

Profiles of Language and Reading Impairment in a Family Study of Autism Spectrum Disorders and Specific Language Impairment.



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Over the past decade, comparing the language profiles of individuals with Autism Spectrum Disorders (ASD) to individuals with Specific Language Impairment (SLI) has been one approach to investigating shared genetic etiology in the language domain for autism. While ASD may include individuals who have significant dysfunction in communication, social interactions, and repetitive and restrictive behaviors, SLI refers to individuals who have no other obvious behavioral, cognitive, or neurological issues other than deficient language. Conflicting results from previous studies either supporting or negating the genetic link suggest that perhaps, previous language phenotypes were not refined enough to address the more subtle constructs that the two disorders may share. The New Jersey Language and Autism Genetics Study (NJLAGS) has been studying families who have at least one individual with a diagnosis of Autism and at least one other individual with SLI, with the goal of identifying language phenotypes to serve as behavioral biomarkers for linkage and association studies. This study is unique in that in addition to the traditional structural aspects of oral language, reading and higher order language constructs are also examined. Each family member received a comprehensive neuropsychological battery and contributed a blood or saliva sample for genetic analyses. Based on testing results, family members were categorized as unaffected, language impairment (LI) and/or reading impairment (RI) and then compared to the verbal ASD probands. **Results:** ASD probands did not significantly differ from the LI group on any language and reading tasks. They scored significantly lower than the RI group on assessments that address overall spoken language ability and metalinguistic language abilities, but significantly higher than the LI+RI group on measures of phonological awareness and word identification. The results of this study suggest that there are enough shared language behaviors of verbal individuals with ASD and those with SLI to support the development of oral and written language phenotypes to be used as behavioral biomarkers for genetics studies of autism.

Methods

Autism Proband (AUT/ASD): Diagnosed using the Autism Diagnostic Interview – Revised (ADI-R), Autism Diagnostic Observation Scale (ADOS), and Diagnostic and Statistical Manual of Mental Disorders - IV (DSM-IV) Autism criteria.

Language Impairment (LI): Individual scored 1 standard deviation below the mean on the Clinical Evaluation of Language Fundamentals (CELF) core score or on 60% of following assessments: CELF subtests (age appropriate measures), Comprehensive Assessment of Spoken Language (CASL) subtests (Ambiguous Sentences, Nonliteral Language, Inference, Meaning from Context, and Pragmatic Judgment), Comprehensive Test of Phonological Processing (CTOPP) subtests (Elision and Nonword Repetition).

Reading Impairment (RI): Individual scored 1 standard deviation below the standard mean on one or more of the following assessments: Gray Oral Reading Test - 4 (GORT4) Overall Reading Quotient, GORT4 Comprehension Standard Score, and Woodcock Reading Mastery Tests (WRMT) – Word Attack and Word Identification.

Language/Reading Impairment (LI+RI): Individual met criteria for both LI and RI.

Table 1: Breakdown of age ranges within the families.

Nuclear family members			
	N	mean age (s.d.)	Range
Fathers	84	44.5 (5.9)	33.09-65.03
Mothers	89	41.9 (6.6)	25.05-59.01
Siblings - male	57	10.8 (5.9)	3.03-33.06
Siblings - female	46	13.1 (8.2)	3.06-49.08
Extended family members			
Grandparents of probands	19	70 (6.6)	60.0-80.0
Aunts and Uncles of probands	20	40.9 (6.3)	33.03-55.06
Cousins of probands	23	11.2 (5.3)	3.02-26.11
Other extended family members	36	35.6 (10.7)	19.0-48.02
Family members meeting criteria for Autism			
Family members meeting criteria for ASD	83	10.8 (7.3)	3.04-36.05
Family members meeting criteria for LI	21	8.5 (3.8)	5.03-19.1
Family members meeting criteria for RI	47	26.7 (22.4)	4.06-79.1
Family members meeting criteria for LI + RI	71	29.5 (19.2)	6.0-79.1
Family members meeting criteria for LI & RI	24	27.5 (19.3)	6.03-79.1
Number of families	95		

Table 2: Mean Values and Standard Deviations of Scores for Each Group on All Variables of the Testing Battery

