# Early-life educational quality and brain health in diverse older adults

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## Introduction

Education attainment is a strong predictor of late life cognition (Jefferson et al., 2011). A recent meta-analysis of international datasets indicates that a higher level of education was associated with increased dementia-free time (Hyun et al., 2022). Many of the previous studies have examined the effect of educational attainment with years of education as the indicator. So far, studies have shown fairly robust protective effects of years of education on cognition. For example, more years of education were associated with better performance in processing speed, working memory, verbal fluency, and verbal episodic memory (Zahodne et al., 2011). And such association was found in both low-education and high-education groups (Zahodne et al., 2015). An event-related potential (ERP) study also found higher education reduces the effect of age on episodic memory deficits and the ERP index of retrieval success, suggesting the protective role of education level on episodic memory aging (Angel et al., 2010). Additionally, scholars have examined the possibility that education functions as a compensatory mechanism in trajectories of cognitive decline. For example, among Alzheimer's dementia (AD) patients, those with lower education exhibit immediate cognitive decline after onset of symptoms, whereas higher education delays further decline for around 7 years until pathology deteriorates (Amieva et al., 2014).

Previous neuroimaging studies have investigated the neural dynamics serving the protective role of educational attainment in both healthy population and AD patients. They found that at a comparable degree of cognitive function, highly educated AD patients exhibit more severe brain atrophy than those with less education (Zhu et al., 2021). Education-related differences in regional cortical thickness were also found in AD patients, such that individuals with more education have smaller cortical thickness in temporal gyrus, inferior and superior parietal gyri, and lateral occipital cortex (Liu et al., 2012). Such findings suggested the compensatory role of education in helping to maintain clinical function in the face of pathology. In cognitively normal populations, a higher level of education was associated with increased cortical thickness, and such association was only limited to older individuals (age >64 years) (Kim et al., 2015; Steffener, 2021). Specifically, greater regional cortical thickness in transverse temporal cortex, insula, and isthmus of cingulate cortex was found in healthy older adults with higher education (Liu et al., 2012). But researchers also suggested a complex and distributed brain pattern of educational effects on cortical thickness in cognitively normal individuals, such that education is associated with larger thickness in right cingulate cortex and lower thickness in right temporal areas (Habeck et al., 2020). Such results showing region-specific associations may provide insight into the specific neural mechanisms underlying the protective effects of education.

Very few studies, however, have investigated how other modifiable early life exposures related to educational attainment are associated with late life brain atrophy. In particular, indicators of educational quality have been found to have implications for late life cognition

(Moorman et al., 2019). Educational quality is often an even stronger predictor of later-life cognition than educational attainment (Brenowitz et al., 2020) as it may capture a greater variety of critical early life experiences that can vary across individuals with the same years of education. In addition, educational quality may represent an upstream factor that influences ultimate educational attainment, as indicators of educational quality have been shown to have a large impact on educational achievement and future educational opportunities (Card et al., 2018; Lafortune et al., 2018). High educational quality is also possibly related to more opportunities to obtain other cognitive promoting resources throughout the life course (e.g., cognitively-demanding occupations), which might be associated with better brain and cognitive health in late life. Thus, it is very important to investigate neuroprotective mechanisms underlying educational quality in healthy aging.

From this background, the current thesis project seeks to address the gap by investigating the associations between early life educational quality and brain health among non-Hispanic Black and White older adults.

## Research Hypotheses

**Aim 1: To examine whether educational quality is associated with mean cortical thickness, averaged across "AD signature" regions (Dickerson et al., 2009).**

H1: Higher educational quality will be associated with greater cortical thickness.

**Aim 2: To examine whether educational quality is associated with cortical thickness in specific regions**.

H2: A mixed pattern of positive and negative associations between educational quality and cortical thickness will be presented across specific regions in line with Habeck et al. (2020).

## Research Design

<u>Data Source</u>

The Michigan Cognitive Aging Project (MCAP) is a prospective, longitudinal study of cognitive decline in English-speaking adults aged 55 and older who, at the time of enrollment, have not been diagnosed with dementia. Starting in 2017, a regionally representative and racially balanced sample of non-Hispanic White and non-Hispanic Black individuals were recruited through voter registration lists along with census data in Wayne and Washtenaw counties in Southeast Michigan. Participants were interviewed at an office in Ann Arbor or Detroit, or in their homes. The Wave 1 sample included 499 participants who completed the neuropsychological assessment. 108 participants in the Wave 1 sample also had available structural MRI data. The final analytic sample will include those with neuroimaging data.

Measures

### Educational quality

*Educational quality of grade school* was self-reported on a scale from 1 (i.e. excellent) to 5 (i.e. poor). These scores are reverse coded so that higher scores represented higher educational quality.

### Neuroimaging outcomes

Structural MRI images were obtained on a 3T General Electric scanner at the University of Michigan fMRI laboratory.

*Cortical thickness* was quantified with FreeSurfer (version 6.0; http://surfer.nmr.mgh.harvard.edu/) using T1-weighted images. Aim 1 analyses will use a composite score calculated by averaging cortical thickness values across hemispheres in nine "AD signature" regions that have been shown to reflect early AD neuropathology (Dickerson et al., 2009). These regions included: rostral medial temporal lobe, angular gyrus, inferior frontal lobe, inferior temporal lobe, temporal pole, precuneus, supramarginal gyrus, superior parietal lobe, and superior frontal lobe. Aim 2 analyses will examine regions individually.

Planned Covariates

This study will control for potentially confounding factors such as race/ethnicity, age, sex/gender, childhood SES, and total intracranial volume. Race/ethnicity was self-reported and represented by two mutually exclusive groups: non-Hispanic Black and non-Hispanic White participants. Age was self-reported. Sex/gender was self-reported as a binary variable (Male or Female). Childhood SES was operationalized as parental education. Parental education was recorded as an average of mother's and father's years of education (0-17). If only one parent's education was recorded, that value was used. Total intracranial volume was derived from T1-weighted images using FreeSurfer version 6.0.

Statistical Analysis

First, descriptive statistics and correlations will be conducted. To address aim 1 of the study, we will perform multiple linear regression to examine the association score between educational quality and the cortical thickness composite. To address aim 2 of the study, we will examine the association between educational quality and nine individual "AD signature" regions. For both aims, we will control for age, sex/gender, race, childhood SES, and intracranial volume.

**Timeline**

| | May '22 | Jun | Jul | Aug | Sep | Oct | Nov | Dec | Jan '23 | Feb | Mar | Apr |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Literature review | **x** | **x** | **x** | | | | | | | | | |
| Proposal submission | | | | **x** | | | | | | | | |
| Data analysis | | | | **x** | **x** | **x** | | | | | | |
| Writing | | | | | | **x** | **x** | **x** | **x** | | | |
| First draft | | | | | | | | | **x** | | | |
| Revision | | | | | | | | | | **x** | **x** | |
| Poster | | | | | | | | | | **x** | **x** | **x** |
| Final draft | | | | | | | | | | | **x** | **x** |

**Mentors**

I will receive support and feedback from Dr. Laura Zahodne, Dr. Ji Hyun Lee, and Jordan Palms. I have been working as a research assistant in Dr. Zahodne's lab since the 2020 fall semester, and I plan to continue this work for the following academic year. I will meet weekly with my primary post-doctoral student mentor Dr. Ji Hyun Lee and receive additional support from Joran Palms, my secondary graduate student mentor. I will also meet with Dr. Zahodne once per month and submit appropriate milestones.

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