BISKUPSKI, Maciej, BARTOSZCZYK, Martyna, OSTAŃSKI, Jan, DANILUK, Aleksander, IWANIUK, Kaja, BUCZEK, Jakub, BIAŁKOWSKA, Zuzanna, SAMCZUK, Maciej, STACHOWICZ, Hubert and OLSZAK, Joanna. Impact of education on cerebral cortex volume, thickness and Alzheimer's disease. Quality in Sport. 2024;16:52206. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.16.52206
https://apcz.umk.pl/QS/article/view/52206

The journal has had 20 points in Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 06.06.2024. Revised: 25.05.2024. Accepted: 03.07.2024. Published: 07.07.2024.

Impact of education on cerebral cortex volume, thickness and Alzheimer's disease

Maciej Biskupski

Human Anatomy Research Group, Medical University of Lublin

https://orcid.org/0009-0000-4040-8068

maciekbisk@gmail.com

Martyna Bartoszczyk

Human Anatomy Research Group, Medical University of Lublin

https://orcid.org/0009-0004-6453-9838

martyna.bartoszczyk@gmail.com

lek. Jan Ostański

Human Anatomy Research Group, Medical University of Lublin

1st Military Clinical Hospital with the Outpatient Clinic, Lublin, Poland

https://orcid.org/0009-0008-6634-7740

janost1911@gmail.com

lek. Aleksander Daniluk
Human Anatomy Research Group, Medical University of Lublin
Stefan Kardynał Wyszyński Province Specialist Hospital in Lublin, Kraśnicka 100 avenue, 20-718 Lublin, Poland
https://orcid.org/0009-0001-3386-285X
aleksanderdaniluk5@wp.pl

lek. Kaja Iwaniuk
Human Anatomy Research Group, Medical University of Lublin
Stefan Kardynał Wyszyński Province Specialist Hospital in Lublin, Kraśnicka 100 avenue, 20-718 Lublin, Poland
https://orcid.org/0009-0001-6350-8499
kaja.iwaniuk@gmail.com

lek. Jakub Buczek
Human Anatomy Research Group, Medical University of Lublin
Stefan Kardynał Wyszyński Province Specialist Hospital in Lublin, Kraśnicka 100 avenue, 20-718 Lublin, Poland
https://orcid.org/0009-0004-1996-5280
jakubbuczek98@gmail.com

lek. Zuzanna Białkowska
Human Anatomy Research Group, Medical University of Lublin
1st Military Clinical Hospital with the Outpatient Clinic, Lublin, Poland
https://orcid.org/0009-0002-5682-8360
zuzanna.bialkowska@gmail.com

lek. Maciej Samczuk
Stefan Kardynał Wyszyński Province Specialist Hospital in Lublin, Kraśnicka 100 avenue, 20-718 Lublin, Poland
Human Anatomy Research Group, Medical University of Lublin
Department of Normal, Clinical and Imaging Anatomy, Medical University of Lublin
https://orcid.org/0009-0002-1857-6967
maciej.samczuk@gmail.com

lek. Hubert Stachowicz
Human Anatomy Research Group, Medical University of Lublin
Stefan Kardynał Wyszyński Province Specialist Hospital in Lublin, Kraśnicka 100 avenue, 20-718 Lublin, Poland
https://orcid.org/0009-0003-5906-1350
hubertsta02@gmail.com

lek. Joanna Olszak
Independent Public Hospital No. 4 in Lublin
https://orcid.org/0009-0004-0211-1449
asia.olszak663@gmail.com

Abstract

Introduction and objective: The purpose of our review was to systematize the knowledge regarding the impact of education on cortical volume and thickness along with assessment of the risk and progress of Alzheimer's disease. We considered the problem among children as well as adults, depending on their level of education and particularized the role of cognitive reserve as a protection from brain damage. Furthermore, we investigate the issue of neuronal tolerance in Alzheimer's disease.

Review methods: The article is a review of 22 original papers, cohort studies and meta-analyses concerning the impact of education on cortical volume and thickness along with the risk and progress of Alzheimer's disease.

