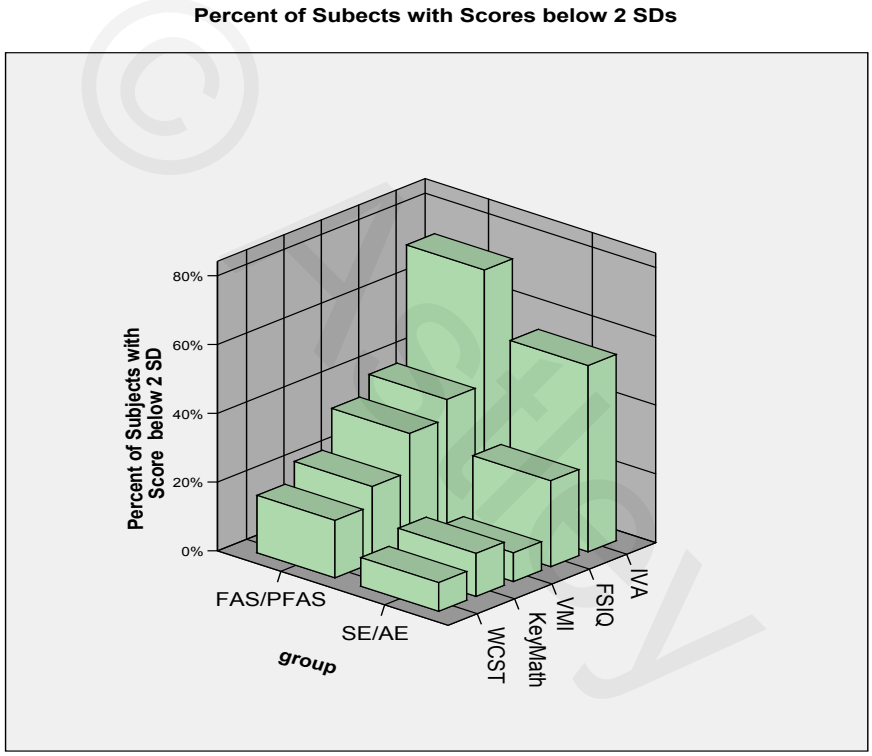
FAS DPN **Clinic** Sample

Days per week of alcohol use during pregnancy



Among the FAS DPN Clinical population, individuals with FAS/PFAS have significantly higher reported prenatal alcohol exposures (number of days of drinking per week during pregnancy) than individuals diagnosed with SE/AE or ND/AE.

FAS DPN **MRI** Sample (20 FAS/PFAS versus 24 SE/AE)



Among the MR study sample, the proportion of subjects with psychological performance 2 or more SDs below the norm was greater among the FAS/PFAS group than the SE/AE group.

FAS DPN Clinic Sample (Adolescent: 8-15 yrs) n = 540

FAS DPN Clinical Sample (8.0-15.9 yrs old) N = 540			
Proportion of Subjects with Characteristic			
	FAS/PFAS	**SE/AE**	**ND/AE**
Characteristic	N=55	N=193	N=289
Female *	47	31	41
Caucasian	62	43	50
Alcohol (high, Rank 4)	56	59	56
Microcephalic *	30	17	1
Abnormal clinical MRI	38% of 8	19% of 21	0
Seizure disorder	10	7	1
Other Neurological	10	11	2
Domain with Significant Impairment			
Intellectual *	45	28	3
Achievement	46	50	13
Neuropsychological *	76	61	22
Language	68	65	19
Adaptive	77	81	51
Psychiatric Disorder	70	68	58
ADD/ADHD	70	60	57
Development	33	43	25

The next three slides provide an overview of the proportion of subjects in each FASD diagnostic subgroup that present with key abnormalities across three age ranges (birth to 3 years, 8-15 years of age, and 16 + years).

FAS DPN **Clinic** Sample **(Birth to 3)** n = 212

FAS DPN Clinical Sample (Birth to 3 yrs) N = 212			
Proportion of Subjects with Characteristic			
	FAS/PFAS	**SE/AE**	**ND/AE**
Characteristic	N=46	N=45	N=121
Female	48	43	41
Caucasian	55	46	46
Alcohol (high, Rank 4)	63	62	61
Microcephalic	83	64	1
Abnormal clinical MRI	40% of 10	60% of 10	0
Seizure disorder	5	12	0
Other Neurological	13	23	3
Domain with Significant Impairment			
Intellectual	--	--	--
Achievement	--	--	--
Neuropsychological	--	--	--
Language	--	--	--
Adaptive	--	--	--
Psychiatric Disorder	--	--	--
ADD/ADHD	--	--	--
Development	50% of 28	49% of 33	31% pf 86

This slide, and the slide before and after this slide, provide an overview of the proportion of subjects in each FASD diagnostic subgroup that present with key abnormalities across three age ranges (birth to 3 years, 8-15 years of age, and 16 + years). This birth to 3 group is too young to assess functional domains like intellect, achievement, language, etc.

