

CREATING A PEDIATRIC IMAGING-GENOMICS DATA RESOURCE

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This application was submitted by a group of investigators at 9 sites distributed throughout the U.S. where there are active developmental research programs involving substantial numbers of typically developing children, and neuroimaging investigators with experience in multi-site imaging initiatives. We will join forces to leverage these ongoing pediatric studies to assemble, over a period of 2 years, a large, cross-sectional imaging-genomics dataset to be used as a shared resource. The major aim of our proposal is to create a database that will include genome-wide association results for a large number of neural architectural phenotypes obtained using multimodal structural imaging.

We propose to offer this database - essentially a map depicting the genomic landscape of the developing human brain - as a resource to the scientific community. Across the sites, investigators will administer the brief NIH Neuroscience Blueprint Toolbox Cognitive assessment; acquire standardized structural and diffusion images, and collect DNA samples in 1575 children and adolescents who are participants in their ongoing studies. The DNA samples will be shipped to a central Genetics Core for analysis, the imaging data will be uploaded for quality control and computational morphometry by the Imaging Core, and other data will be uploaded to the Coordinating Core, where an aggregate database of demographic, behavioral, imaging, and genomics deliverables will be compiled from 1400 individuals and maintained for shared access. A large, cross-sectional pediatric dataset would fill a significant gap that currently prevents description of gene and gene-by-age effects on neural architecture in children (i.e., main effects of genetic variation and gene effects on developmental trajectories) that are likely to be relevant to variability in behavioral and neuropsychiatric outcomes. Preliminary results of analyses of large adult cohorts suggest that common genetic variation accounts for substantial variability in brain morphology. The age-span of participants in these studies has made it possible to detect gene-by-age interactions relevant to variability in brain aging. Unfortunately because there are no well-powered studies with data from individuals spanning the childhood and adolescent age range, it is not known whether these neural phenotypes are present in children; and if they are, whether they can be observed early in development or evolve as ongoing remodeling of neural structures proceeds during childhood.

This project will address the discrepancy between currently available imaging-genetics data in children of different ages and those available in adults. In addition to providing an informative data resource, the project would create a collaborative hub of investigators prepared to participate in an imaging-genomics adjunct study of the National Children's Study, which is in the early planning stages at this time.

Public Health Relevance Statement: The aim of this project is to assemble, over a period of 2 years, a large, cross-sectional imaging-genomics dataset to be used as a shared resource for investigations of genetic bases of neural phenotypes and age-by-genotype interactions that may represent genetically-mediated differences in developmental trajectories.