University of California, Davis

Center for Children's Environmental Health

Childhood Autism Risks from Genetics and The Environment

The CHARGE Study

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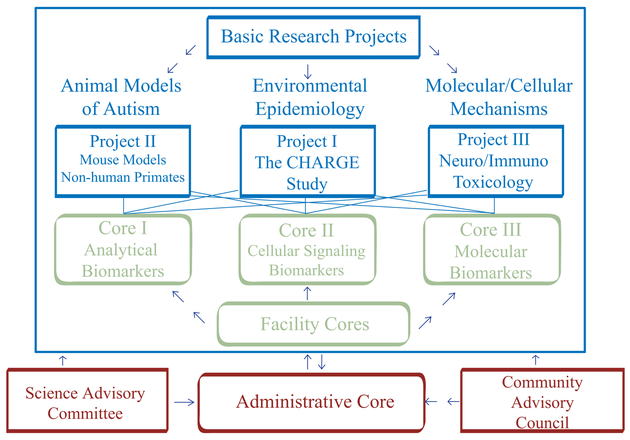
UC Davis Center for Children's Environmental Health Organizational Structure



What is our goal?

The CHARGE study is a project of the NIEHS/EPA Center for Children's Environmental Health at UC Davis, that has been designed by parents and researchers committed to understanding the causes of autism and other neurodevelopmental disabilities. These serious, lifelong disorders interfere with a person's ability to function in everyday activities. By studying children with different patterns of development we will learn more about factors that can increase risks for these disabilities.

What kinds of causes do we study?

We are investigating:
Environmental toxins
Medical history
Lifestyle factors both before and after birth

We also look at susceptibility factors that may affect brain development, including:
Metabolites such as lipids, sugars and amino acids
Cell to cell communication molecules
Gene activity
Immune system function and status

Who participates in the CHARGE study?

Three groups:
Children with autism
Children with developmental delay or mental retardation but not autism (MR/DD)
Children with typical or expected development (GP)

Who is eligible to participate?

Between the ages of two and five
Born in selected areas of California
Parents speak either English or Spanish
Living with at least one biologic parent

Study Design

Recruitment

- Children with autism (n=700) from State of California Regional Center system
- Children with mental retardation/developmental delay (n=600) from State of California Regional Center System
- Typically developing children (n=700) randomly sampled from California live births occuring in same birth years and counties as cases

Courtesy of Association of Regional Center Agencies (ARCA)

Data Collection

Regional Center Record Abstraction

Maternal Interview
- Demographic and lifestyle factors, medical, reproductive, occupational and residential histories

Clinical Assessments
- Cognitive, Behavioral and Medical

Specimen Collection
- Blood, urine, buccal swab and hair

Medical Record Review
- Obstetric, labor/delivery, neonatal, pediatric, dental

Take-home Questionnaires
- Abberant Behavior Checklist, Multiple Language Questionnaire, Sleep and GI Survey

Preliminary Results

Subject Enrollment

	Number of Families in Clinical Process	Number of Families Completed Clinical Process
Autism Group	126	118
MR/DD Group	19	20
Typically Developing Group	36	26
Total	181	164

Biological Sample Analysis (highlights)

Analytical Core (Core I) is attempting to cast a wide net and use the electrospray time of flight mass spectrometer to look in a semi quantitative way at a large variety of metabolites in urine and serum of autistic children including:

- Tryptophan metabolites (serotonin is a tryptophan-derived neurotransmitter)
- Neuroactive peptides, such as casomorphin from casein or gliadinomorphin form gluten (neuroactive peptides that exert an "opioid-like" effect in the brain)
- Oxilipins (oxidized lipids derived from the arachidonic acid and linoleic acid cascades) which are recognized as mediators of inflammatory and proliferative responses.

The Analytical Core is also measuring blood Hg and a wide range of other metals using ICP-MS (Inductively Coupled Plasma Mass Spectrometer) technology.

Cellular Activation/Signaling Core (Core II) is profiling serologic samples from autistic and matched control children to:

- define blood levels of key neurotrophins and neuropeptides in plasma.
- ascertain what tissue-specific antibodies are found in sera of patients with autism using a variety of neuronal antigens by immunoblot.

Molecular Biomarkers Core (Core III) is applying expression microarray and single-gene approaches to identify patterns of altered gene expression that form significant associations with autism in human populations, or which are coupled to specific environmental factors in animal models. Specifically the core is examining the association between autism and single-gene polymorphisms at six loci:

- Adenosine Deaminase, Serotonin transporter (5-HT), Glutathione S-transferase, Reelin, dopamine beta-hydroxylase, and monoamine oxidase A.