The Effects of the Duration of Formal Education on Adult Brain: A Voxel-Based Morphometry – (Diffeomorphic Anatomical Registration Using Exponentiated Lie algebra) DARTEL Study

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ÖZET:
Okul eğitiminin süresinin erişkin beyni üzerine olan etkisi: Bir voksel tabanlı morfometri - DARTEL çalışması

Amaç: Son dönemde yapılan çalışmalar çevresel uyaranların sürekli verilmesinin beyinde yapısal değişiklikleri tetikleyebileceğini göstermiştir. Okul eğitimi sırasında, insan beyni sadece yeni bilgiler ile karşılaşmamakta, eski bilgilerini de çağırarak yenileri ile birleştirmektedir. Biz bu çalışmada, yoğun öğrenme sürecinin yaşandığı okulda geçirilen sürenin beyin üzerindeki etkisini voksel tabanlı morfometri (VBTM) – DARTEL yöntemini kullanarak araştırmayı amaçladık.
Yöntem: Bu çalışmaya 47 sağlıklı erişkin dahil edildi. SCID-NP ile taranan hastaların daha sonra 1.5 T gücündeki Siemens Manyetik Rezonans Görüntüleme cihazı ile beyin görüntüleri alındı. T1 ağırlıklı görüntüler SPM 5'te (Statistical Parametric Mapping software) VBTM protokolü kullanılarak değerlendirildi.
Bulgular: VBTM değerlendirmesi sonucunda sağ ön hipokampus hacminin eğitim ile korele olduğu tespit edildi. Bilateral oksipital loblarda (BA 18) ve sağ serebullum da eğitim süresinin artmasına paralel gri madde artışı tespit edildi. Sağ parietal korteks (BA 7) ve sağ orta frontal kortekste (BA 8) ise gri madde miktarı eğitim süresi ile negatif korelasyon göstermekteydi.
Sonuçlar: Bu çalışmanın sonuçları beyinin yeni uyaranın tespiti, semantik ve uzay bellek ve görsel sistemler ile ilgili alanlardaki gri madde hacmi ile okulda geçirilen süre arasında ilişki olduğunu göstermiştir. Bu ilişki ilgili alanlarının yoğun uyarımı ile ilişkili olabilir.

Anahtar sözcükler: Eğitim, manyetik rezonans görüntüleme, voksel tabanlı morfometri, DARTEL, hipokampus

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ABSTRACT:
The effects of the duration of formal education on adult brain: a voxel-based morphometry - (diffeomorphic anatomical registration using exponentiated lie algebra) DARTEL Study

Objective: Recent studies neuroimaging showed that continues environmental stimuli can induce structural changes in the brain. Compared to later life, during formal education in school and university; human brain is not only continuously stimulated with new information but also retrieves the already learned information and extends it with the new one. In this study, we explored the effects of this extensive learning process on brain structure by using voxel-based morphometry (VBM) –DARTEL method.
Method: Forty-seven healthy adults were included in this study. After screened carefully by SCID-NP, all subjects were scanned by Siemens 1.5T Magnetic Resonance Imaging machine. T1 weighted images were analyzed by SPM 5 (Statistical Parametric Mapping software) via VBM protocol.
Results: Our VBM results showed that the right anterior hippocampus gray matter volume was correlated with the duration of formal education. We also observed that education showed positive correlations with Brodmann (BA) 18 in the occipital lobes and with the right cerebellum. However, the right parietal cortex (BA 7) and the right middle frontal cortex (BA 8) showed negative correlations with education.
Conclusion: Our study showed that there is an association between the duration of formal education and the gray matter volume of brain regions related to the detection of novel stimuli, semantic and spatial memory and visual system which might be related to extensive learning process during formal education years.

Key words: Education, Magnetic Resonance Imaging, Voxel-based Morphometry, DARTEL, Hippocampus

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INTRODUCTION

Among other species in the world, Homo sapiens is the most successful species to create its own culture, art, and technology. This success was achieved by unique capabilities of human brain especially on higher cognitive functions and emotion processing. Every generation of human species created its own knowledge on culture and technology and taught this enormous information to the next generation. In the modern world, most of the teaching is taking places in the formal education system starting from elementary school to college education and the students are systematically influenced by the rich environmental stimuli in those years.