Variable	SEGMENTAL LANGUAGE							
	UNAFFECTED		ASD		LI			
	MEAN (SD)	N	MEAN (SD)	N	MEAN (SD)	N		
CELF - Core Score	120	110.79 (8.41)	21	71.49 (21.90)	33	71.77 (21.81)	18	108.89 (9.15)
CELF - Comprehension and Following Directions	121	110.71 (8.37)	21	63.84 (21.31)	33	64.25 (21.31)	18	104.67 (9.78)
CELF - Formulated Sentences	128	111.85 (8.85)	25	67.90 (23.32)	32	69.27 (23.32)	18	109.99 (9.51)
CELF - Word Structure	128	111.85 (8.85)	25	67.90 (23.32)	32	69.27 (23.32)	18	109.99 (9.51)
CELF - Recalling Sentences	128	111.85 (8.85)	25	67.90 (23.32)	32	69.27 (23.32)	18	109.99 (9.51)
CELF - Word Classes Expressive Score	128	111.85 (8.85)	25	67.90 (23.32)	32	69.27 (23.32)	18	109.99 (9.51)
CELF - Word Classes Receptive Score	128	111.85 (8.85)	25	67.90 (23.32)	32	69.27 (23.32)	18	109.99 (9.51)
CELF - Word Classes Total Score	128	111.85 (8.85)	25	67.90 (23.32)	32	69.27 (23.32)	18	109.99 (9.51)
CELF - Word Definitions	112	112.16 (1.78)	18	63.1 (28.26)	30	69.82 (28.26)	14	104.19 (2.48)
CELF - Preschool Sentence Score	112	112.16 (1.78)	18	63.1 (28.26)	30	69.82 (28.26)	14	104.19 (2.48)
CELF - Preschool Expressive Vocabulary	112	112.16 (1.78)	18	63.1 (28.26)	30	69.82 (28.26)	14	104.19 (2.48)
CELF - Preschool Sentence Structure	112	112.16 (1.78)	18	63.1 (28.26)	30	69.82 (28.26)	14	104.19 (2.48)
CELF - Preschool Word Structure	112	112.16 (1.78)	18	63.1 (28.26)	30	69.82 (28.26)	14	104.19 (2.48)
CTOPP - Elision	128	111.85 (8.85)	25	67.90 (23.32)	32	69.27 (23.32)	18	109.99 (9.51)
CTOPP - Nonword Repetition	128	111.85 (8.85)	25	67.90 (23.32)	32	69.27 (23.32)	18	109.99 (9.51)
SUPRASEGMENTAL LANGUAGE								
CASL - Ambiguous Sentences	117	109.82 (13.22)	21	77.91 (21.49)	19	74.09 (21.49)	14	106.11 (14.27)
CASL - Inference	124	109.82 (13.22)	21	77.91 (21.49)	19	74.09 (21.49)	14	106.11 (14.27)
CASL - Meaning from Context	119	109.82 (13.22)	21	77.91 (21.49)	19	74.09 (21.49)	14	106.11 (14.27)
CASL - Nonliteral Language	123	109.82 (13.22)	21	77.91 (21.49)	19	74.09 (21.49)	14	106.11 (14.27)
CASL - Pragmatic Judgment	123	109.82 (13.22)	21	77.91 (21.49)	19	74.09 (21.49)	14	106.11 (14.27)
WRITTEN LANGUAGE								
WRAT - Spelling	131	107.48 (11.83)	23	65.79 (21.74)	31	68.41 (21.74)	16	102.97 (17.55)
Woodcock - Word Attack	131	111.44 (10.78)	24	68.47 (18.84)	31	69.87 (18.84)	15	104.89 (15.87)
Woodcock - Word Identification	131	110.14 (10.61)	23	65.12 (20.93)	31	68.11 (20.93)	15	102.05 (15.83)
GORT4 - Accuracy	114	113.08 (13.88)	21	64.84 (21.37)	33	67.84 (21.37)	17	109.31 (13.90)
GORT4 - Comprehension	111	113.08 (13.88)	21	64.84 (21.37)	33	67.84 (21.37)	17	109.31 (13.90)
GORT4 - Fluency	114	113.08 (13.88)	21	64.84 (21.37)	33	67.84 (21.37)	17	109.31 (13.90)
GORT4 - Rate	114	113.08 (13.88)	21	64.84 (21.37)	33	67.84 (21.37)	17	109.31 (13.90)
GORT4 - Overall Reading Quotient	114	113.08 (13.88)	21	64.84 (21.37)	33	67.84 (21.37)	17	109.31 (13.90)
WRMT - Performance IQ	129	109.42 (14.80)	23	63.89 (21.45)	33	69.88 (21.45)	12	104.04 (17.77)

Variability in N can be attributed to age specific measures of language and reading ability. The following results are based on a subset of the original sample; 53 families who have completed the entire study to date.

Statistical Methods

SPSS software was used to conduct all statistical analyses.