Abbreviated description of the state of knowledge: Studies have shown that education is associated with an increase in intelligence, which determines the dynamics of brain cortex changes among children. In adults, the thickness of individual brain areas - primarily the temporal and frontal poles - enhances with the increase of their education level. The dynamics of changes in cortical measurements are correlated with education both in healthy adults and in patients with Alzheimer's disease. A healthy lifestyle, common for those with higher education, has a positive impact on cortical thickness and lowers the risk of developing Alzeihmer's disease. Moreover, education comes with better neuronal tolerance for

accumulated proteins, yet few studies take notice of more dynamic progress of the disease among adults with higher education.
Summary: Research has confirmed the impact of education on cortical volume and thickness. The risk and progress of Alzheimer’s disease are also reflected in the patient’s level of education nevertheless the literature is ambiguous regarding this issue.

Keywords: intelligence, education, volume, thickness, cerebral cortex, Alzheimer's disease

Introduction and objective

The cerebral cortex, due to its complex structure and a wide range of functions, has become the subject of research and interest for many scholars. A particularly significant aspect of these studies is determining the influence of education on its anatomy. Equally important is addressing the issue of neurodegenerative diseases, including Alzheimer's disease, and their role in disrupting the normal structure and function of the brain. The purpose of this review article is to systematize the knowledge concerning the impact of education on brain cortex measurements such as volume and thickness together with the risk and progress of Alzheimer’s disease.

The cerebral cortex is a superficial layer of gray matter, formed by the cell bodies of neurons. It belongs to the telencephalon and forms the cerebral hemispheres, covering the surface of gyri and sulci. It is divided into the palaeocortex, the archicortex, and the neocortex. The neocortex, with the highest degree of development, constitutes the majority, accounting for over 90%. It consists of 6 layers composed of billions of pyramidal and non-pyramidal cells. The palaeocortex and archicortex show a lower degree of development, differing in structure, containing only 3 layers. They can be found within the limbic system and rhinencephalon. The two deepest sulci of the cortex, the central and lateral sulcus, determine the division of the cortex into lobes: frontal, temporal, parietal, and occipital. The functional division of the brain cortex distinguishes it into motor, sensory, visual, auditory, taste, olfactory, and associative cortex, each characteristic of a specific brain region [1]. The volume of the cerebral cortex is about 643 cm^3 in men and about 597 cm^3 in women [2]. Its thickness varies between 1.6 and 4 mm and differs in the areas of individual gyri and sulci. The surface area equals about 1000 cm^2 per hemisphere [3].

Both the new cortex, especially in associative areas, and the archicortex in the limbic system participate in cognitive processes, learning, and memory. Education influences the brain at the synaptic level. Integrating external stimuli and forming new neural connections are the basis of the learning process, and the repeated circulation of impulses in new connections ensures the memorization of new information [4].

Disorders in the structure and function of the cerebral cortex can occur due to neurodegenerative diseases. They lead to progressive damage and loss of neuron populations. Most of them are associated with the excessive accumulation of proteins with abnormal conformation, which may persist for many years before the onset of the first clinical symptoms. Among them, amyloidoses, tauopathies, synucleinopathies, and TDP-43 proteinopathies are distinguished. Within one disease entity, there may be the accumulation of several types of proteins, as in the case of Alzheimer's disease, where both extracellular β-amyloid deposits and intracellular aggregates of tau protein are observed [5]. Amyloid plaques shape within the new cortex, while tau protein tangles initially occupy the area of the entorhinal cortex and hippocampus and, with disease progression, spread to the neocortex's associative areas. The TDP-43 protein is also increasingly recognized in pathological deposits. Alzheimer's disease is the most common cause of dementia and is considered a global public health priority. In addition to episodic memory loss, patients develop cognitive and motor disturbances and difficulties in performing basic activities. This disease leads to dependence, disability, and even death [6].

Review methods

In our review, a total of 22 original papers, cohort studies, and meta-analyses were utilized to investigate the indirect and direct impact of education on the volume and thickness of the cerebral cortex (13) as well as on the risk and progression of Alzheimer's disease (9).
The following databases were used: PubMed, Web of Science, Google Scholar, Scopus. The following keywords were used: intelligence, education, volume, thickness, cerebral cortex, Alzheimer's disease, nutrition, alcoholism.

The time frame considered for the studies was 1995-2023 (studies older than 8 years were predominantly used in the section concerning the negative influence of education on the course of Alzheimer's disease, as emphasized in the conclusions).

Description of state of knowledge

Impact of Education on Intelligence

To determine how education affects the volume and density of the brain's cortex, it is crucial to define how education shapes intelligence. Cognitive ability (or intelligence) [7] is precisely the foundation for potential changes in brain structure, making an understanding of its role a key aspect in analyzing the impact of education on the brain. It is through this correlation that conclusions can be drawn about how education influences (or doesn't influence) the thickness of the brain's cortex.

