



R.C.P.U. NEWSLETTER

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Genetics of Autism

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Introduction

Autism Spectrum Disorders (ASD) are neurodevelopmental disorders characterized by impairments in social interaction, communication and restricted and repetitive behavior. ASD is composed of three main categories: classic infantile autism, Aspergers, and pervasive developmental disorder, not otherwise specified (PDD-NOS).

Classic infantile autism is a condition of impaired sociability, empathy, and ability to read other people's moods and intentions; therefore resulting in inappropriate social interactions (Rapin et al., 2008). Individuals with classic autism often display rigidity and perseveration, including repetitive movements and activities, and a need for sameness. They have impaired language, communication, and imaginative play (Rapin et al., 2008). Asperger disorder differs from classic infantile autism because speech is often not delayed and IQ is typically greater than 70. Hyperlexia (above average reading ability combined with below average verbal abilities) may also occur (Rapin et al., 2008). PDD-NOS occurs in children who do not meet the specific criteria for classic autism but have pervasive impairment and odd behaviors. The prevalence of ASD is approximately 1 in 150 and it occurs more often in males than in females, with a ratio of 4:1 (Zhao et al. and Folstein, 1985).

Genetic Testing in Autism

About 5-10% of cases of classic infantile autism is due to an identifiable genetic disorder which, in many cases, has a known inheritance pattern and a specific recurrence risk (Simonoff, 1998). This paper briefly notes some of the more common genetic causes of classic autism, but does not specifically review them. Fragile X syndrome is one of the more significant identifiable genetic causes of classic autism (Muhle et al., 2004). Testing for Fragile X is typically ordered on almost all individuals with a developmental handicap who are undergoing genetic

evaluation. Fragile X is a mental retardation syndrome seen mainly in males because the gene is located on the X chromosome; however, it can occur in females. Fragile X is classified as a DNA triplet repeat disorder. Rett syndrome is also an identifiable genetic cause for Autism, but it is less common of Autism than Fragile X. Rett syndrome is a condition that occurs almost exclusively in females, and is characterized by: regression of developmental milestones, seizures, stereotypic hand movements and purposeless use of hands. Molecular testing for Rett syndrome is performed by DNA sequencing the MECP2 gene as well as deletion/duplication testing for this gene.

Testing for chromosomal microduplication/deletion disorders has recently been improved by the development of new molecular testing known as chromosome microarray or comparative genomic hybridization. The most common micro duplication syndrome that has been found to be associated with autism is 15q11.2 and occurs in approximately 1% of all children with autism (Muhle et al., 2004). Other identifiable genetic causes for autism that may be tested for include metabolic diseases. The appropriate testing for these diseases usually includes: serum amino acids, urine organic acids, and plasma acylcarnitine levels.

Evidence that Autism is Genetic

For families with a child with ASD who does not on of these identifiable causes, the risk of recurrence is often unknown and must be estimated. Studies on twins have shown that the concordance rate for autism is approximately 60% for monozygotic and about 4.5% for dizygotic twins (Cook et al., 2001). In addition, a concordance rate of approximately 90% for monozygotic twins was found for ASD, including cognitive delays and/or social problems, while only 10% of dizygotic twins were found to be concordant (Muhle et al., 2004). The higher rate of monozygotic concordance illustrates the strong influence of inherited genes, and suggests that multiple genes can be

related to the cause of autism and autism-related traits (Freitag, 2007). This type of inheritance, where a combination of multiple genes and environment plays a role in the development of a condition or syndrome, is referred to as multifactorial inheritance.

Recurrence Risks

Most families of a child with an ASD come to genetics clinic with questions regarding recurrence risk. After the identifiable genetic causes have been ruled out, recurrence risk estimates can be provided. The risk of recurrence is variable and depends on the degree of relationship to the affected child. Below is a table listing the reported recurrence risk estimates obtained from multiple studies. These risk estimates are listed according to how the person asking the question is related to the affected person.

Person Asking the Question	Recurrence Risk for Classic Autism	Recurrence Risk for PDD-NOS/Aspergers	Recurrence Risk for Cognitive or Language Delays
Affected Proband	5-50%	Not Available	Not Available
Parents with Affected male child	3-8%	5%	10-20%
Parents with Affected female child	3-8%	7-8%	10-20%
Siblings of Affected Proband	Not Available	Not Available	Not Available
Aunt/Uncle of Affected Proband	0.18%	1%	Not Available
Cousin of Affected Proband	0.12%	1%	Not Available
Parent of 2 Affected Probands	25%	Not Available	Not Available

Genetic Counseling

Genetic counseling plays a very important role in the genetic evaluation of a child with an ASD. Genetic Counselors enable accurate risk information to be provided to the family in an objective and informative way. Genetic Counselors also provide resources to these families as well as information regarding research and experimental treatments currently being used.