FAS DPN Clinic Sample (Adult: 16+ years) n = 141

FAS DPN Clinical Sample (Adults (16+ years) N = 141			
Proportion of Subjects with Characteristic			
	FAS/PFAS	**SE/AE**	**ND/AE**
Characteristic	N=17	N=53	N=71
Female	59	38	51
Caucasian	65	59	54
Alcohol (high, Rank 4)	42	62	51
Microcephalic	41	27	4
Abnormal clinical MRI	0% of 2	36% of 11	0
Seizure disorder	0	10	0
Other Neurological	7	10	3
Domain with Significant Impairment			
Intellectual	20	36	2
Achievement	58% of 12	76% of 43	17% of 41
Neuropsychological	83	67	18
Language	50% of 10	69% of 32	26% of 35
Adaptive	75% of 4	85% of 15	100% of 8
Psychiatric Disorder	100	72	84
ADD/ADHD	44	55	59
Development	--	--	--

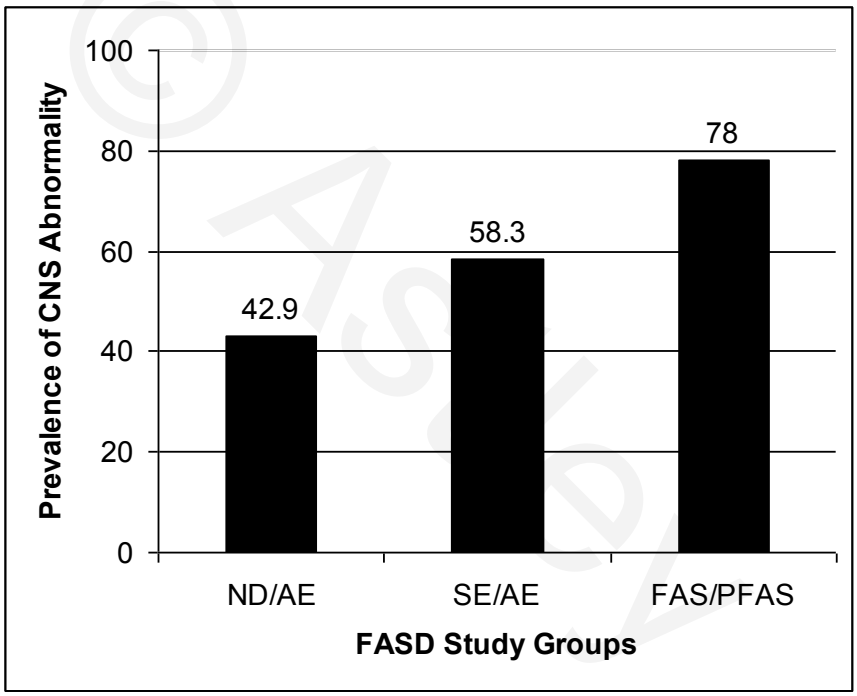
This slide, and the previous two slides, provide an overview of the proportion of subjects in each FASD diagnostic subgroup that present with key abnormalities across three age ranges (birth to 3 years, 8-15 years of age, and 16 + years).