Based on a long-term cohort study, a positive correlation between education and intelligence has been demonstrated [8]. While the correlation is not large, it is statistically significant, amounting to approximately 1-5 IQ points for each additional year of education. Several potential explanations for this relationship have been proposed. One possibility is that education helps develop cognitive skills, such as memory, attention, and problem-solving. These skills are crucial for success in various areas of life, including work, interpersonal relationships, and health. Another possibility is that education aids in acquiring knowledge, which may improve performance in intelligence tests. Finally, education may also play a role in the socialization process, assisting individuals in developing skills and attitudes essential for success in society [9].

The relationship between education and cerebral cortex volume

Research on the association between intelligence and the volume of the brain cortex is one of the key areas in neurobiological studies. Shaw et al. made a study aiming to explore the relationship between intelligence and the development of the brain cortex in children and adolescents was published in the journal Nature. The study revealed that the thickness of the brain cortex in childhood is not significantly linked to the level of intelligence. Participants were categorized into three groups (highly intelligent - IQ 121-149, very intelligent - IQ 109-120, and average intelligence - IQ 83-108) based on tests assessing verbal, non-verbal, and reasoning skills (according to the Wechsler intelligence scale). Subsequently, they underwent MRI examinations. It was demonstrated that highly intelligent children and adolescents exhibited more dynamic changes in the thickness of the brain cortex during development. They experienced a phase of accelerated and prolonged cortical growth, followed by equally intense processes of thinning, compared to less intelligent children. However, intelligence did not directly impact the thickness of the brain cortex [10].

In adults, studies have shown that education indeed influences cortical thickness. An example of such research, allowing us to draw such conclusions, is the study conducted by Jason Steffener. Using magnetic resonance imaging, he measured the cortical thickness in 391 healthy individuals aged 19-80. His research showed that there are regions of the brain cortex whose thickness correlates with the education level of the participants. These regions include the left hemisphere's superior temporal gyrus and insula, as well as the right hemisphere's superior, middle, and inferior temporal gyrus, part of the operculum, and triangular part of the inferior frontal gyrus, superior frontal gyrus, frontal pole, and temporal pole. The study also revealed that differences in cortical thickness over the years varied depending on the education level. Individuals with low education levels experienced a significant decline in cortical thickness early in life, which gradually equalized and became insignificant later in life. Similar effects were observed in the group with moderate education levels. Highly educated individuals, on the other hand, had smaller differences in cortical thickness early in life but experienced greater declines in cortical thickness in later years compared to other groups [11].

Furthermore, a study involving 60 Italian and Hong Kong citizens showed that individuals proficient in at least two languages have a thicker brain cortex than monolingual individuals, despite having undergone the same number of years of education. This underscores the significant importance of language learning in the course of education [12].

The most likely explanation for the correlation between education and the thickness of the brain cortex is the increase, under the influence of education, in cognitive and brain reserves. Cognitive reserve refers to the brain's ability to maintain normal cognitive functions despite age-related changes or brain damage, while brain reserve pertains to the physical resilience of the brain to damage or diseases. It is assumed that education provides cognitive stimulation and intellectual challenges that can aid in building neural connections (resulting in increased cortical thickness) and enhance brain plasticity [13].

It is worth expanding the research perspective on the impact of education on the thickness of the cerebral cortex, taking into account intermediate aspects. An intriguing phenomenon suggests that individuals with higher levels of education are generally more physically active than less educated individuals (partly due to healthier attitudes and a larger budget for physical activities) [14]. Simultaneously, there are studies indicating that physical activity may be linked to the thickness of the brain cortex. A study conducted in 2016 by Korean scientists, involving 1842 participants who underwent MRI examinations to measure cortical thickness, and completed a questionnaire assessing their physical activity, demonstrated that longer exercise duration (≥1 hour/day), but not intensity or frequency, was associated with increased average cortical thickness, particularly in the frontal area. Another noteworthy conclusion from this analysis, confirming previous study results, is that more educated individuals had a thicker cortex compared to similarly physically active less educated individuals [15].

