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Introduction

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A B S T R A C T

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. 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. Within this Special Issue, readers will find much information about the rationale and objectives of the study, the broad ranging assessment protocols and new as well as traditional methodologies applied at baseline, the recruitment and retention strategies, and the anticipated final composition of the cohort. Information is also provided about how the study is coordinated and conducted, how decisions are made, how data quality is monitored, and how ethical standards are protected. In this introduction we will focus instead on the position of the ABCD Study in the changing landscape of biomedical research.

1. Rationale for the study

Few DCN readers will need reminding that the living human brain ranks among the most complex entities under scrutiny by the scientific community today; and most will be keenly aware that a focus on its development adds an additional layer of complexity due to continuous change, at multiple scales, in its biology and functional organization. In recent decades, human brain imaging research has revealed a surprisingly long period of continuing biological development and concurrent functional re-organization of neural circuits, extending well into the third decade of life. This long developmental arc in the life of a human being reflects a unique genome apparently selected to equip the species with a brain best distinguished by its capacity to model and adapt intelligently to its environment, in order to ensure its own survival and that of its affiliates. It is in the nature of such a species that variability in behavioral outcomes will occur not just because of variation in individual genomes but, disproportionately, due to variation in physical and social environments and gene-environment interactions.

1.1. Need for the study

Numerous studies of origins of mental and substance use disorders, but also of academic and workforce disengagement, have highlighted the pivotal role of adolescence in the trajectories toward these outcomes; and as the field has focused more sharply on this important stage of development, multiple factors have been associated with different outcomes in youth, including genetic variation, attributes of the environment, individual experiences, and behavioral traits of the youth themselves. But a major goal of biomedical research is to identify causal factors that mediate adverse health outcomes, so that the causal chains can be identified and broken. Unfortunately, when single or multiple outcomes emerge gradually through dynamic interaction between gene and environment, retrospective reconstruction of the causal events may be impossible. The developmental research community has long appreciated the potential for prospective group studies of individuals developing in different environments to reveal the dynamics that lead to diverging trajectories; but only recently has it been possible to access noninvasively some of the personal factors known to play important roles in the outcomes, such as genomic and epigenetic variation, biological development of the brain, and individual experiences and environmental exposures. Further, simultaneous evaluation of multiple social, cultural and policy systems presumed instrumental in mediating or moderating risks can be incorporated into causal modeling of developing phenotypes. For these reasons and others, previous studies of adolescent brain development and associated health and mental health outcomes, have lacked the size, scope, and methodological standardization to provide definitive, replicable answers to questions about causal, mediating, and moderating effects of the multiple factors likely to influence these phenotypes, for good or for ill. Now, however, with new noninvasive technologies in hand, and considering the gravity of the problems and questions posed in ABCD, human developmental scientists have the opportunity to create the data resources from which evidence-based models of the causal chains leading to healthy as well as adverse outcomes can be constructed. Emergent models from such

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comprehensive and detailed data developed in an open science framework can produce novel interventions to enhance health and prevent or mitigate adverse developmental outcomes.

1.2. Scope of the study

Although estimating risk for adverse behavioral and mental health outcomes in individuals based on previous research enjoys only limited success, the existing evidence implicates many plausible causes, and leaves little doubt that the 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 many forms of genetic variation, most of which are likely to be of individually modest effect. In other words the genetic architecture of a risk phenotype is likely to be very complex. Finally, it is increasingly evident that the impact of environmental and experiential factors on various developmental outcomes will differ as a function of the genetic variables, and also differ as a function of culture and family structure. For this reason, 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. As a large scale multi-disciplinary project, ABCD also reflects the development of team science critical to truly understanding human adolescence.

2. Key objectives of the study

The primary objective of the ABCD study is to produce for the scientific community an informative, high-dimensional data resource, populated by assessments with strong validity and good quality. 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 U.S.
- To define the factors predictive of variability in individual developmental trajectories (e.g., of cognitive and emotional development, academic progress, etc.).
- To examine the roles of genetic vs. environmental factors on development, as well as 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, pubertal changes, physical activity, sleep, as well as sports and other injuries on brain development and other outcomes.
- To further elucidate the onset and progression of mental disorders, factors that influence their course or severity; and the relationship between mental disorders and substance use.
- To determine how exposure to various levels and patterns of alcohol, nicotine, cannabis, caffeine, and other substances affect developmental outcomes, and how earlier developmental differences relate to use patterns.

