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The Adolescent Brain Cognitive Development Study

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The Adolescent Brain Cognitive Development (ABCD) Study is a longitudinal, observational study of over 10,000 youth recruited at 21 sites throughout the United States. School-based recruiting strategies are used to enroll a diverse cohort of 9- and 10-year-old children with the goal of following youth for at least 10 years. A team of epidemiologists and biostatisticians has designed the sampling methods to ensure that the cohort resembles the U.S. population as closely as possible on sociodemographic variables. Comprehensive biennial assessments and more limited interim assessments measure health, mental health, neurocognition, family, cultural, and environmental variables; substance use, genetic, and other biomarkers; and structural and functional brain development. A full description of these protocols, with lists of the instruments and methods used for each assessment domain, can be reached from the Scientists page of the ABCD Study website (ABCDDStudy.org).

WHY CONDUCT ABCD NOW?

Brain imaging research reveals that developing human brain systems undergo continuous biological and functional change, at multiple scales, well into adulthood. This long arc of development reflects a unique genome apparently selected to equip us with the capacity to develop a complex model of the world and revise it continuously through intelligent adaptation to the changing environment. It follows that variability in human phenotypes will emerge during development in part because of variation in individual genomes, but also, disproportionately, due to variation in physical and social environments and gene-environment interactions. Previous studies of the course of mental and substance use disorders, and also of academic and workforce disengagement, for example, have highlighted the pivotal role of adolescence in the trajectories toward these functional

outcomes. In studies of this important stage of development, multiple factors have been associated with adverse outcomes in youth, including genetic variation, attributes of the environment, individual experiences, and behavioral traits of the youth themselves. However, when these outcomes emerge gradually through dynamic interaction between gene and environment, retrospective reconstruction of the causal events is extremely challenging and can be misleading.

Prospective, longitudinal studies of individuals developing in different environments have the potential to reveal the dynamics that lead to diverging trajectories; but only recently has it been possible to access noninvasively some of the factors known to play important roles in the outcomes, such as genomic and epigenetic variation, biological development of the brain, and individual experiences and exposures. Now, however, with new noninvasive technologies in hand, and considering the gravity of the educational, health, and mental health problems we face as a society, human developmental scientists are obliged to create the data resources from which evidence-based models of emerging behavioral phenotypes can be constructed. Effective interventions to prevent or mitigate negative outcomes depend critically on such large-scale data and new models.

WHY THE LARGE SIZE AND SCOPE OF THE STUDY?

Although it is not yet possible to predict risk for adverse behavioral and mental health outcomes in individuals accurately, the existing evidence implicates a number of plausible modifiers of risk, and leaves little doubt that environmental factors contributing to the disparities will be many and varied. Similarly, although there is strong evidence that genetic factors play a role, it is likely that the outcomes will be influenced by multiple genetic variants, most of which are likely to be of individually modest effect. In other words the genetic archi-

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texture of a risk phenotype is likely to be very complex. Finally, it is increasingly evident that the impact of environmental and experiential factors on specific developmental outcomes will differ as a function of the genetic variables, and may also differ as a function of culture and family structure.

With this study, and others like it, we enter a new era in human behavioral neuroscience, which has been labeled population neuroscience. Since some outcomes of interest are relatively uncommon in the general population, it is necessary to observe a large number of developing youth in order to identify those factors and interactions that best distinguish these outcomes. For these reasons, large-scale, high-dimensional, longitudinal data resources are urgently needed by the scientific community, and these cannot be acquired without broad collaboration and careful harmonization of key data elements. The ABCD Study represents a major commitment by a consortium of researchers to create such a broad collaboration, focusing on the behaviorally critical, and biologically complex, period of development surrounding adolescence.

WHAT ARE THE OBJECTIVES OF THE STUDY?

In many ways, the primary goal of the ABCD Study is to produce an informative, high-dimensional open data resource, populated by assessments with strong validity and good quality that the broadest scientific community can use. However, the design and selection of the protocols has been guided by several key objectives, listed below.

- To develop national standards for normal brain development in youth, by defining the range and pattern of variability in trajectories of brain development observed in children growing up in the United States.
- To define the factors related to and predictive of variability in behavioral trajectories (e.g., of cognitive and emotional development, academic progress, etc.).
- To examine the roles of genetic versus environmental factors on development, as well as their interactions (e.g., by analysis of data from 800 twin pairs embedded within the cohort, and through genomic analyses).
- To estimate the effects of health, physical and creative activities, and sleep, as well as sports injuries and other injuries on brain development and other outcomes.
- To determine how exposure to various levels and patterns of alcohol, nicotine, cannabis,

caffeine, and other substances affect developmental outcomes, and how pre-exposure developmental differences relate to use patterns.

- To further elucidate the onset and progression of mental disorders and the factors that influence their course or severity; and to examine the relationship between mental disorders and substance use.

ABCD IS AN OPEN SCIENCE STUDY

The ABCD Study shares with the research community, as soon as is practicable, the entire evolving data resource, as a means of accelerating progress in the field. Unprocessed brain imaging data are shared almost continuously through the National Institute of Mental Health (NIMH) Data Archive, as part of the “fast-track” sharing arm of the study. In addition, updated, cumulative sets of curated data, along with workflows used to produce the derived data, are shared in annual versioned releases. ABCD is therefore a significant contributor to the data resources that support the new era of “big data” in biomedical research, and it complements most other studies by increasing the depth of phenotyping and adding important prospective developmental data.

To ensure that the accumulated data are of acceptable quality, the ABCD consortium must establish robust data review procedures and closely monitor the quality of all types of data as well as ensure that the protocols provide both stable construct validity over time and necessary modifications as the cohort matures. Furthermore, the consortium attempts to adapt to emerging improvements in behavioral phenotyping methods that could enhance the study, and identify other relevant data streams, for example, of environmental factors, that can be integrated temporally and geographically with ongoing assessments of the participants. Thus, new data types and new computational workflows are expected to appear in future data releases.

The ABCD Study, more than most similar studies, will push the envelope with an aggressive timeline of data sharing and reduced barriers to access designed primarily to protect the privacy of participants and maintain records of the use of the data. Moreover, the sharing of associated workflows and specific algorithms will provide additional value to the larger scientific community beyond that of the data themselves. This new model will inevitably create challenges for conventional practices of scientists, reviewers, and editors, as multiple attempts to answer similar scientific questions with the same

data will be under way almost simultaneously by independent investigators and groups. However, the data use agreement is designed to maximize transparency in the science, by requiring those who use the data resource to reference a versioned release of the data so that other investigators can repeat, expand, and challenge the results—particularly important in this era of renewed focus on scientific rigor and reproducibility. New standards for responsible use of large shared databases are emerging and are likely to guide editorial practices in the future, but the benefits of such databases for increasing transparency, enabling rapid replication, and generally accelerating scientific progress should outweigh the challenges.

Finally, the ABCD Study may set new records for the number and disciplinary reach of scientists engaged by a single study. Over 200 investigators are actively engaged to date, and as the study evolves and the data emerge, a large number of additional scientists are expected to participate in the evolving design, data collection, analysis and interpretation, and many novel uses of the data. Furthermore, the availability of the data may draw scientists from wide-ranging disciplinary backgrounds to the cause of understanding development of the human brain and finding innovative approaches for preventing adverse health and mental health outcomes and thus improving life trajectories.