FAS DPN Clinic Sample

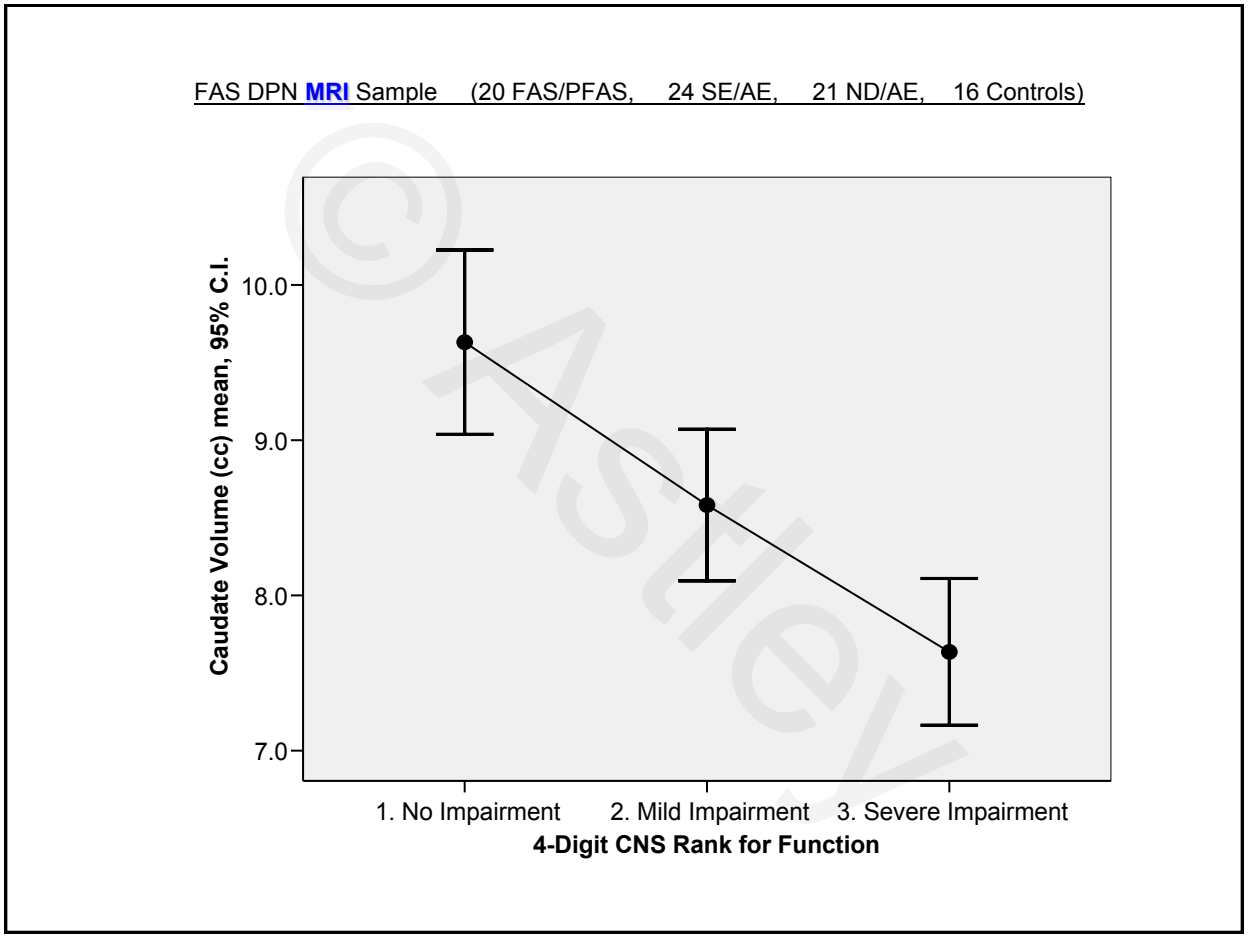
FAS DPN Clinic Sample (n = 1,336)				
Diagnostic Outcomes by Age Group				
Age at Diagnosis	**Sample Size**	**FAS/PFAS**	**SE/AE**	**ND/AE**
	n	%	%	%
Birth to 3.9	212	22	21	57
4.0 to 7.9	443	13	28	59
8.0-15.9	540	10	36	54
16-53	141	12	38	50
All Ages	1,336	13	31	56

Age distribution across the three FASD diagnostic classifications among the FAS DPN clinical sample.

FAS DPN **MRI** Sample (20 FAS/PFAS, 24 SE/AE, 21 ND/AE, 16 Controls)



The number of subjects in each FASD study group, with 1 or more brain regions that were 2 or more SDs below the mean of the healthy, unexposed Control group, increased significantly as one advanced from the ND/AE to the SE/AE to the FAS/PFAS group. This graph demonstrates that even when the FAS facial phenotype was missing and the level of brain dysfunction was mild to moderate (4-Digit CNS Rank 2 in ND/AE group), there was a significant increased risk of underlying structural brain abnormality relative to the Control group.