Other significant factors that may influence the varying thickness of the brain cortex in individuals with different education levels are dietary habits. Based on a study involving a whopping 780,000 participants, it was shown that more educated individuals are less likely to develop alcoholism [16], which may contribute to a thicker brain cortex in these individuals. Chronic alcohol consumption can lead to a significant bilateral decrease in cortical thickness, especially in the regions of the temporal and insular gyri as well as precentral and dorsolateral prefrontal gyri [17]. Moreover, an analysis of the dietary habits of the population of London observed that more educated individuals tend to follow a healthier and more diverse diet, characterized by higher fiber, fruit, vegetable, and fish consumption, as well as a more balanced and varied intake of nutrients. Conversely, a low level of education is generally associated with a diet rich in carbohydrates, sweets, red meat, higher calorie intake, and larger average portion sizes [18]. At the same time, Chinese scientists wrote a paper based on the analysis of cortical thickness in 51,665 individuals from 60 different cohort studies worldwide, indicating, among other things, that increased fat consumption in the diet leads to a bilateral decrease in the thickness of the superior frontal gyrus and the posterior part of the middle frontal gyrus, while increased consumption of fresh fruits causes thickening of the insular cortex [19].

The latest studies on the impact of education on the human brain, involving 1731 Koreans, provided specific numerical data on how education increases the thickness of the brain cortex, and notably, the thickness of the white matter and the total intracranial volume. An additional year of education (accounting for the influence of gender and age of the study participants) is associated with an increase in the volume of the brain cortex by 1.41-1.67 ml, white matter by 1.28-1.39 ml, and the total intracranial volume by 4.39 ml [20].

The impact of education on the risk and course of Alzheimer's disease

Education has been recognized as playing a significant role in the risk and progression of Alzheimer's disease (AD). Studies have shown that individuals with higher levels of education are less susceptible to developing AD and experience a slower decline in cognitive function compared to those with lower levels of education. This is evidenced by the analysis of 54,162 participants (17,008 of whom had AD, while the rest constituted the control group) in a study conducted by British scientists, which revealed that an additional increase in intelligence by 10-15 IQ points (equivalent to about 3.6 years of education) reduces the risk of developing AD by approximately 36% [21]. In 2001, an article published in the American Journal of Alzheimer's Disease and Other Dementias provided evidence that individuals with more years of education who developed AD had a slower rate of cognitive decline. Interestingly, each additional year of education also increased the likelihood of AD symptoms occurring earlier (by approximately 1.4 months earlier) [22].

There are several possible explanations for this relationship. One possible explanation for this protective effect is the cognitive reserve (mentioned earlier), which refers to the brain's ability to compensate for damage or pathology by utilizing alternative neural networks. It has been proven that individuals with higher levels of education have greater cognitive reserve, allowing them to better cope with progressive cognitive impairment associated with AD [23]. The protective function of education during the course of AD is also supported by a study showing that individuals with higher education levels had significantly more deposited amyloid Aβ compared to those with lower education levels, despite comparable levels of cognitive function decline [24]. Another observation supporting this relationship is that with an increase in education, there is an increased tolerance of the cortical neurons to the neurotoxic accumulation of intracellular, twisted tau proteins [25]. More educated individuals also lead healthier lifestyles [26], adhere more strictly to healthy eating habits, and use fewer substances, leading to better maintenance of brain structure and, consequently, cognitive function in old age, making them less susceptible to AD [27].

Despite the positive correlations between education and a milder course of Alzheimer's disease, there are also studies (significantly older) showing a more dynamic development of AD in better-educated individuals, indicating an ambiguous impact of education on the course of AD. Among 494 clinically diagnosed Alzheimer's patients in Chicago, those with higher education levels exhibited a more rapid decline in cognitive function. Participants in the study were subjected to tests, including episodic memory, verbal fluency, recognition ability, and overall mental state, at least twice at 6-month intervals. Despite better initial results in these tests, individuals with longer periods of education showed a slightly accelerated loss of cognitive function at later stages of the disease, compared to those with shorter periods of education [28]. A study conducted on 156 patients using the MMSE test also demonstrated greater disease progression in better-educated individuals. The MMSE test assessed cognitive abilities on a scale from 0 to 30 points and was conducted among participants at least twice, with annual intervals. Individuals with moderate education experienced an average annual decline of 1.2 MMSE points, while those with higher education experienced an average decline of 1.3 MMSE points. Additionally, it was shown that among participants with an initial MMSE score of 15 points, the disease progression was 44% faster in those with higher education compared to individuals with below-average education [29, 30].