3. An open science paradigm

By embracing an open science model, the ABCD Study is designed to share with the entire research community, as soon as is practicable, the entire expanding data resource, as a means of accelerating progress in the field. Brain imaging data will be shared almost continuously, and the entire, updated, cumulative set of curated data, along with workflows used to produce the derived data, will be shared in annual versioned releases, through the NIMH Data Archive. In this way, ABCD follows the precedents set in previous studies such as the Alzheimer's Disease Neuroimaging Initiative (ADNI), the Human Connectome Project (HCP), and the Pediatric, Imaging, Neurocognition, and Genetics (PING) Study. In all of these studies the data are shared with the larger community soon after they are collected, and for the longitudinal studies, while data collection is still ongoing. Of course, the NIH "All of Us" study will aggregate health records from an even larger cohort of patients following a similar open science model. ABCD is a significant contributor to the data resources that invigorate this new era of "big data" research, and it complements most earlier studies by increasing the depth of phenotyping and adding important prospective developmental data.

In this context, the priority assigned in the research to selection of measurement domains and metrics, and to data quality, is even higher than usual, because these factors will be rate limiting in future attempts to use the resource. With this in mind, the ABCD consortium sites were selected to collectively contain diversified expertise in both content and methods (e.g., neuroimaging, neurocognition, adolescent development, family studies, substance use, mental health, longitudinal methodology, analytics) and established robust data review procedures and close quality monitors of all types of data. The protocols provide both stable construct validity over time, necessary modifications as the cohort matures, and incorporate new, developmentally tailored methodologies. Furthermore, it will be important for the consortium to adapt to emerging improvements in behavioral phenotyping methods that could enhance the study, and identify other relevant data streams, e.g., of environmental factors, that can be integrated temporally and geographically with ongoing assessments of the participants. This will ultimately involve many more members of the scientific community than are presently involved. Furthermore, already there are hopes for some degree of harmonization with other large-scale longitudinal studies planned or underway in the US and abroad to leverage even more powerful analyses, faster replication, and hypothesis-driven exploration.

With this study, and others like it, we enter a new era in human behavioral neuroscience, which has been labeled population neuroscience. The ABCD Study more than most other examples, will push the envelope with its data sharing practices. The timeline of data sharing will be very aggressive and barriers to access very low both inside and outside the consortium. 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 will inevitably create new challenges for scientists, reviewers, and editors, as multiple attempts to answer similar scientific questions with the same data will be underway almost simultaneously by researchers within the consortium as well as independent investigators and groups in the broader scientific community. ABCD policies articulated in the data use agreement are explicitly designed to maximize transparency in the science, creating an opportunity for direct replication and model testing. All publications making use of the data resource must reference a versioned release of the data so that other investigators can repeat, expand, and challenge the results. 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 would seem to vastly outweigh the challenges they present. Although some have voiced concerns that large-scale studies will place too many resources in the hands of too few, in reality it may be that the opposite is true, given the large number of scientists who will be engaged in the associated (continuously evolving) design, methods development, data collection, analysis and interpretation, and novel uses of the data. Furthermore, when, to some extent, resources allocated to data collection are decoupled from those supporting

computational modeling of the results, scientists from more wide-ranging disciplinary backgrounds may be drawn into the cause of understanding development of the human brain and mitigating suffering associated with adverse health, mental health and behavioral outcomes. Finally, the unprecedented breadth of the developmentally sensitive data may generate novel frameworks through which more effective prevention and early intervention can emerge.

Conflict of Interest

None.

Update

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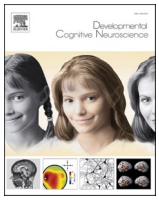

Erratum

Erratum

The purpose of this publisher correction is to inform readers that the final version of the articles linked with this correction were replaced with a corrected version in April 2019. The corrected version contains a Declaration of Interest statement which the publisher inadvertently omitted from the original version.

The Publisher apologizes for any inconvenience this may cause."

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