



Co-Occurrence of Behavioral, Psychiatric, and Medical Issues In Families Ascertained for Autism and Language Learning Impairment

Zena Fermano¹, Judy Flax¹, Abby Hare¹, Barbie Zimmerman-Bier⁴,
Christopher W. Bartlett³, Liping Hou⁵, Steven Buyske^{1,2}, Linda Brzustowicz¹

¹Rutgers University, Department of Genetics, Piscataway, NJ; ²Rutgers University, Department of Statistics, Piscataway, NJ

³The Battelle Center for Mathematical Medicine, The Research Institute at Nationwide Children's Hospital and Department of Pediatrics, The Ohio State University, Columbus, OH, ⁴Saint Peter's University Hospital, New Brunswick, NJ, ⁵National Institute of Health, Bethesda, MD



Introduction: Converging evidence suggests that in families where there is an individual with an autism spectrum disorder (ASD), relatives may also exhibit behavioral, medical, and/or psychiatric characteristics that are milder but qualitatively similar to the defining features of autism. This observation has been coined the *Broad Autism Phenotype –BAP* (see Losh et al., 2008). Furthermore, research suggests that these conditions occur more frequently in families where there is an individual diagnosed with autism when compared to control families. Before undertaking any family linkage and association analyses, strong phenotypic characterization of these family members is essential.

The **New Jersey Language and Autism Genetics Study (NJLAGS)** has studied families ascertained through (at least) one proband with autism and a second proband with a significant language-learning impairment. Each family member has also been directly assessed to identify family members who exhibit elevated scores on ratings of (1) language deficits, (2) rigid personality traits/social aloofness, and (3) medical and psychiatric inventories, yet do not meet any of the criteria for autism. The primary goal is to *create behavioral biomarkers related to language and other conditions associated with autism*. Once proband criteria are met, the family completes a comprehensive neuropsychological battery and donates a blood sample for DNA analysis.

Study Ascertainment & Methods: Autism probands are diagnosed using the ADI-R, the ADOS, and a comprehensive physician's examination including the DSM-IV.

• **Language-Learning Impaired probands** are diagnosed by a licensed Speech/Language Pathologist and is defined as a family member with oral and/or written language skills significantly below his/her peers:

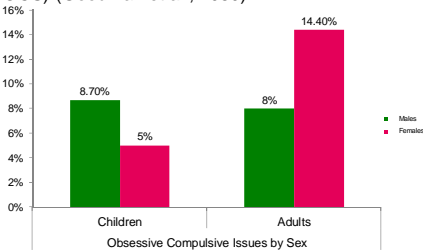
- 1) reflected on comprehensive standardized oral (speaking and listening) and written (reading and spelling) language tests, or
- 2) as significant weaknesses in specific language domains (not necessarily reflected in a global language score) combined with a history of language and/or reading issues and subsequent interventions.

Study I: Occurrence of Obsessive-Compulsive Issues and Social Impairments in NJLAGS Family Members based on Quantitative Assessment (excluding ASD probands)

Quantitative Assessments for Obsessive-Compulsive Issues:

Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (Goodman et al., 1989)

Children's Yale-Brown Obsessive Compulsive Scale (CYBOCS) (Goodman et al., 1989)

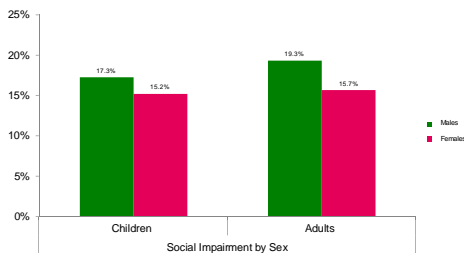


❖ CY-BOCS & Y-BOCS: For this study, total score ≥ 16 represents OCD behaviors in the "affected" range (Grados et al., 2001; personal correspondence with Dr. L Schill).