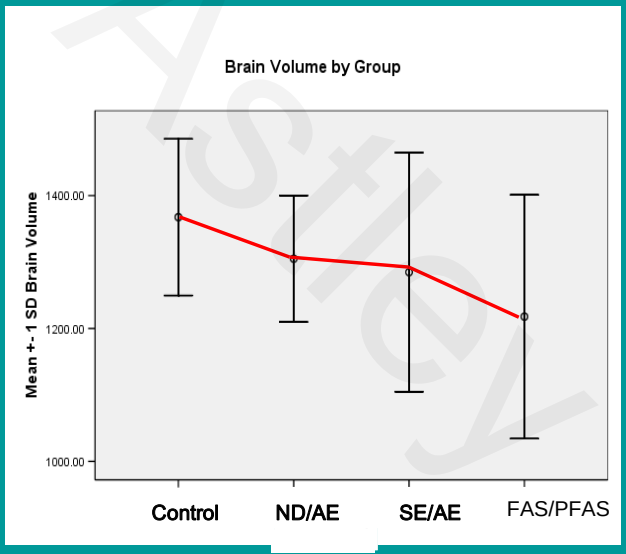


Mean absolute caudate volume decreased as a global measure of brain function (the 4-Digit Code CNS Rank) increased from no impairment to mild impairment to severe impairment.

FASD MRI, MRS, fMRI Study: Results

Key Structural Findings

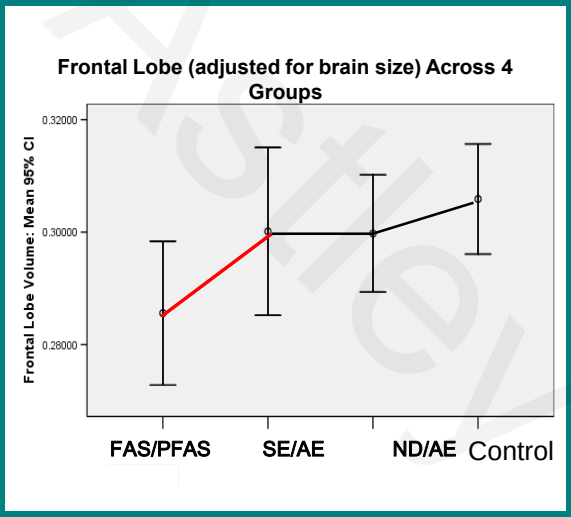
All brain regions become progressively smaller (absolute size) as you advance across the 4 Diagnostic Groups from Controls to FAS / PFAS.



FASD MRI, MRS, fMRI Study: Results

Key Structural Findings

The frontal lobe is significantly smaller in FAS/PFAS relative to Severe ARND, Mild ARND, and Controls, even after adjustment for overall brain size.

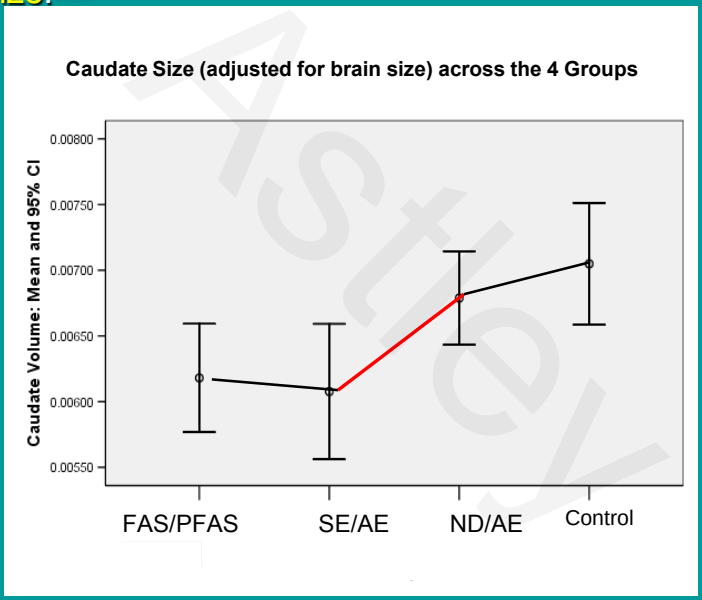


The one CNS structural feature that distinguished the FAS/PFAS group from all other groups was a significantly, and disproportionately smaller frontal lobe volume. Although the FAS/PFAS and SE/AE groups both have comparably severe CNS dysfunction, only the group with the FAS facial phenotype (the FAS/PFAS group) has disproportionately smaller frontal lobe volumes.

FASD MRI, MRS, fMRI Study: Results

Key Structural Findings

The caudate is significantly smaller in both FAS/PFAS and Severe ARND, relative to Mild ARND and Controls, even after adjustment for overall brain size.



In contrast to the Frontal Lobe (previous slide) the volume of the caudate was significantly and disproportionately smaller in both the FAS/PFAS and SE/AE groups relative to the ND/AE and Control groups. What the FAS/PFAS and SE/AE groups have in common is severe CNS