



Differences in educational opportunity predict white matter development

Ethan Roy^{a,*}, Amandine Van Rinsveld^a, Pierre Nedelec^b, Adam Richie-Halford^{a,c},
Andreas M. Rauschecker^b, Leo P. Sugrue^b, Ariel Rokem^d, Bruce D. McCandliss^a, Jason
D. Yeatman^{a,c}

^a Graduate School of Education, Stanford University, Stanford, CA, USA

^b Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, USA

^c Division of Developmental-Behavioral Pediatrics, Stanford University, Stanford, CA, USA

^d Department of Psychology and eScience Institute, University of Washington, Seattle, WA, USA

ARTICLE INFO

Keywords:

White Matter
Education
Development
Socioeconomic Status

ABSTRACT

Coarse measures of socioeconomic status, such as parental income or parental education, have been linked to differences in white matter development. However, these measures do not provide insight into specific aspects of an individual's environment and how they relate to brain development. On the other hand, educational intervention studies have shown that changes in an individual's educational context can drive measurable changes in their white matter. These studies, however, rarely consider socioeconomic factors in their results. In the present study, we examined the unique relationship between educational opportunity and white matter development, when controlling other known socioeconomic factors. To explore this question, we leveraged the rich demographic and neuroimaging data available in the ABCD study, as well the unique data-crosswalk between ABCD and the Stanford Education Data Archive (SEDA). We find that educational opportunity is related to accelerated white matter development, even when accounting for other socioeconomic factors, and that this relationship is most pronounced in white matter tracts associated with academic skills. These results suggest that the school a child attends has a measurable relationship with brain development for years to come.

1. Introduction

Students who attend high-quality schools demonstrate higher academic achievement both in terms of reading and math scores (Baker et al., 2001; Chetty et al., 2015; Heck, 2000; Rivkin and Schiman, 2015), as well as long-term outcomes such as college admissions and social mobility (Chetty et al., 2011; Duncan et al., 2007; Murnane et al., 1995). A common suggestion in the scientific literature (Ng, 2018; Yeager and Dweck, 2012), and popular press (McCandliss and Toomarian, 2020; Boaler, 2013), is that the relationship between educational opportunity and academic outcomes reflects the influence that high-quality educational experiences might exert on brain development. Despite the well-established links between school quality and academic achievement, the specific relationship between educational opportunity and brain development remains unexplored.

Past studies, however, have demonstrated a relationship between brain development and various non-academic socioeconomic and environmental factors (Brito and Noble, 2014). For example, diffusion

MRI has revealed that higher family income predicts differences in white matter properties in adulthood (Dufford et al., 2020) and that parental income moderates the relationship between cognitive flexibility and tissue properties across a range of white matter tracts (Ursache et al., 2016). Furthermore, the influence of genetic heritability on white matter structure has been shown to be higher for individuals from high income backgrounds (Chiang et al., 2011). Together these findings suggest that the financial resources available to an individual during childhood influence and interact with brain development in complex ways that are not fully understood.

Additionally, lower levels of parental education have been linked to differences in white matter structure across multiple white matter tracts, including those purportedly underlying academic skills, such as the left arcuate fasciculus, left superior longitudinal fasciculus (SLF) and left inferior longitudinal fasciculus (ILF) (Noble et al., 2013; Ozernov-Palchik et al., 2019; Vanderauwera et al., 2019). These studies offer a variety of different (and sometimes conflicting) accounts of the relationship between white matter, parental education, and cognitive

* Corresponding author.

E-mail address: ethanroy395@gmail.com (E. Roy).

skills, with some results finding a brain-behavior relationship in individuals with lower levels of parental education (Ozernov-Palchik et al., 2019) and others suggesting that the relationship between parental education and cognitive behaviors is completely mediated by white matter properties (Noble et al., 2013; Vanderauwera et al., 2019). What none of these studies address is why parental education affects white matter structure. In other words, are differences in parental education a proxy for a variety of environmental factors (broadly encompassed by the construct of SES) that influence white matter development? Or are there specific aspects of a child's environment that are responsible for the link between measures of SES and brain structure?

Typical measures of socioeconomic status (SES) do not elucidate the specific aspects of an individual's environment that drive differences in white matter development. The hormone cortisol has been shown to mediate the relationship between stressful life experiences and white matter properties (Simon et al., 2021), suggesting that environmental stress, which has been linked to aspects of SES (Luby et al., 2013), plays a role in white matter development. Furthermore, other specific environmental factors, such as home language (Turesky et al., 2022), screen use (Hutton et al., 2020), early childhood nutrition (Isaacs et al., 2010; Ottolini et al., 2020), and adverse childhood events (Hanson et al., 2013; Choi et al., 2009) have also been linked to differences in white matter properties. Together, these findings suggest that typical measures of SES, such as parental income or education, may act as proxies for a confluence of other environmental factors that are more directly related to white matter development.

However, across these studies examining the link between SES and white matter development, an individual's academic environment has gone unexplored. Although traditional measures of SES are highly correlated with school achievement (Reardon et al., 2021), it remains unclear the extent to which the specific school, and more generally the educational environment, that a child ends up in influences white matter development above and beyond the myriad of correlated factors that are wrapped up in indices of SES.

It bears mentioning that educational intervention studies have demonstrated that educational experiences can drive changes in brain structure and function over remarkably short timescales. These studies have shown that a short-term, intensive reading intervention lead to changes across a range of white matter tracts, including left arcuate and left ILF, and that these changes correspond to changes in reading skill (Huber et al., 2018, 2021; Meisler et al., 2023). In the domain of mathematics, intensive learning experiences have been shown to "normalize" functional activity in students with mathematical learning difficulties (Iuculano et al., 2015) and participation in specific math curricula drives changes in neurotransmitter concentration in the middle frontal gyrus and predicts longitudinal changes in mathematical reasoning (Zacharopoulos et al., 2021).

Although these findings serve as a proof-of-concept that educational experience can shape brain development in a manner that facilitates the development of academic skills, the samples used in these studies included a small number of participants in an intervention setting and were not representative of the population at large (Henrich et al., 2010). Moreover, the intensive and highly controlled interventions employed by these studies are far from representative of the typical differences among American schools. Furthermore, these studies did not include measures of SES in their analyses; It is possible or even likely that interventions have variable effects on brain development and learning depending on a child's sociodemographic background (Romeo et al., 2018; Hermida et al., 2015).