- Independent sample T-tests were conducted to identify differences in test variable means between the ASD and LI groups and the ASD and RI groups.
 - Bonferroni correction: $\alpha = 0.05 / 21$ variables = 0.002
- Independent sample T-tests were conducted to identify differences in test variable means between male and female individuals.
 - Bonferroni correction: $\alpha = 0.05 / 21$ variables = 0.002

Results

Table 3: Comparison of testing variable means between ASD individuals and LI individuals

Variable	Segmental					Independent Samples T-test
	ASD	LI	difference	95% CI	p-value	
CELF-PPVT	5.54 (4.45)	4.11 (3.89)	1.43	(-1.35, 4.48)	0.338	
CELF-PPSS	5.70 (3.93)	5.63 (2.77)	-0.08	(-2.05, 1.86)	0.932	
CELF-WSS	5.13 (4.26)	4.07 (3.13)	1.05	(-0.35, 2.44)	0.522	
CELF-RSS	4.64 (3.39)	4.27 (2.23)	0.37	(-1.92, 2.61)	0.679	
CELF-WCS	6.31 (2.89)	5.95 (2.40)	0.37	(-1.27, 2.44)	0.683	
CELF-WSS	7.73 (5.17)	7.82 (5.07)	0.21	(-2.35, 2.75)	0.866	
CTOPP-LES	8.14 (3.89)	5.25 (3.08)	2.81	(-1.84, 0.78)	0.008	
CTOPP-RS	8.30 (2.72)	8.86 (2.80)	-1.49	(-3.08, 1.10)	0.086	
Suprasegmental						
CSLASS	77.91 (12.49)	74.00 (17.77)	3.91	(-1.28, 5.06)	0.568	
CSLNS	70.10 (14.95)	74.50 (16.20)	-4.4	(-10.25, 19.05)	0.536	
CSLMS	71.09 (16.31)	78.72 (18.59)	-7.67	(-15.75, 17.68)	0.104	
CSLNS	70.80 (20.85)	78.39 (15.83)	8.37	(2.45, 12.44)	0.003	
CSLPS	70.32 (20.35)	78.92 (14.69)	8.62	(-1.01, 18.35)	0.078	
Written						
WRATSS	95.78 (12.74)	89.61 (18.11)	6.17	(-1.16, 13.47)	0.147	
WRMFASTO	98.67 (18.84)	89.87 (13.81)	8.73	(-1.71, 21.24)	0.065	
WRMFASTO	99.12 (20.99)	88.21 (18.44)	11	(-1.24, 36.03)	0.042	
GRT4-RSS	8.94 (3.77)	7.91 (3.72)	1.03	(-2.87, 1.90)	0.681	
GRT4-WSS	8.61 (4.80)	8.82 (3.90)	-0.21	(-2.15, 1.74)	0.933	
GRT4-PPSS	6.59 (3.57)	5.87 (3.94)	0.72	(-0.43, 1.86)	0.393	
GRT4-RSS	7.35 (3.02)	6.65 (3.28)	0.74	(-1.26, 2.77)	0.349	
GRT4-RQ	77.12 (19)	75.14 (15.59)	2.78	(-1.47, 8.92)	0.633	

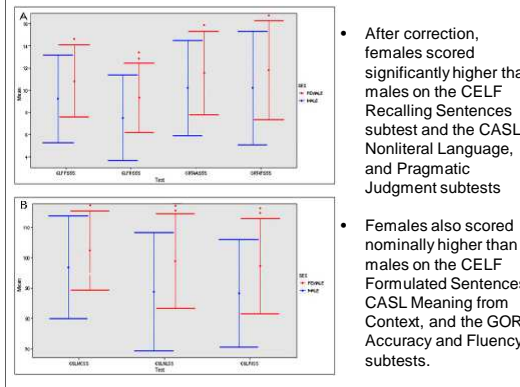
- After correction for multiple testing, individuals with ASD did not have significantly different mean scores on any of the language tests when compared to individuals with LI.
- Nominally, individuals with ASD did score higher on the Elision and Word Identification tasks than individuals with LI.

Table 4: Comparison of testing variable means between ASD individuals and RI individuals