Summary

In summary, research confirms the impact of education on the volume of the cerebral cortex, both through shaping intelligence, developing skills, creating new neuronal connections, and the inclination towards a healthy lifestyle. Changes in the cerebral cortex are evident throughout the development of exceptionally intelligent children. Also, individuals with higher education levels show regions of the brain cortex where thickness is greater, but with advancing age, they experience higher declines compared to those with lower education levels. The increase in brain volume and cortex thickness is likely associated with an increased cognitive and brain reserve, which ensures the maintenance of mental efficiency and protects the brain from damage and diseases. Consequently, a positive impact of education on a milder course of Alzheimer's disease and lower risk of onset has been demonstrated. However, in some (significantly older) studies, a more dynamic loss of cognitive abilities in individuals with higher education was observed. The ambiguous influence of education on the course of Alzheimer's disease remains a subject for further research on this topic.

Disclosures:

All authors have read and agreed with the published version of the manuscript. **Conflict of interest:** The authors declare no conflict of interest. **Funding statement:** No external funding was received to perform this review. **Statement of data availability:** not applicable **Statement of institutional review committee:** not applicable **Statement of informed consent:** not applicable **Author's contribution:** conceptualisation: Maciej Samczuk, Zuzanna Białkowska; methodology: Maciej Biskupski, Martyną Bartoszczyk; software: Aleksander Daniluk, Kaja Iwaniuk; check: Zuzanna Białkowska, Jan Ostański; formal analysis: Hubert Stachowicz, Maciej Biskupski; investigation: Martyną Bartoszczyk, Maciej Biskupski; resources: Aleksander Daniluk, Kaja Iwaniuk; data curation: Maciej Biskupski, Joanna Olszak; writing-rough preparation: Jan Ostański, Hubert Stachowicz; writing-review and editing: Zuzanna Białkowska, Jakub Buczek; visualisation: Aleksander Daniluk; supervision: Maciej Samczuk; project administration: Joanna Olszak; receiving funding: Maciej Samczuk
Corresponding author: Maciej Biskupski, maciekbisk@gmail.com

References

1. Patestas MA. A Textbook of Neuroanatomy. 2nd ed. Wiley-Blackwell, 2016.

2. Ritchie SJ, Cox SR, Shen X, et al. Sex Differences in the Adult Human Brain: Evidence from 5216 UK Biobank Participants. Cereb Cortex. 2018;28(8):2959-2975. https://doi:10.1093/cercor/bhy109

3. Glasser MF, Smith SM, Marcus DS, et al. The Human Connectome Project's neuroimaging approach. Nat Neurosci. 2016;19(9):1175-1187. https://doi:10.1038/nn.4361

4. Konturek SJ. Human physiology. 3rd ed. Edra Urban & Partner, 2019.

5. Dugger BN, Dickson DW. Pathology of Neurodegenerative Diseases. Cold Spring Harb Perspect Biol. 2017;9(7):a028035. Published 2017 Jul 5. https://doi:10.1101/cshperspect.a028035

6. Lane CA, Hardy J, Schott JM. Alzheimer's disease. Eur J Neurol. 2018;25(1):59-70. https://doi:10.1111/ene.13439

7. Goleman D. Emotional intelligence. Media Rodzina, 2021.

8. Hegelund ER, Grønkjær MS, Osler M, et al. The influence of educational attainment on intelligence. Intelligence. 2020;78. 101419. https://doi.org/10.1016/j.intell.2019.101419

9. Ritchie SJ, Tucker-Drob EM. How Much Does Education Improve Intelligence? A Meta-Analysis. Psychol Sci. 2018;29(8):1358-1369. https://doi:10.1177/0956797618774253

10. Shaw P, Greenstein D, Lerch J, et al. Intellectual ability and cortical development in children and adolescents. Nature. 2006;440(7084):676-679. https://doi:10.1038/nature04513

11. Steffener J. Education and age-related differences in cortical thickness and volume across the lifespan. Neurobiol Aging. 2021;102:102-110. https://doi:10.1016/j.neurobiolaging.2020.10.034

12. Abutalebi J, Guidi L, Borsa V, et al. Bilingualism provides a neural reserve for aging populations. Neuropsychologia. 2015;69:201-210. https://doi:10.1016/j.neuropsychologia.2015.01.040

13. Foubert-Samier A, Catheline G, Amieva H, et al. Education, occupation, leisure activities, and brain reserve: a population-based study. Neurobiol Aging. 2012;33(2):423.e15-423.e4.23E25. https://doi:10.1016/j.neurobiolaging.2010.09.023

14. Kari JT, Viinikainen J, Böckerman P, et al. Education leads to a more physically active lifestyle: Evidence based on Mendelian randomization. Scand J Med Sci Sports. 2020;30(7):1194-1204. https://doi:10.1111/sms.13653

