Educational attainment does not influence brain aging

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Education has been related to various advantageous lifetime out-
comes. Here, using longitudinal structural MRI data (4,422 observa-
tions), we tested the influential hypothesis that higher education
translates into slower rates of brain aging. Cross-sectionally, educa-
tion was modestly associated with regional cortical volume. How-
ever, despite marked mean atrophy in the cortex and hippocampus,
education did not influence rates of change. The results were repli-
cated across two independent samples. Our findings challenge the
view that higher education slows brain aging.

education | aging | cerebral cortex | hippocampus | reserve

Do higher levels of education attained in childhood and early
adulthood slow the rate of brain and cognitive decline in
later adulthood and old age? Prominent accounts of heterogeneity
in neural and behavioral aging postulate that this is the case, ar-
guing that education acts as a modifiable protective factor (1) or
cognitive reserve (2, 3) of human neurocognitive aging. However,
findings from cross-sectional studies provide only inconclusive
support for an association between education and neurocognitive
level in aging (4–7), and the longitudinal support for an influence
of education on age-related neurocognitive change is even more
elusive. In fact, a comprehensive review recently concluded that
level of education does not reliably influence the rate of cognitive
decline in aging (8). Also, associations between secular improve-
ments in average education and historical changes in rates of
cognitive change are generally weak (9). In relation to brain
changes, longitudinal data are sparse and provide no support for
an education–brain aging relation (6, 10). Therefore, we con-
ducted a large-scale test of the hypothesis of a longitudinal rela-
tion between education and brain aging. Brain aging was
operationalized as brain atrophy measured longitudinally by
structural MRI. This metric does not capture the multitude of
dimensions of brain aging, but is commonly used and very sensitive
to normal and pathological aging.

Results

We considered MRI-based measures across the cortical mantle
and the hippocampus from several regional samples within
Lifebrain (LB) (11) and from the UK Biobank (UKB) (12).
There were marked individual differences in education levels in
LB ($n = 735$; age range = 29–91 y; Fig. 1A) and UKB ($n = 1,289$;
age range = 47–79 y; 630 with college/university and 659 with
nonuniversity education). The main analyses of longitudinal

brain aging were performed with mixed models, using age
(at baseline), sex, and scanner as covariates, and the interaction
term *education × time (since first scan)* as the variable of interest.
The longitudinal coverage was up to 11.2 y and three test waves.
Models were run with and without intracranial volume (ICV) as
an additional covariate.

Longitudinal analyses in LB (1,844 scans), revealed no sig-
nificant relationship between education and vertex-wise volume
change across the cortex. Similarly, when restricting the analysis
to regions where volume loss was significantly larger with higher
age (Fig. 1B), we found no support that higher education was
related to less volume loss (Fig. 1C). Hippocampus atrophy in
aging is well documented, and we found a marked age-related
reduction in hippocampus volume with increasing age regardless
of whether ICV was included as covariate ($F = 141.4$, $P < 2e^{-16}$,
edf [effective degrees of freedom] = 8.51) or not ($F = 137.2$, $P < 2e^{-16}$, edf = 8.52). Crucially, rates of hippocampus volume
change were not influenced by level of education ($F = 1.51$, $P = 0.22$; Fig. 1D).

Longitudinal analyses in UKB (2,578 scans) showed that re-
gions in posterior association cortices and lateral and medial
frontal and temporal cortex displayed more change with in-
creasing age (Fig. 2A), but levels of education did not influence
rate of change in these cortical regions (Fig. 2B). A vertex-wise
mega-analysis of LB and UKB data pooled together confirmed
the lack of an effect of education on cortical change (no vertices
survived conventional criteria for multiple comparison correc-
tions). Hippocampus volume loss was seen with ($F = 102.2$, $P < 2e^{-16}$) and without ($F = 98.74$, $P < 2e^{-16}$) covarying for ICV, but
again level of education did not influence rate of hippocampal
change (Fig. 2C; $t = -0.45$, $P = 0.65$) (Fig. 2C).

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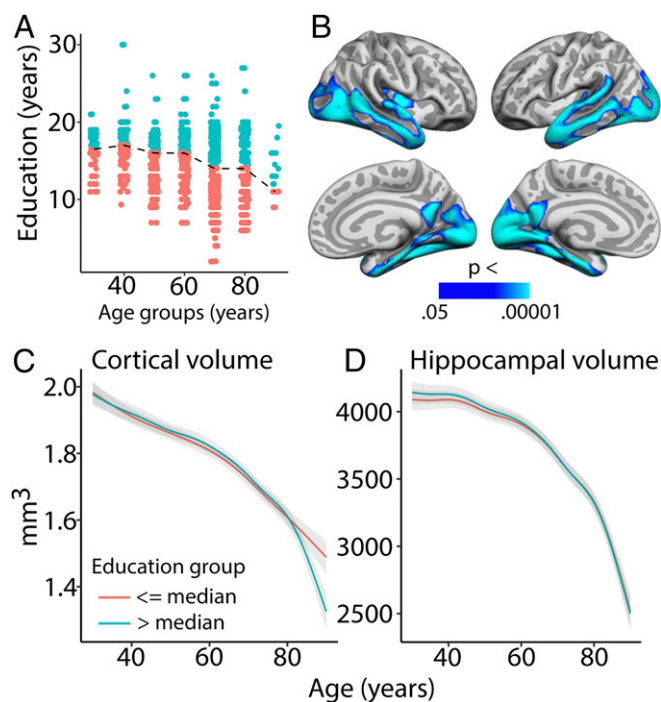
Fig. 1. Longitudinal education—brain-aging relations in LB. (A) Marked individual differences in education in all age groups. (B) Cortical regions showing more volume loss with increasing age, i.e., nonlinear age changes ($P < 0.05$, corrected for multiple comparisons; see *SI Appendix*). (C) Education was not related to rate of change in the atrophy-prone cortical regions in B. (D) There was significant hippocampus volume loss but no influence of education on rate of change. Education groups in C and D are based on a median split (indicated by the dashed line in A and used for illustrative purposes). The shaded areas around the lines denote 95% CI.