Although careful recruitment strategies can lead to socio-demographically diverse study populations, it is nearly impossible to capture the vast range of educational experiences of students across the United States in a typical brain imaging study. Recent efforts to collect and share large-scale neuroimaging datasets (Alexander et al., 2017; Bycroft et al., 2018; Casey et al., 2018; Harms et al., 2018; Jernigan

et al., 2016) have now opened the door for researchers to explore the interplay between brain development, cognitive skills, and environmental and demographic factors. The ongoing ABCD study (Casey et al., 2018) is particularly well positioned to examine the relationship between school quality and brain development in a large and representative sample. This study is following a cohort of approximately 10,000 children from across the United States longitudinally to understand brain development throughout adolescence. In addition to neuroimaging data, the ABCD study collects rich demographic and behavioral data on each participant, including traditional measures of SES, household and neighborhood cohesion, and educational opportunity, as measured by the Stanford Education Data Archive (SEDA; see Methods for overview) (Reardon et al., 2021). This rich set of neuroimaging and demographic data presents the first opportunity to understand the relationship between brain development and the diversity of educational environments experienced by students across the United States.

In the current study, we test the hypothesis that differences in white matter development are related to the quality of an individual's educational environment, while controlling for the multitude of factors indexed by traditional measures of SES. We first leverage the individual white matter tract data generated through automated-fiber quantification (AFQ) (Kruper et al., 2021; Yeatman et al., 2012a) to test the hypothesis that educational opportunity relates to white matter development in specific tracts underlying academic skill, such as reading and math. We find that FA in the bilateral arcuate fasciculus, left posterior arcuate, and the corpus callosum are related to educational opportunity, even when controlling for other measures of socioeconomic status. We then train a brain-age model to test the hypothesis that educational opportunity relates to accelerated white matter development. This model suggests that an individual's educational opportunity may influence white matter development throughout the brain, though this relationship may be more pronounced in white matter tracts associated with academic skills.

2. Methods and materials

2.1. Participants

The participants in the present study come from the ABCD study, a ten-year longitudinal study that includes both neuroimaging and behavioral data collected from children aged 9–10 from 21 study sites across the United States (Casey et al., 2018). The data used in the present analysis come from the baseline and 2-year follow up visits of the ABCD study and can be found in the ABCD curated annual data release 4.0 (<https://nda.nih.gov/abcd/>). The baseline observation included 6410 individuals who had the necessary neuroimaging and demographic data and the longitudinal data included 4770 individuals with the necessary data at both time points.

2.2. Covariates of Interest

In both the cross-sectional and longitudinal models, we included a range of demographic and developmental factors as covariates including participant age, log-transformed income-to-needs ratio, parental education, family cohesion, neighborhood cohesion, biological sex, and pubertal status. All of these measures are readily available or calculated using the data present in the ABCD data release 4.0.

2.2.1. Income-to-needs ratio

Log-transformed income-to-needs ratio was calculated using the approach outlined in Weissman et al. (2023), which combines family income and household size data. Briefly, in the ABCD study, parents report family income on a scale of 1–10, where each interval represents an income range. The midpoint of the reported range was then calculated for each participant. This dollar amount was then divided by the poverty threshold for a household of a given size. The thresholds used in

this calculation come from the 2017 report by the U.S Census Bureau (Bureau, 2024). This value was then log-transformed.

2.2.2. Parental education

The ABCD study records parental reports of the highest level of education they have completed. This is measured on an ordinal scale ranging from “Never attended school” to “Doctoral Degree”. In the present analysis, this is operationalized as the average level of parental education of both parents/guardians.

2.2.3. Non-academic environment

Family home environment was measured using the average of the nine questions present on Family Environment Scale-Family Conflict (Moos and Moos, 1994). A higher score on this measure indicates higher levels of conflict within an individual’s household and family environment. Neighborhood cohesion was assessed by taking the average of the ten items present on the ABCD Parent PhenX Community Cohesion measure (Hamilton et al., 2011). For this measure, a higher score indicates that the participant perceives their neighborhood and surrounding community as safer and more cohesive.

2.2.4. Pubertal status

Pubertal status was assessed using the PDS (Petersen et al., 1988), a measure designed to mimic the Tanner scale to assess the development of secondary sex characteristics during the onset of puberty. In line with past research using PDS in the ABCD sample (Holm et al., 2023; Beck et al., 2023), pubertal status was calculated by taking the average of the seven PDS items present on the parental PDS survey collected at each time point.

2.2.5. Educational opportunity

Educational opportunity was operationalized using linked data from the Stanford Education Data Archive (SEDA) (Reardon et al., 2021). This dataset leverages standardized test scores from 3rd to 8th grade students in nearly every single school district in the United States to generate two distinct measures for a given school district: intercept and slope. The details on how these two measures are calculated are outlined in detail in Reardon et al. (2021).

Some scholars interpret these scores as a metric of general school or teacher performance and emphasize that external influences can impact test performance, which makes these scores inappropriate for evaluating school or teacher quality (Baker et al., 2010; Darling-Hammond et al., 2012). However, others consider these scores to be a metric of the educational opportunities afforded to the students in a given school district. According to this interpretation, the educational opportunities provided by a given school or district not only reflect properties of those schools but also external factors, including parental, community, and early childhood experiences that support learning the reading and mathematics concepts assessed on standardized tests, as well as toxin exposure (Jacqz, 2022) or community conflict that may negatively impact test scores (Drescher et al., 2022; Reardon, 2019, 2013).

More specifically, SEDA intercept refers to the average standardized test score for third graders from a given school district relative to the national average and can be thought of as an index of the household, community level, pre-school, and early elementary school educational opportunities provided by a school or district (Drescher et al., 2022; Reardon, 2019). On the other hand, SEDA slope is a measure of year-to-year growth in standardized test scores for students from a given school or district relative to the national average. This can be thought of as the educational opportunity provided to students by a specific school or district between 3rd and 8th grade.