References

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Centers for Autism and Related Disorders (CARD) centers in Florida:

The Center for Autism and Related Disabilities (CARD) provides assistance with the goal of optimizing the potential of people with autism and related disabilities. Located at six university sites throughout Florida, CARD develops programs offering support and training for individuals, families, professionals, and peers throughout Florida. CARD offers support within the natural contexts of homes, residences, child care programs, schools, and communities. Services provided by CARD include (1) consultation to caregivers and professionals on how best to work with an individual with a disability; (2) training sessions on how to work effectively with individuals with autism and related disabilities; and (3) family referral to federal, state, and local service agencies. CARD serves both children and adults of all levels of intellectual functioning who have autism, pervasive developmental disorders, autistic-like disabilities, dual sensory impairments, or sensory impairments with other disabling conditions. CARD services are designed to build on the

capacities of state and local resources. The Center is funded by the Florida Legislature through the Florida Department of Education and all services are provided free of charge.

CARD Center Locations:

University of Florida at Jacksonville:

CARD UF Jacksonville
6271 St. Augustine Road, Suite 1
Jacksonville, Florida 32217
Phone: (904) 633-0760
Fax: (904) 633-0751

Counties served: Baker, Clay, Duval, Flagler, Nassau, St. John's

University of Florida / Gainesville:

University of Florida
PO Box 100234
Gainesville FL 32610-0234

(800)754-5891 or (352)273-0581

Fax (352)846-3703

Counties served: Alachua, Bradford, Citrus, Columbia, Dixie, Gilchrist, Hamilton, Hernando, Lafayette, Levy, Marion, Putnam, Suwannee, Union

University of South Florida:

CARD-USF MHC2113A
13301 Bruce B. Downs Blvd.
Tampa FL 33612-3899
(800) 333-4530 or (813) 974-2532
Fax (813) 974-6115

Counties served: Charlotte, Collier, Desoto, Glades, Hardee, Hendry, Highlands, Hillsborough, Lee, Manatee, Pasco, Pinellas, Polk, Sarasota

University of Central Florida:

CARD/University of Central Florida
PO Box 162202
Orlando FL 32816-2202

(888) 558-1908 or (407) 737-2566
Fax (407) 823-6180

Counties served: Brevard, Lake, Orange, Osceola, Seminole, Sumter, Volusia

Florida Atlantic University:

Florida Atlantic University CARD
Dept. of ESE
Florida Atlantic University
777 Glades Road
Boca Raton, FL 33431

(888) 632-6395 or (561) 297-2023
Fax: (561) 297-2063

Counties served: Indian River, Martin, Okeechobee, Palm Beach, St. Lucie

Florida State University:

CARD/Florida State University
625-B North Adams Street
Tallahassee FL 32301
(800) 769-7926 or (850) 644-4367
Fax (850)644-3644

Counties served: Bay, Calhoun, Escambia, Franklin, Gadsden, Gulf, Holmes, Jackson, Jefferson, Leon, Liberty, Madison, Okaloosa, Santa Rosa, Taylor, Wakulla, Walton, Washington

University of Miami:

CARD/University of Miami
Department of Psychology
PO Box 248768
Coral Gables FL 33124
(800) 9-AUTISM or (305) 284-6563
Fax (305) 284-6555

Counties served: Broward, Dade, Monroe

Additional Resources:

Autism Society of America

Publishes the "Advocate," an informative quarterly magazine.

7910 Woodmont Avenue
Suite 300

Bethesda MD 20814-3067

Phone: 800-3AU-TISM (800-328-8476); 301-657-0881

Fax: 301-657-0869

Email: Advocate@autism-society.org

www.autism-society.org

GeneTests

University of Washington, Seattle
www.genetests.org

University of Florida

Division of Genetics and Metabolism
PO Box 100296

Gainesville, FL 32610

Phone: 352-392-4104

Fax: 352-392-3051

www.peds.ufl.edu/divisions/genetics/programs/autism_card.htm

About the RCPU

The Raymond C. Philips Research and Education Unit began in 1978 when the legislature established section 393.20 of what is now known as the "prevention" legislation. It is named after Raymond C. Philips, who was the Superintendent of Gainesville's Tacachale (formerly Sunland) Center for 38 years, and was an acknowledged state and national leader in services for mentally retarded persons. The Unit is run through the Division of Pediatric Genetics, University of Florida, and is funded through a contract with the Department of Children and Families.

The purpose of the R.C.P.U. is to treat, prevent, and/or ameliorate mental retardation through medical evaluations, education and research. The unit provides direct evaluations and counseling to families and promotes service, education, and prevention projects.

Some of the conditions currently under study at the RCPU involve Angelman, Velo-Cardio-Facial, Prader-Willi, Fragile X, Williams and Smith-Lemli-Opitz syndromes.

The R.C. Philips Unit is a resource for all Floridians interested in the diagnosis, treatment and prevention of mental retardation. Staff members are available for consultation and for educational programs for health professionals and for the community at large.

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