15. Lee JS, Shin HY, Kim HJ, et al. Combined effects of physical exercise and education on age-related cortical thinning in cognitively normal individuals. Sci Rep. 2016;6:24284. Published 2016 Apr 11. https://doi:10.1038/srep24284

16. Rosoff DB, Clarke TK, Adams MJ, et al. Educational attainment impacts drinking behaviors and risk for alcohol dependence: results from a two-sample Mendelian randomization study with ~780,000 participants. Mol Psychiatry. 2021;26(4):1119-1132. https://doi:10.1038/s41380-019-0535-9

17. Dai X, Yu J, Gao L, et al. Cortical thickness and intrinsic activity changes in middle-aged men with alcohol use disorder. Alcohol. 2023;106:15-21. https://doi:10.1016/j.alcohol.2022.10.001

18. Azizi Fard N, De Francisci Morales G, Mejova Y, et al. On the interplay between educational attainment and nutrition: a spatially-aware perspective. EPJ Data Sci. 2021;10:18 https://doi.org/10.1140/epjds/s13688-021-00273-y

19. Li C, Chen Z, He S, Chen Y, Liu J. Unveiling the influence of daily dietary patterns on brain cortical structure: insights from bidirectional Mendelian randomization. Food Funct. 2023;14(23):10418-10429. Published 2023 Nov 27. https://doi:10.1039/d3fo02879h

20. Kim RE, Lee M, Kang DW, Wang SM, Kim D, Lim HK. Effects of education mediated by brain size on regional brain volume in adults. Psychiatry Res Neuroimaging. 2023;330:111600. https://doi:10.1016/j.pscychresns.2023.111600

21. Anderson EL, Howe LD, Wade KH, et al. Education, intelligence and Alzheimer's disease: evidence from a multivariable two-sample Mendelian randomization study. Int J Epidemiol. 2020;49(4):1163-1172. https://doi:10.1093/ije/dyz280

22. Fritsch T, McClendon MJ, Smyth KA, et al. Effects of educational attainment on the clinical expression of Alzheimer's disease: results from a research registry. Am J Alzheimers Dis Other Demen. 2001;16(6):369-376. https://doi:10.1177/153331750101600606

23. van Loenhoud AC, van der Flier WM, Wink AM, et al. Cognitive reserve and clinical progression in Alzheimer disease: A paradoxical relationship. Neurology. 2019;93(4):e334-e346. https://doi:10.1212/WNL.0000000000007821

24. Roe CM, Mintun MA, D'Angelo G, Xiong C, Grant EA, Morris JC. Alzheimer disease and cognitive reserve: variation of education effect with carbon 11-labeled Pittsburgh Compound B uptake. Arch Neurol. 2008;65(11):1467-1471. https://doi:10.1001/archneur.65.11.1467

25. Hoenig MC, Bischof GN, Onur ÖA, et al. Level of education mitigates the impact of tau pathology on neuronal function. Eur J Nucl Med Mol Imaging. 2019;46(9):1787-1795. https://doi:10.1007/s00259-019-04342-3

26. Raghupathi V, Raghupathi W. The influence of education on health: an empirical assessment of OECD countries for the period 1995-2015. Arch Public Health. 2020;78:20. Published 2020 Apr 6. https://doi:10.1186/s13690-020-00402-5

27. Karama S, Bastin ME, Murray C, et al. Childhood cognitive ability accounts for associations between cognitive ability and brain cortical thickness in old age. Mol Psychiatry. 2014;19(5):555-559. https://doi:10.1038/mp.2013.64

28. Wilson RS, Li Y, Aggarwal NT, et al. Education and the course of cognitive decline in Alzheimer disease. Neurology. 2004;63(7):1198-1202. https://doi:10.1212/01.wnl.0000140488.65299.53

29. Teri L, McCurry SM, Edland SD, Kukull WA, Larson EB. Cognitive decline in Alzheimer's disease: a longitudinal investigation of risk factors for accelerated decline. J Gerontol A Biol Sci Med Sci. 1995;50A(1):M49-M55.

30. Teri L, McCurry SM, Edland SD, Kukull WA, Larson EB. Cognitive decline in Alzheimer's disease: a longitudinal investigation of risk factors for accelerated decline. J Gerontol A Biol Sci Med Sci. 1995;50A(1):M49-M55. https://doi:10.1093/gerona/50a.1.m49