Both SEDA intercept and slope are in z-score units and relative to national norms. Thus, a school with a SEDA intercept and slope of zero performs at the national average in terms of third grade test scores and in terms of how much students grow from year to year. A school with a SEDA intercept of -1 and slope of zero performs 1 standard deviation

below the national average, and students progress at the average rate, meaning the discrepancy in achievement is maintained throughout schooling. Because the ABCD study began when participants are in either 4th or 5th grade, SEDA intercept is the most relevant measure of the educational opportunity that a participant has experienced up until the first ABCD measurement.

2.3. Diffusion MRI acquisition and processing

The neuroimaging data used in this analysis come from the baseline and Year 2 follow-up sessions collected across the 21 ABCD study sites. An overview of the data acquisition and preprocessing protocols can be found in Casey et al. (2018) and Hagler et al. (2019). Briefly, multi-shell, high angular-resolution imaging scans were collected on each participant during each scan session. These data underwent manual quality control and were then minimally preprocessed using a pipeline that included eddy-current correction, motion correction, B_0 distortion correction, and gradient warp correction (Hagler et al., 2019).

These preprocessed diffusion images were then processed with pyAFQ (Krupar et al., 2021). Briefly, fiber orientation distributions were estimated in each voxel using constrained spherical deconvolution (Tournier et al., 2007) implemented in DIPY (Garyfallidis et al., 2014) before probabilistic tractography was used to generate streamlines throughout the white matter. As originally described in Yeatman et al. (2012a), 30 major white matter tracts were identified from these streamlines. Each tract was then sampled to 100 nodes. At each node, fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD) were calculated using the diffusion kurtosis model (DKI) (Jensen et al., 2005; Henriques et al., 2021). There is substantial overlap between the anterior forceps and anterior frontal callosal tracts, as well as between the posterior forceps and occipital callosal tracts identified by pyAFQ. Because of this, we excluded the anterior and posterior forceps from our analysis, leaving us with 28 total tracts (see Supplemental Fig. 1 for overview of the tracts identified by pyAFQ used in this analysis).

To account for potential non-biological variance in the diffusion MRI signal introduced by scanner differences across the 21 ABCD sites, ComBat harmonization (Fortin et al., 2017, 2018; Johnson et al., 2007) was performed on the diffusion metrics calculated by pyAFQ. Harmonization was performed using the neurocombat_sklarn Python library (Fortin et al., 2018; Johnson et al., 2007).

2.4. Univariate mixed-effect modeling

We constructed a series of linear mixed-effects models to explore univariate relationships between FA in the left arcuate and demographic, developmental, and socioeconomic factors while controlling for various random effects in white matter properties. These models included family structure nested within scanner site as random effects (Saragosa-Harris et al., 2022) and either log-transformed income-to-needs ratio, parental education, family cohesion, neighborhood cohesion, sex, SEDA intercept or pubertal status as a single fixed-effect predictor. We focused these analyses on the left arcuate, as past studies have shown this tract to relate to both reading skill and measures of SES (Vanderauwera et al., 2019; Huber et al., 2018; Yeatman et al., 2012b). As a control measure, we also fit the same sequence of models predicting FA in the right arcuate to assess whether these univariate relationships occur across the white matter or are specific to the left arcuate.

2.5. Multivariate mixed-effect modeling

Because measures of socioeconomic status are highly correlated with each other, any observed relationship between white matter properties and any one index of SES may actually be driven by a separate, yet correlated measure. To test the hypothesis that there is a specific

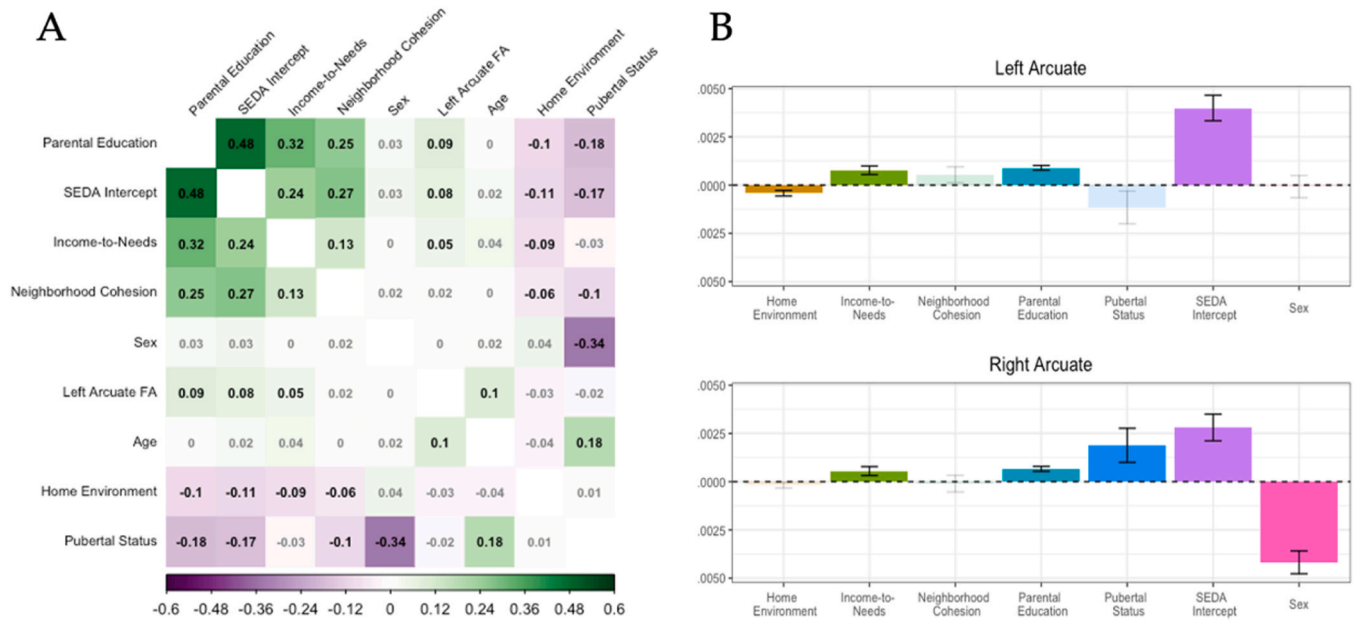


Fig. 1. A. Correlation matrix illustrating the univariate relationships between mean FA in the left arcuate, SEDA intercept, and other demographic and socioeconomic factors. Coefficients in bold represent correlations where FDR-corrected $p < 0.05$. B. Beta-weights for linear mixed-effects models predicting mean FA in the left and right arcuate from a single predictor, specified on the x-axis. Each model included a random effects structure of family structure nested within scanner site. The colors of each bar denote each predictor variable. Error bars represent the standard error of each beta-coefficient. Bars that are bolded illustrate the beta-weights with FDR-corrected $p < 0.05$.

relationship between educational opportunity and white matter properties, while accounting for other developmental and socioeconomic effects, we modeled the relationship between SEDA intercept and FA across all the white matter tracts identified by pyAFQ.