Variable	Segmental					Independent Samples T-test
	ASD	RI	difference	95% CI	p-value	
CELF-PPVT	5.54 (4.45)	5.47 (3.70)	0.27	(-1.24, 9.09)	0.965	
CELF-PPSS	5.70 (3.93)	6.09 (3.51)	-3.47	(-1.69, 3.24)	<0.001	
CELF-WSS	5.13 (4.26)	4.30 (4.07)	0.83	(-3.09, 3.84)	0.769	
CELF-RSS	4.64 (3.39)	6.92 (4.93)	-2.38	(-7.26, 4.91)	0.005	
CELF-WCS	6.31 (2.89)	6.83 (4.86)	-2.92	(-8.28, 4.53)	0.001	
CELF-WSS	7.73 (5.17)	10.46 (3.28)	-2.78	(-6.60, 4.97)	0.013	
CTOPP-LES	8.14 (3.89)	7.00 (3.49)	1.08	(-2.89, 0.74)	0.242	
CTOPP-RS	8.30 (2.72)	8.00 (3.55)	0.29	(-1.77, 1.19)	0.761	
Suprasegmental						
CSLASS	77.91 (12.49)	86.11 (4.27)	8.3	(3.99, 17.60)	0.079	
CSLNS	70.10 (14.95)	88.18 (20.12)	-18.08	(-29.35, 33.20)	0.021	
CSLMS	71.09 (16.31)	91.07 (12.40)	-19.98	(-31.09, 28.81)	0.001	
CSLNS	70.80 (20.85)	88.70 (17.30)	-17.96	(-27.77, 27.35)	<0.001	
CSLPS	70.32 (20.35)	88.95 (17)	-18.63	(-30.26, 27.01)	0.001	
Written						
WRATSS	95.78 (12.74)	92.97 (17.12)	2.78	(-3.16, 5.58)	0.511	
WRMFASTO	98.67 (18.84)	94.89 (15.57)	3.82	(-1.48, 4.24)	0.363	
WRMFASTO	99.12 (20.99)	92.05 (15.93)	7.25	(-1.24, 30.02)	0.082	
GRT4-RSS	8.94 (3.77)	7.91 (3.95)	1.03	(-1.18, 3.31)	0.372	
GRT4-WSS	8.61 (4.80)	6.81 (3.92)	1.85	(-2.37, 2.67)	0.509	
GRT4-PPSS	6.59 (3.57)	7.35 (4.84)	-0.76	(-1.43, 2.95)	0.484	
GRT4-RSS	7.35 (3.02)	7.79 (5.0)	-0.3	(-1.45, 2.11)	0.845	
GRT4-RQ	77.12 (19)	80.98 (15.31)	-3.86	(-15.29, 13.00)	0.403	

- As a group, individuals with RI had significantly higher scores on the CELF Formulated Sentences and Word Classes subtests, the CASL Meaning from Context, Nonliteral Language, and Pragmatic Judgment subtests than individuals with ASD.
- Nominally, individuals with RI also scored significantly higher on the CELF Recalling Sentences and Word Definitions subtests and the CASL Inference subtest.

Figure 1A and 1B: Significant mean differences in testing variables between male and female participants.



- After correction, females scored significantly higher than males on the CELF Recalling Sentences subtest and the CASL Nonliteral Language, and Pragmatic Judgment subtests.
- Females also scored nominally higher than males on the CELF Formulated Sentences, CASL Meaning from Context, and the GORT Accuracy and Fluency subtests.

Rates of Impairment

Table 5: Rates of Impairment in the NJLAGS sample.

Nuclear Family (excluding ASD probands)	Unaffected LI or RI	LI only	RI only	LI+RI	TOTAL LI	Total tested
	Fathers	31 (70%)	1 (2%)	8 (18%)	4 (9%)	13 (30%)
Mothers	39 (80%)	1 (2%)	7 (14%)	2 (4%)	10 (20%)	49
Brothers	14 (30%)	9 (25%)	4 (11%)	4 (11%)	22 (61%)	36
Sisters	13 (45%)	2 (7%)	8 (28%)	6 (21%)	16 (58%)	29
TOTAL nuclear family	97 (61%)	13 (8%)	32 (20%)	16 (10%)	61 (39%)	219
Extended Family	41 (72%)	3 (5%)	8 (14%)	5 (9%)	16 (28%)	57
Verbal ASD	9 (31%)	10 (34%)	0 (0%)	10 (34%)	20 (68%)	29
Total (nuclear and extended families)	147 (60%)	26 (11%)	40 (16%)	31 (13%)	97 (40%)	244

- By design, all 53 families had at least one individual with an SLI diagnosis.
- In nuclear families the rate in excess of the original 53 proband was 9 other family members with a diagnosis of SLI/LLI (13%).
- When all nuclear and extended family members were included as well as the ASD probands who met criteria for LI and/or RI, the rate increased to 44 other members over and above the original 53 (18%).
- This is a rate higher than the rates of SLI in the general population (Tomblin et al., 1997).

Conclusions

- There were no significant difference between the mean scores of individuals with LI and ASD and few significant differences between the mean scores of the RI and ASD groups.
- We recognize that ASD and SLI are complex disorders and that in many respects they are distinctly different disorders. However, there were enough similarities in performance to support using language ability as a behavioral biomarker in family studies of autism.
- This similarity also suggests that these families, which are enriched for LI, may also be enriched for genetic factors that are related to the language impairment that is relevant to both SLI and ASD.
- The high rates of LI in our families (after excluding SLI probands) also suggests a genetic component linking LI and ASD. In these families