Infant Eye Movement Links Genetic Susceptibility with Social Impairment in Autism

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Disclosure of Interests

• Industry Consulting:
  – Roche Pharmaceuticals

• Stock Equity: None

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  The Social Responsiveness Scale (SRS-2)

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  Missouri Autism Centers of Excellence
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Recurrence Rates and Inherited Transmission in Autism

**MZ concordance:** 90+%  
**DZ concordance:** 20%  
**Non-twin sib recurrence:** 18%  
**General population risk** 1%

“SPORADIC” (60%)

FAMILIAL (40%)

De novo (germ line)

Rare inherited

Common var. (polygenic)

Rare inherited
As the numbers rise, the effects of variants of intermediate potency will become discoverable.

Figure 2 | Diagnostic yield for ID over time. Graphical overview of the diagnostic yield for moderate to severe intellectual disability (ID) (excluding Down syndrome, which represents 6–8% of all ID) over time. Solid line indicates the mean of published studies, and the shaded background indicates the lower and upper boundaries of reported diagnostic yields. In the 1970s, conventional karyotyping became a routine diagnostic test and provided a conclusive diagnosis in 3–6.5% of ID cases. The
“Additive Genetic overlap”: Common variants conferring background genetic risk for one disorder confer background genetic risk for another disorder (eg. ADHD/ASD; SCHZ/Bipolar Disorder)

“Pleiotropy”: A rare mutation causes two different syndromes on two different backgrounds
ASD – Epilepsy – ID – Schizophrenia
Medication for Attention Deficit–Hyperactivity Disorder and Criminality

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METHODS

Using Swedish national registers, we gathered information on 25,656 patients with a diagnosis of ADHD, their pharmacologic treatment, and subsequent criminal convictions in Sweden from 2006 through 2009. We used stratified Cox regression analyses to compare the rate of criminality while the patients were receiving ADHD medication, as compared with the rate for the same patients while not receiving medication.

A Phenotypic Index of Family Genetic Background

QUANTITATIVE AUTISTIC TRAITS
Diagnosis of autism spectrum disorder: reconciling the syndrome, its diverse origins, and variation in expression

John N Constantino, Tony Charman

“...A tale of 3 distributions”

Figure 2. Distribution of Social Responsiveness Scale (SRS) scores as a function of sex (n=1576).

General Population

Male First Degree Relatives

Sisters of ASD Index Cases

www.thelancet.com/neurology
Where’s the lesion?

Scores for Symptom Clusters map to clinical affectation status, and are highly inter-correlated in affected *and* unaffected populations.

Attention to eyes is present but in decline in 2–6-month-old infants later diagnosed with autism

Warren Jones\textsuperscript{1,2,3} & Ami Klin\textsuperscript{1,2,3}

Figure 2 | Growth charts of social visual engagement for typically developing children and children diagnosed with ASD. a, b, Fixation to eyes, mouth, body and objects from 2 until 24 months in TD (a) and ASD (b) children. c, d, Contrary to a congenital reduction in preferential attention to eyes in ASD, children with ASD exhibit mean decline in eye fixation. e–h, Longitudinal change in fixation to eyes (e), mouth (f), body (g), and object (h) regions; between-group comparisons by functional ANOVA. Thick lines
Biological correlates of genetic background in early development

Figure 3. Salience maps for typically-developing 2-year-olds (top) and for 2-year-olds with autism (bottom). Images at right show color data scaled from black to transparent and overlaid on the still image from the video scene.

Courtesy, Ami Klin and Warren Jones, Emory University
Social visual engagement in infants is under stringent genetic control

Constantino et al., under review
Autism Treatment in the First Year of Life: A Pilot Study of Infant Start, a Parent-Implemented Intervention for Symptomatic Infants

S. J. Rogers · L. Vismara · A. L. Wagner · C. McCormick · G. Young · S. Ozonoff
The distribution of social and cognitive impairments in a population of children with a specific genetically-defined syndrome is often wide, and for 22q11.2 and 16p11.2 manifest correlations with “genetic background” distributions indexed by variation in the subjects’ parents.

**HIGHLY-PENETRANT MUTATIONS RESULT IN PREDICTABLE PATHOLOGICAL SHIFT FROM WHAT WOULD BE “EXPECTED” ON THE BASIS OF AN INDIVIDUAL’S GENETIC BACKGROUND**

*Figure 1: Cognitive effects of copy number variant syndromes in full-scale intelligence quotient scores (A) The intelligence quotient (IQ) distribution curve in individuals with deletion 22q11.2 (red line) is shifted 2 SD to the left of the IQ distribution in the general population (mean 100; SD: 15; light blue line). Individuals with deletion 16p11.2 have a mean IQ of 76.1 (dark blue line), which is significantly lower than the mean IQ of their non-carrier first-degree relatives (108.3; green line). The higher IQ of first-degree relatives compared to the general population was previously discussed by Zufferey and colleagues as likely due to ascertainment bias. For both copy number variant syndromes, many deletion carriers have IQ scores within the normal range (>70); this is often referred to as incomplete penetrance when cognitive function is viewed as a qualitative, dichotomous trait (normal intelligence vs. intellectual disability) based on a cutoff of 70 points of IQ (dotted line), but may be better interpreted as variable expressivity of a continuous, quantitative trait.*
Moreno-DeLuca, Ledbetter et al., JAMA Psychiatry 2015
Developmental Theories for the 1990s: Development and Individual Differences

Sandra Scarr
University of Virginia

Scarr, Sandra. *Developmental Theories for the 1990s: Development and Individual Differences.* Child Development, 1992, 63, 1–19. Understanding both typical human development and individual differences within the same theoretical framework has been difficult because the 2 orientations arise from different philosophical traditions. It is argued that an evolutionary perspective can unite the study of both species-typical development and individual variation. Research on determinants of development from many perspectives can be understood within an evolutionary framework in which organism and environment combine to produce development. Species-normal genes and environments and individual variations in genes and environments both affect personality, social, and intellectual development. These domains are used as examples to integrate theories of normal development and individual differences. Within the usual samples of European, North American, and developed Asian countries, the results of family and twin studies show that environments within the normal species range are crucial to normal development. Given a wide range of environmental opportunities and emotional supports, however, most children in these societies grow up to be individually different based on their individual genotypes. Understanding the ways in which genes and environments work together helps developmentalists to identify children in need of intervention and to tailor interventions to their particular needs.

[Child Development, 1992, 63, 1–19. © 1992 by the Society for Research in Child Development, Inc. All rights reserved. 0009-3920/92/6301-0015$01.00]
It is proposed here that each child constructs a reality from the opportunities afforded by the rearing environment, and that the constructed reality does have considerable influence on variations among children and differences in their adult outcomes.

**CONSTRUCTING EXPERIENCES FROM ENVIRONMENTS**

The idea that people make their own environments (Scarr & McCartney, 1983) runs counter to the mainstream of developmental psychology.
Different people, at different developmental stages, interpret and act upon their environments in different ways that create different experiences for each person. In this view, human experience is the construction of reality, not a property of a physical world that imparts the same experience to everyone who encounters it.
The entire theory depends on people having a varied environment from which to choose and construct experiences. The theory does not apply, therefore, to people with few choices or few opportunities for experiences that match their genotypes. This caveat applies particularly to children reared in very disadvantaged circumstances and to adults with little or no choice about occupations and leisure activities.

Two-Generation Psychiatric Intervention in the Prevention of Early Childhood Maltreatment Recidivism

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