Based on previous research in smaller samples linking specific white matter tracts to academic skills, we hypothesized that educational opportunity would specifically relate to FA in the left arcuate fasciculus (ARC), left posterior arcuate fasciculus (pARC), bilateral inferior longitudinal fasciculus (ILF), bilateral superior longitudinal fasciculus (SLF), and uncinate fasciculus (UNC), as these tracts have all been previously implicated in academic skills, such as reading and arithmetic (Tsang et al., 2009; Wandell and Yeatman, 2013; Polspoel et al., 2019; Navas-Sánchez et al., 2014). To test this hypothesis, within each tract, we fit a linear mixed-effects model predicting mean harmonized fractional anisotropy (averaged over the length of tract) at the first ABCD observation from SEDA intercept while also controlling for age, log-transformed income-to-needs ratio, parental education, family cohesion, neighborhood cohesion, sex, and pubertal status. Family structures nested within scanner site were included as random effects in each model (Saragosa-Harris et al., 2022).

2.6. Growth modeling

In addition to our cross-sectional models, we also investigated the longitudinal development of the left and right arcuate. Because past longitudinal studies have linked the development of left arcuate and gains in reading skill (Huber et al., 2018; Yeatman et al., 2012b; Van Der Auwera et al., 2021), we again chose to center this analysis around this tract and its right hemisphere counterpart. To investigate the developmental dynamics of these two white matter tracts, we fit a series of linear growth models (Grimm et al., 2016) predicting mean FA over time (operationalized as years since initial MRI scan). In these models, we again included individuals nested within family structures nested within scanner sites as random effects. To control for known developmental, demographic, and socioeconomic effects, we also included initial age, pubertal status, sex, log-transformed income-to-needs ratio, parental education, family cohesion, neighborhood cohesion, and sex as

fixed-effects. Our main predictors of interest in these models were time, SEDA intercept, tract (right or left arcuate), and their interactions.

To investigate intraindividual change in the white matter properties of the left and right arcuate and the relationship of this change with educational opportunity, we constructed a series of growth models (Grimm et al., 2016) specified as follows:

$$FA_{ijk} = \beta_{0ijk} + \beta_{1ijk}(Time\ in\ Study_{ijk}) + e_{ijk}$$

where each participant's FA at a given scan session, t , is modeled as a function of a participant specific intercept (β_{0ijk}), a participant specific slope (β_{1ijk}), and a residual error term (e_{ijk}). To examine interindividual differences, the participant specific coefficients were modeled as:

$$\beta_{0ijk} = \gamma_{00ij} + \gamma_{01}(SEDAIntercept_{ijk}) + u_{0ijk}$$

$$\beta_{1ijk} = \gamma_{10ij} + \gamma_{11}(SEDAIntercept_{ijk}) + u_{1ijk}$$

where the γ coefficients on SEDA Intercept refer to, on average, how baseline FA and FA development differ with SEDA intercept and u_{0ijk} and u_{1ijk} refer to residual error at the individual level. These models also included initial age, log-transformed income-to-needs ratio, parental education, family home environment, neighborhood cohesion, and pubertal status as covariates.

Our final growth model, which examined FA development in the left and right arcuate simultaneously, included two additional parameters, $\gamma_{02}(Hemisphere_{ijk})$ and $\gamma_{12}(Hemisphere_{ijk})$, which allowed us to directly test the hypothesis that educational opportunity is related to differences in FA development between the left and right arcuate. In this model γ_{00ij} and γ_{10ij} are modeled at the family structure level as:

$$\gamma_{00ij} = \alpha_{00i} + v_{0ij}$$

$$\gamma_{10ij} = \alpha_{10i} + v_{1ij}$$

where v_{0ij} and v_{1ij} refer to residual error at the family structure level and α_{00i} and α_{01i} are modeled at the level of scanner site as:

$$\alpha_{00i} = a_0 + w_{0i}$$

$$\alpha_{10i} = a_1 + w_{1i}$$

where w_{0i} and w_{1i} refer to residual error at each scanner site and a_0 and a_1 are the mean FA and rate of FA development, respectively, at each scanner site.

These models were fit in R version 4.2.1 (R Core Team, 2022) using the *lme4* package (version 1.1.30) (Bates et al., 2015).

2.7. Brain-age gap analysis

Although the bundle-wise analyses allowed us to explore multivariate relationships between socioeconomic factors and the development of individual white matter tracts, linear-mixed effects models are not well suited to model global white matter development. To better understand the link between educational opportunity and global white matter development, we trained a convolutional neural network (ResNet (He et al., 2015)) implemented in the Python library AFQ-Insight (Rokem et al., 2023; Richie-Halford et al., 2021) to predict age based on the harmonized pyAFQ outputs from the baseline and Year 2 follow-up scans. We chose this model over other approaches because deep learning models have been shown to generate state-of-the-art age predictions from tractometry data (Rokem et al., 2023).

The data used to train and evaluate this model were split into three splits: a training set, a test set, and a validation set. To prevent peeking, longitudinal observations from the same participant were placed in the same split. The validation set contained 20 % of the observations, while the remaining 80 % was distributed across the training and test sets. To prevent overfitting, the model was then trained on varying proportions of the training and test sets, allowing us to determine the point at which

the model performance did not improve with the addition of more training data (Supplemental Fig. 2).