❖ There were no statistically different rates among males and females in children $X^2(1, N = 86) = 0.450, p = .502$; nor any differences in rates between males and females in adults $X^2(1, N = 192) = 1.97, p = .161$.

❖ A higher rate of obsessive compulsive behaviors was reported in NJLAGS families (excluding the ASD probands) as compared to the reported rates of OCD in the U.S. population which are reported as 0.4% in children and 1% in adults (Kessler et al., 2005, Wang et al, 2005, and Weissman et al., 1994).

Quantitative Assessment for Social Impairments: Social Responsiveness Scale (SRS) (Constantino, 2002)



❖ SRS: Raw Scores ≥ 54 (females) and ≥ 65 (males) represents moderate to severe range of social impairment and are considered "affected" for this study (Constantino et al., 2003, 2004; personal correspondence with Dr. J Constantino).

❖ Approximately one-fifth of all NJLAGS family members (excluding ASD probands) reported social issues. There were no statistically different rates among males and females in children $X^2(1, N = 98) = 0.078, p = .780$; nor any differences in rates between males and females in adults $X^2(1, N = 171) = 0.395, p = .530$.

STUDY II: Occurrence and Co-Occurrence of Language, Psychiatric, and Medical Issues in NJLAGS Families Based on Family History Data

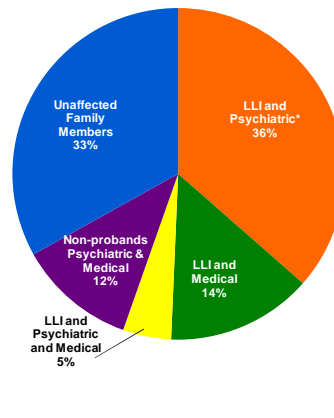
Subjects:

36 NJLAGS Families
174 Individual Surveys

Questionnaire Details:

- ❖ Questions rated history and level of proficiency in language, reading, and academics as superior through impaired.
- ❖ Family members with a rating of *below average* and *impaired* were considered **affected**.
- ❖ Questions regarding psychiatric issues (i.e. Anxiety Disorder, Bipolar Disorder, ADD/ADHD, etc.) were scored as present or not.
- ❖ Questions regarding medical and health issues (i.e. autoimmune issues, gastrointestinal issues, etc.) were scored as present or not.

Co-Occurrence of Medical, Psychiatric, and Behavioral Issues in Family Members (excluding ASD probands)



*9% of these family members report ADD/ADHD

Two-thirds of NJLAGS family members (excluding the ASD probands and including the LLI probands), reported at least one other co-morbid psychiatric impairment or medical impairment that is often associated with autism.

Co-Occurrence of Medical and Psychiatric Issues in ASD probands

Medical/Psychiatric Issue*	Percentage
ADD/ADHD	58%
Allergies	33%
Gastrointestinal Issues	25%
Autoimmune Diseases	8%
Seizures	3%

*these categories are not mutually exclusive

❖ Greater than 50% of all ASD probands were reported to have concomitant ADD/ADHD.

❖ A third of the sample reported some type of seasonal or food allergy while another quarter experienced gastrointestinal problems and to a lesser degree autoimmune diseases and seizures.

Preliminary Conclusions & Future Directions

❖ Ongoing analyses of the NJLAGS study suggest that in families who were ascertained for a history of autism and language-based learning disorders, there appears to be a greater risk for other behavioral, psychiatric, and medical disorders in comparison to the general population.

❖ These findings: 1) support the theory of a broader view of autism and related disorders in families, 2) support the notion of a greater genetic risk for certain disorders in these families studied, and 3) highlight the potential genetic heterogeneity in autism research and the need to explore multiple behavioral biomarkers in families.

❖ NJLAGS families have been genotyped and linkage and association analyses are ongoing. While the speech and language phenotypes and subsequent genotyping associated with both disorders remain the primary aims, other behavioral biomarkers are currently being explored.

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For questions, please contact: fermano@biology.rutgers.edu