We used hypothesis testing with Bayes factors (BF) to quantify the evidence in favor of the null hypothesis of no relation of education with longitudinal brain aging. Given similar patterns of results for the cortex and hippocampus in both samples, the Bayesian analysis was restricted to the computationally less demanding hippocampal region in LB where education was coded as a continuous variable. We used mean-zero Gaussian priors with an uninformative prior followed by a sensitivity analysis with an informative prior. Based on previous studies of the effect of education on brain aging (5, 10), the informed prior stated that hippocampal volume loss (about 50 mm³ per y, or 1%) would be slowed by around 0.5 mm³/y for each year of education. The uninformative prior's SD was set at 10 times the main effect (SD = 500 mm³/y), and yielded a BF corresponding to very strong evidence in favor of the null ($BF_{01} = 1,170$). The informative prior assigned a very large prior probability that the effect of interest was close to zero (SD = 0.5 mm³/y). The obtained $BF_{01} = 1.29$ implies that the posterior probability is even more concentrated around zero than the informative prior, thus favoring the null hypothesis.

Finally, in both LB and UKB, cross-sectional analyses revealed modest associations of education with regional cortical volume around left central sulcus (Fig. 2D; LB: cluster extension, 5,298 mm²; cluster P values < 0.019–0.0002; UKB: 30,800 mm², P < 0.013–0.0002). Even in these cortical regions where education was related to intercept no relation was seen for slope (Fig. 2E). A large-scale ($n = 19,646$) cross-sectional UKB study reported a very small positive education–hippocampus volume association (12), but in the present smaller samples no significant cross-sectional associations were observed in LB or UKB between education and hippocampus volume.

Discussion

Taken together, the results from two large-scale datasets totaling almost 4,500 observations and over 2,000 individuals provided no support for the hypothesis that higher education translates into slower rates of brain aging. Instead, parallel rates of change were seen in cortical regions and in the hippocampus. It remains an open question whether other measures of brain aging than structural MRI are related to education levels.

Cross-sectionally, in both LB and UKB, education was modestly related to regional cortical volume, but even in the cortical regions where education was related to volume no relation was seen for rate of change. Thus, our brain-aging findings mimic those previously demonstrated for cognitive aging (8) by showing that education to some degree is related to level (intercept) but not rate of change (slope). A positive association between level of education and level of neurocognitive functioning has been reported in some past studies (5, 8, 12) (but see ref. 6), and is consistent with the notion of a "passive" reserve (13), which posits that individuals with higher education have an initial advantage over individuals with lower education that they may carry through their adult lives. It is this advantage, not attenuated longitudinal change, that reduces the risk among more educated individuals to be diagnosed with dementia and delays them reaching a threshold below which independent living is no longer possible. There is evidence for a genetic association of educational attainment with cortical surface area (14) and cognitive functions (15), indicating that shared genetic influences may account for cross-sectional relations of education with neurocognitive levels.

In conclusion, education is linked to many advantageous outcomes, but the present findings challenge theoretical and empirical claims that higher education slows brain aging.

Materials and Methods

MRIs were processed using FreeSurfer, version 7.1. All participants gave informed consent, subprojects were approved by the relevant ethical review board, and the Lifebrain project was approved by Regional Committees for Medical Research Ethics–South East Norway. Screening criteria were not identical across studies, but participants were recruited to be cognitively
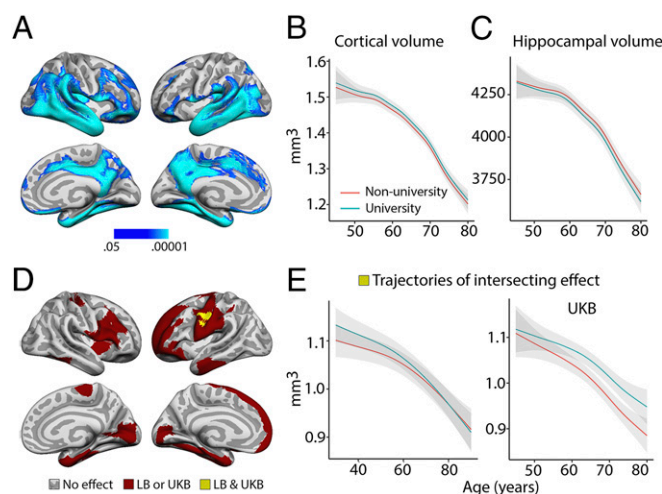
Fig. 2. Longitudinal education—brain-aging relations in UKB. (A) Cortical regions showing more volume loss with increasing age ($P < 0.05$, corrected). (B) Education was not related to rate of change in the atrophy-prone cortical regions in A. (C) There was significant hippocampus volume loss but no influence of education on rate of change. (D) Cross-sectional education—brain-volume relations in LB and UKB ($P < 0.05$, corrected). (E) In the regions in D where a cross-sectional effect of education was seen in both LB and UKB (yellow), no differences in longitudinal rate of change were seen in relation to education in LB or UKB (red, low education; blue, high education). The shaded areas around the lines denote 95% CI.

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healthy and did not suffer from neurological conditions known to affect brain function, such as dementia. All samples consisted of community-dwelling participants, some were convenience samples, whereas others were contacted on the basis of population registry information. Details on samples, MRI acquisition and processing, statistical analyses, and data and code availability are presented in *SI Appendix*.

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