We found that model performance plateaued when the model was trained on 56% of the overall sample. This model attained an R^2 score of 0.22 on the unseen validation set. To prevent data leakage in our brain age models, we then generated two additional train-test splits to ensure that brain age predictions for each individual were generated from a model that was trained on data that did not include that individual. We then trained two additional models on 56% of the overall sample to generate brain age predictions for the individuals used as the training set of the initial brain age model. Across these three models, the average R^2 score was 0.19 on the unseen data with an average MAE of 0.834 years. It should be noted that the variance explained by these models is smaller than other brain age models (Rokem et al., 2023) due to the restricted age range in the ABCD sample. Nevertheless, the residuals from this model, or the difference between the model's predicted age and each participant's observed age, can be thought of as the brain-age gap (BAG), a relative measure of how accelerated or delayed an individual's brain is maturing.

We then calculated the BAG for each individual, using the prediction from the model that was not trained on that individual's data. The residuals of these brain age models were then used as the outcome measure of a linear-mixed effects model to explore the relationship between educational opportunity and brain-age. Our baseline model included age, log-transformed income-to-needs ratio, parental education, family cohesion, neighborhood cohesion, sex, and pubertal status as fixed-effects (and the same random effects structure as previous models), allowing us to control for known demographic, socioeconomic, and developmental factors related to brain development (Simon et al., 2021; Holm et al., 2023). We then added SEDA intercept as an additional

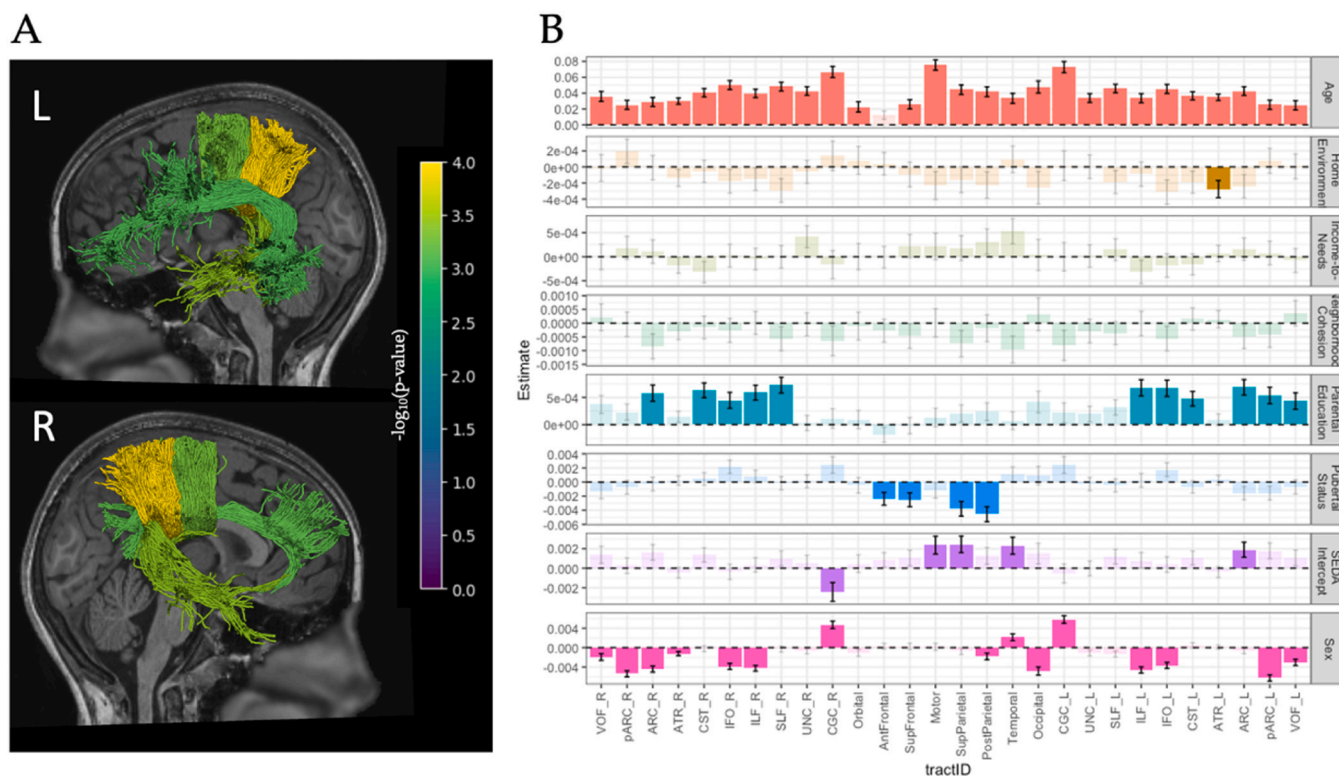


Fig. 2. A. Renderings of the five white matter tracts significantly related to SEDA intercept. These include the left arcuate fasciculus, right cingulate bundle, and the motor, superior parietal, and temporal bundles of the corpus callosum. Shading represents the $-\log_{10}(p\text{-value})$ for the beta-weight on SEDA intercept from the models predicting FA in each tract (1.301 corresponds to a p-value of 0.05). This association was strongest in the left arcuate (yellow in the top panel). B. Beta-coefficients for the fixed effects of the models predicting FA in each major white matter tract. The x-axis represents a specific bundle identified by pyAFQ. Each row and color in the figure refers to the fixed-effect in each model. Error bars represent the standard error of each beta-coefficient. Bars that are bold illustrate the beta-weights with FDR-corrected $p < 0.05$.

predictor to the baseline model in order to test the hypothesis that educational opportunity is related to global white matter development. All linear-mixed effects models were carried out with R version 4.2.1 (R Core Team, 2022) using the *lme4* package (version 1.1.30) (Bates et al., 2015).

Code to replicate the analyses and figures presented in this manuscript can be found at: https://github.com/earoy/white_matter_education

3. Results

3.1. Diffusion properties of the left arcuate are related to socioeconomic factors

We began our analysis by calculating correlations between SEDA intercept and other measures of socioeconomic status thought to influence SEDA scores. As expected, SEDA intercept is highly correlated with traditional measures of socioeconomic status (Fig. 1A), such as log-income-to-needs ratio ($r = 0.238$, $p < 0.001$) and parental education ($r = 0.477$, $p < 0.001$). The relationships between these various indices of SES raise the possibility that measures such as parental education and household income could act as proxies for other factors, like educational opportunity, that might more directly influence brain development.

After observing these correlations between various socioeconomic factors, we then attempted to replicate the results from past studies linking white matter and socioeconomic factors by calculating the correlation between mean FA in the left arcuate and a range of demographic and developmental factors, including age, pubertal status, sex, family cohesion, log-transformed income-to-needs ratio, parental education, neighborhood cohesion, and SEDA intercept. We found small, yet significant correlations (Fig. 1A) between mean FA in the left arcuate and parental education ($r = 0.093$; $p_{\text{corrected}} < 0.001$), income-to-needs ratio ($r = 0.046$; $p_{\text{corrected}} = 0.022$), SEDA intercept ($r = 0.076$; $p_{\text{corrected}} < 0.001$) and age ($r = 0.097$; $p_{\text{corrected}} < 0.001$), but not between sex, family cohesion, neighborhood cohesion, or pubertal status (all $p_{\text{corrected}} > 0.05$).

However, these correlations do not account for individual and site-level random effects that might relate to white matter properties. To account for these random effects, we then fit a series of univariate models using each socioeconomic or developmental factor as a single predictor of FA in the left arcuate. Similar to the correlation analyses, these models revealed significant relationships between mean FA in the left arcuate and parental education, SEDA intercept, and income-to-needs ratio (all $p_{\text{corrected}} < 0.001$; Fig. 1B). Additionally, these models identified a slight yet significant relationship between home environment and mean FA in the left arcuate ($\beta = -0.0004$, $p_{\text{corrected}} = 0.004$).

Interestingly, the models predicting FA in the right arcuate also suggested significant relationships between mean FA and parental education, income-to-needs ratio, and SEDA intercept (all $p_{\text{corrected}} < 0.05$) as well as significant effects of pubertal status ($\beta = 0.002$, $p_{\text{corrected}} = 0.032$) and biological sex ($\beta = -0.004$, $p_{\text{corrected}} < 0.001$).

3.2. The relationship between educational opportunity and tissue properties varies across the white matter

The results from our multivariate models predicting FA across each individual white matter tract are presented in Fig. 2. Examining the beta-coefficients from these models revealed significant relationships between FA and SEDA intercept in the left arcuate, right cingulate cingulum (CGC), and three colossal tracts (all FDR-corrected $p < 0.05$; Fig. 2, second row from bottom).

However, as expected, FA in many tracts was also related to other environmental, developmental, and demographic factors (see Fig. 2B for overview of these relationships). Parental education was linked to FA in the bilateral arcuate, CST, IFOF, ILF, left posterior arcuate, left VOF, and the right SLF, whereas pubertal status was negatively related to FA in a

collection of four colossal bundles. Furthermore, age was positively related to higher FA across the entirety of the white matter and males, on average, demonstrated lower FA compared to females across most white matter tracts, with the exception of the left and right CGC and temporal portion of the corpus callosum.

3.3. Development of the left and right arcuate is moderated by educational opportunity

The two growth models predicting mean FA in the left and right arcuate revealed significant changes in FA in both tracts within each participant across the two observations (both $p < 0.001$; See Supplemental Materials for full model outputs). These models also revealed a significant relationship between SEDA intercept and mean FA across both tracts, suggesting that, on average, individuals with greater educational opportunities have higher FA in both the left and right arcuate. When we added a SEDA intercept by time interaction to both growth models, Wald tests comparing the full and reduced models revealed that the addition of the interaction term significantly improved the fit for model predicting FA in the left arcuate ($\chi^2(1) = 36.632$, $p < 0.001$) but not the right arcuate ($\chi^2(1) = 1.676$, $p = 0.196$).

The combined growth model based on data from both the left and right arcuate fasciculus revealed that, on average, FA was lower in the right arcuate compared to the left ($\gamma_{02} = -0.023$; $p < 0.001$) and that FA increased over time in both tracts ($a_1 = 0.002$; $p < 0.001$). Furthermore, Wald tests comparing growth models with and without a tract by time interaction suggested that the average rate of FA development similar across both tracts ($\chi^2(1) = 0.605$, $p = 0.437$). Interestingly, individuals in environments with higher SEDA intercept scores, on average, had higher FA in both tracts ($\gamma_{01} = 0.002$, $p = 0.01$) and also demonstrated significantly faster rates of FA development across both the right and left arcuate ($\gamma_{11} = 0.0013$; $p < 0.001$). This interaction was slightly, yet significantly, more pronounced in the left arcuate compared to the right ($\gamma_{12} = -0.001$; $p = 0.004$; Fig. 3). For a full summary of the longitudinal growth model, see Supplemental Table 1.

3.4. Educational opportunity is linked with accelerated white matter development

A Wald test comparing the full and reduced mixed-effects models predicting brain-age gap (BAG) revealed that SEDA intercept significantly improved model fit ($\chi^2(1) = 6.651$, $p = 0.009$). The coefficients of the full model that included SEDA intercept revealed a significant negative relationship between BAG and age ($\beta = -0.471$; $p < 0.001$; See Supplemental Table 2 for full model output), suggesting that our model underestimates the brain-age of older participants and over estimates the brain age of younger participants. This is a known phenomenon with brain age models (Butler et al., 2021) and can be interpreted as regression to the mean.

Additionally, the model revealed a significant relationship between BAG and pubertal status ($\beta = 0.042$; $p < 0.001$). Interestingly, this model also revealed a significant relationship between the BAG and SEDA intercept ($\beta = 0.022$; $p = 0.009$; Fig. 3). There were no further significant relationships between BAG and other demographic and environmental predictors (all $p > 0.05$).

4. Discussion

In the present study, we leveraged the unique epidemiological sample from the ABCD study, combined with data from the Stanford Education Data Archive, to explore the relationship between an individual's white matter development and the educational opportunities provided by their early childhood and elementary school environments. The scale of the ABCD study, coupled with the rich demographic measures present in the data, provides the very first opportunity to examine how the diverse educational experiences found across the United States'

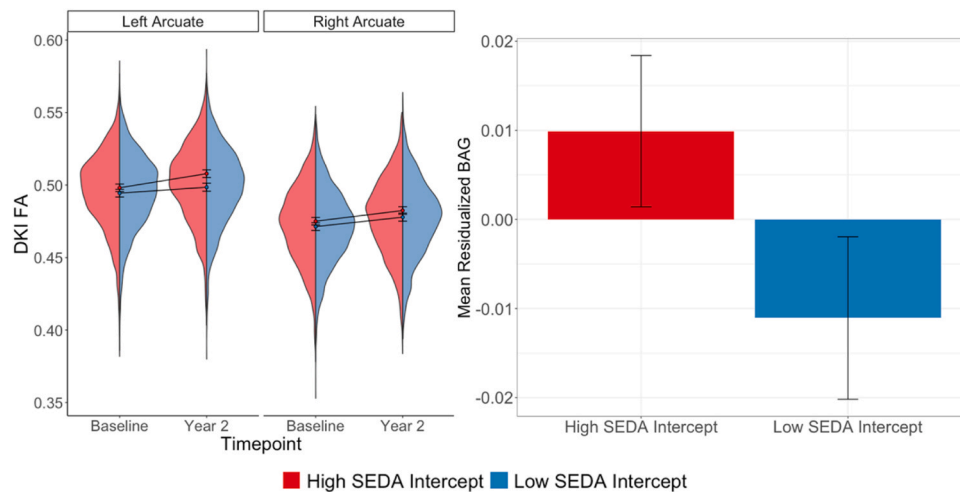


Fig. 3. Left: Growth trajectories for Diffusion Kurtosis (DKI) FA in the left and right arcuate across the first two observations of the ABCD study. The red and blue lines represent the average DKI FA growth trajectories for individuals in high (Intercept = 1) or low SEDA (Intercept = -1) intercept schools, respectively. Gray lines represent the observed changes in FA in the left and right arcuate for each individual present in the dataset. Right: Mean residual values for the model predicting Brain-Age Gap from a reduced model that excludes SEDA intercept as a predictor, but retains all other random and fixed-effects. Each bar represents either the top (red) or bottom (blue) 20% of participants based on their SEDA intercept scores. Error bars represent one standard error from the mean.

educational system relate to brain development, while also accounting for other environmental factors.

These analyses showed that SEDA intercept, a measure of early educational environment, was associated with fractional anisotropy in the left and right arcuate fasciculi, left posterior arcuate, and the corpus callosum, even when accounting for other socioeconomic factors known to relate to white matter, such as parental education or household income. These tract-wise results demonstrate that the school a child attends is related to the development of some white matter tracts above and beyond the myriad of other socioeconomic variables that characterize a child's environment.

However, these models also revealed significant relationships between developmental and socioeconomic factors, such as age, sex, pubertal status, and parental education and FA in a range of white matter tracts. These results are in line with past studies linking socioeconomic (Simon et al., 2021) and developmental (Lebel et al., 2019) factors with white matter development and illustrate that, although educational environment is uniquely linked to FA in some tracts, other environmental and developmental forces are also related to tissue properties across the white matter.

When examining the longitudinal relationship between white matter properties and educational environment over the course of 2 years, the rate of FA development in both the right and left arcuate was related to higher SEDA intercepts. This relationship was slightly, yet significantly, more pronounced in the left arcuate compared to the right arcuate. This finding suggests that educational environment might more strongly influence development of the left arcuate, a white matter tract that purportedly supports reading skill (Yeatman et al., 2011), and is in line with results from intervention studies showing that changes in the properties of the left arcuate correspond to gains in reading (Huber et al., 2018).

Additionally, a global analysis of the white matter using a brain-age modeling approach revealed a relationship between SEDA intercept and levels of white matter maturation, suggesting that an individual's early educational opportunities are related to accelerated patterns of global white matter development, even when accounting for factors such as income-to-need ratio, family cohesion, and neighborhood stability. However, across the cross-sectional, longitudinal, and brain-age models, we also observed significant associations between white matter maturation and both parental education and pubertal status, suggesting that additional developmental and environmental factors relate to white matter development. These results replicate past findings linking

parental education with differences in white matter development (Noble et al., 2013) but also extend the results of Holm et al. (2023), suggesting that puberty is related to accelerated patterns of both white matter development and structural properties of the brain measured through T1-weighted imaging.

To the best of our knowledge, these results are the first to show a specific link between educational environment and white matter development in a sample of this magnitude. Although these data are purely observational and do not allow for causal reasoning, this type of investigation into the specific links between socioeconomic factors and white matter development is only possible in large-scale datasets, such as the ABCD study. As seen in the current results, measures of socioeconomic status are highly correlated with one another, meaning that some indices of SES, such as household income, may confound other measures of SES in studies of brain development. Large samples are necessary to tease apart these relationships and assess how these potentially confounding measures relate to brain development. Thus, the fact that SEDA intercept predicts tissue properties of specific white matter tracts, as well as global brain-age measures, even when controlling for other developmental and environmental factors, implicates a specific relationship between an individual's educational environment and their white matter development.

The interpretation of SEDA intercept as a measure of the educational opportunities available to a learner in early childhood and elementary school (Drescher et al., 2022; Reardon, 2019) suggests that early educational experiences are related to the development of white matter tracts throughout elementary school and into middle school. This parallels behavioral and educational policy research that has shown that gaps in reading and mathematics at the onset of elementary school, on average, persist throughout the course of K-12 education (Reardon, 2013; García and Weiss, 2015; Duff et al., 2022) and that early measures of academic skills serve as strong predictors of later academic success and life outcomes (Chetty et al., 2011; Duncan et al., 2007). However SEDA measures are subject to multiple interpretations and intervention studies will be required to test causal effects of changing a student's educational environment (Baker et al., 2010; Darling-Hammond et al., 2012; Drescher et al., 2022; Reardon, 2019).

An issue that remains to be resolved in future longitudinal research is whether early childhood educational opportunities continue to track white matter development throughout late elementary school and into adolescence or if the year-to-year educational opportunities afforded by

a school (SEDA slope) also shape white matter later in development. The full longitudinal ABCD sample will make it possible to model the interplay between educational opportunity and white matter development over longer timescales. Nevertheless, the findings that SEDA intercept is related to increased rates of FA development in the left arcuate indicate that differences in early educational opportunity are not only linked to differences in academic outcomes but also relate to the developmental trajectories of white matter throughout childhood and into adolescence.

Furthermore, the observed relationship between SEDA intercept and the brain-age gap suggest that early educational opportunities may not only influence the development of certain white matter tracts underlying academic skills, but also relate to white matter development throughout the brain more broadly. Studies in animal models have shown that environmental enrichment leads to an increase in cellular activities related to myelination, such as the proliferation of oligodendrocyte progenitor cells and alterations of the oligodendrocyte transcriptome in a wide range of brain regions (Forbes and Gallo, 2017; Nicholson et al., 2022; Goldstein et al., 2021). Evidence from human neuroimaging data suggests that environmental stress and caregiving settings relate to differences in white matter properties throughout the brain (Bick et al., 2015; Lebel and Deoni, 2018). Taken together, these results suggest that general enrichment of an individual's educational environment may drive global changes in white matter, whereas opportunities to meaningfully engage in specific subject areas may impact the white matter tracts subserving academic skills. Future studies are necessary to isolate the white matter changes driven by opportunities to engage in a particular academic subject area from those due to aspects of the educational environment that are independent of the specific academic content matter.

Future studies investigating the interplay between educational environment, brain development, and academic skills will be well served by including both functional and diffusion MRI data. The present analyses rely solely on diffusion MRI data and are therefore limited in their ability to drive conclusions about brain function. Future learning intervention research should leverage novel techniques combining functional and structural neuroimaging data (Grotheer et al., 2022, 2019) to understand how educational environments drive learning related changes in functionally defined sub-bundles within major white matter pathways.

Unfortunately, because the SEDA data are derived from school-level standardized test scores, they do not provide any insight into the specific aspects of the educational opportunities present within a given school district. A student's experience in the classroom and subsequent learning opportunities can be impacted by socio-cultural equity, language use, student-teacher relationships, the curriculum adopted by the school district, and classroom organization (Goldberg et al., 2022; Watts et al., 2021; Limlingan et al., 2020; Hamre et al., 2012), none of which necessarily manifest in a school's standardized test scores.

Although the present study provides a first step towards understanding the relationship between educational environment and white matter, the multifaceted nature of these measures present a challenge for fully understanding how different aspects of an individual's early learning environment relate to brain development. Future intervention studies conducted in collaboration with educational practitioners and more nuanced measures of the opportunities present in an educational environment are needed to better understand these relationships.

Furthermore, because each participant has at most two observations, our longitudinal models are limited in the types of relationships captured by difference scores. White matter properties have been shown to follow non-linear growth trajectories over the lifespan (Lebel and Deoni, 2018; Yeatman et al., 2014), however, with only two observations, one cannot effectively model non-linear relationships. Future research using the full longitudinal ABCD sample will have to explore the developmental dynamics of the white matter over the course of adolescence and determine whether the observed relationship between

FA development and SEDA is best described by a linear or non-linear trajectory.

In summary, these results suggest that the educational opportunities provided to a learner in early elementary school are related to subtle differences in white matter maturation, even when accounting for other socioeconomic factors. We observe a link between white matter development and educational environment and find that this relationship is strongest in the white matter tracts typically associated with academic skills. Future research is needed to inform the design of interventions and educational policies addressing inequities in education from a neuroscientifically-informed perspective. The current study provides the first direct evidence for the relationship between educational opportunity and brain development at scale and sheds light on the complex interaction between environmental factors, brain development, and learning.

CRediT authorship contribution statement

Ariel Rokem: Formal analysis, Software, Writing – review & editing. **Bruce D McCandliss:** Conceptualization, Funding acquisition, Supervision, Writing – review & editing. **Leo P Segrue:** Data curation, Writing – review & editing. **Ethan Roy:** Conceptualization, Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Jason D Yeatman:** Conceptualization, Formal analysis, Funding acquisition, Supervision, Writing – original draft, Writing – review & editing. **Adam Richie-Halford:** Data curation, Formal analysis, Writing – review & editing, Software. **Andreas M Rauschecker:** Data curation, Writing – review & editing. **Amandine Van Rinsveld:** Conceptualization, Formal analysis, Writing – review & editing. **Pierre Nedelec:** Data curation, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

Acknowledgments

Data used in the preparation of this article were obtained from the Adolescent Brain Cognitive DevelopmentSM (ABCD) Study (<https://abcdstudy.org>), held in the NIMH Data Archive (NDA). This is a multisite, longitudinal study designed to recruit more than 10,000 children age 9–10 and follow them over 10 years into early adulthood. The ABCD Study® is supported by the National Institutes of Health and additional federal partners under award numbers U01DA041048, U01DA050989, U01DA051016, U01DA041022, U01DA051018, U01DA051037, U01DA050987, U01DA041174, U01DA041106, U01DA041117, U01DA041028, U01DA041134, U01DA050988, U01DA051039, U01DA041156, U01DA041025, U01DA041120, U01DA051038, U01DA041148, U01DA041093, U01DA041089, U24DA041123, U24DA041147. A full list of supporters is available at <https://abcdstudy.org/federal-partners.html>. A listing of participating sites and a complete listing of the study investigators can be found at https://abcdstudy.org/consortium_members/. ABCD consortium investigators designed and implemented the study and/or provided data but did not necessarily participate in the analysis or writing of this report. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or ABCD consortium investigators. The ABCD data repository grows and changes over time. The ABCD data used in this report came from <https://doi.org/10.15154/1523041>. This work was funded by Eunice Kennedy Shriver National Institute of Child Health and

Human Development grant R01HD095861 to JDY and the National Institute of Mental Health grant 1RF1MH121868-01 to AR. Additionally, BDM was funded through the Stanford Educational Neuroscience Initiative.

Ethical considerations and approvals

The research sites involved in the ABCD study rely on a central Institutional Review Board at the University of California, San Diego. Before participating in the study, parental/guardian consent was obtained, as well as assent from participants. The analyses conducted in the present study were authorized under a Data Use Certification issued by the NIMH Data Archive.

Data statement

The raw diffusion MRI data and the demographic data used for these analyses, including SEDA scores are available through the NIH Data Archive. Instructions for accessing the ABCD data can be found here: <https://nda.nih.gov/abcd/>. The pyAFQ outputs were generated using the publicly available pyAFQ software package (<https://yeatmanlab.github.io/pyAFQ/>). These derivatives are not publicly available but can be replicated using the available raw data.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.dcn.2024.101386](https://doi.org/10.1016/j.dcn.2024.101386).

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