Recent brain morphometry studies showed that rich environment or training may change the brain structure (1-4). Animal studies showed that new cell formation especially in the hippocampus might be one factor responsible for these structural changes (5). Although current imaging technologies allow us a limited amount of information about the cell proliferation in vivo human brain, high resolution magnetic resonance imaging (MRI) studies showed that three months training on 3 ball juggling or 2 weeks practicing on mirror reading might induce gray matter changes in the brain (3,6). It is worth noticing that gray matter changes by juggling training vanished after training was stopped (6). This kind of reversal might not be seen in all kind of trainings. For example, medical students showed an increased gray matter volume in hippocampus and parietal cortex after an extensive studying for their final examination for three months (2). Three months after the examination, gray matter changes in the parietal cortex reversed but hippocampal volume continued to increase. This might be due to the processing of learned information that continues long after it is learned. Therefore, education in the formal years might have more impact on gray matter compared to short-term trainings. Indeed, studies (1,4,7) testing the brain reserve hypothesis (7) which proposes that high pre-morbid intelligence, education, and a stimulating life style provide ‘reserve capacity’ for the effects of aging and diseases on brain function, showed that education might have protective effect against brain atrophy in the old age.

In this study, we aimed to explore the effects of the duration of formal education on the adult brain. We hypothesized that duration in the formal education would be associated with specifically hippocampal volume in addition to other structural changes in the brain, as having a gateway function in memory formation. Here, we used a voxel-based morphometry approach to examine the regional effects of education on the human brain.

METHODS

Subjects

Forty-seven healthy volunteers (mean age: 30.6±7.2 yeas; 28 females, 19 males) were included in the study and screened by a psychiatrist with SCID-NP (Structured Clinical Interview for DSM-IV) non-patient version (Table 1). Subjects with the following criteria were excluded during the screening: having any DSM-IV axis I diagnosis, a first degree relative with psychotic disorders, any ongoing unstable medical disorder (including diabetes mellitus, hypertension and hypothyroidism), and a history of head trauma with more than 3 minutes of unconsciousness. Subjects were right-handed, actively working in a job which were what they had beeen trained for.. Fifteen subjects were occasionally drinking alcohol, which was not more than a few drinks per week, and twelve subjects were nicotine users who did not smoke cigarette more than 1 pack/day. This study was approved by Institutional Review Board and was done under the principles of Helsinki Declaration. All subjects were informed in detail by one of the researcher before the study and gave their informed consents.

MRI acquisition

The imaging was performed on a 1.5 Tesla MR unit (Magnetom Vision Symphony Upgrade, Siemens, Erlangen, Germany) with a circularly polarized head coil. Three-dimensional (3-D) T1-weighted images, using a magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence, were acquired with the following parameters: echo time (TE)= 3.93 ms, repetition time (TR)= 1600 ms, 2 mm coronal slices without gap, flip angle= 15°, NEX = 1, field of view (FOV)= 25 cm.

Voxel-based morphometry - DARTEL protocol

Voxel-based morphometry (VBM) was performed using SPM5 (Statistical Parametric Mapping, Wellcome Trust Center for Imaging Neuroscience, London, UK) (8). The VBM pre- processing included five steps:

(1) Check for scanner artifacts and gross anatomical abnormalities for each subject,

(2) Set image origin at the Anterior Commissure,

(3) Segment the images with Gaussian Mixture model implemented in SPM 5. This model is based on mixture of Gaussians and is extended to incorporate a smooth intensity variation and non-linear registration with tissue probability maps,

(4) Use “Diffeomorphic Anatomical Registration using Exponentiated Lie algebra” (DARTEL) toolbox to have a high-dimensional normalization protocol. We followed John Ashburner's chapter in its standard version including the MNI (Montreal Neurological Institute) space transformation (9),

(5) Check for homogeneity across sample and use the standard version of the smoothing (i.e., 8). After this pre-processing we obtained smoothed modulated normalized data that we used for the statistical analysis.

Statistical Analyses

We performed regression analyses using the number of years in the formal education as a regressor to evaluate the correlation between regional gray matter volumes and education. Sex, age and whole brain volumes were included in the design matrix of General Linear Model (GLM) as covariates to eliminate their possible effects on gray matter volume. In SPM analyses, we applied a threshold of p<0.001(uncorrected) across the whole brain. For all statistical tests, we excluded all voxels with a gray or a white matter value < 0.15 to avoid possible edge effects around the border between gray and white matter, and to include only voxels with sufficient gray matter proportion. The MNI coordinates of the significant voxels were converted to Talairach coordinates by Ginger ALE software.

Table 1: Socio-demographic and total brain volume variables of the studied group

Variables	Mean±SD (N=47)
Age (years)	30.64±7.1 (range 20-50)
Sex (male/female)	19/28
Education (years)	14.09±3.28 (range 5-18)
Total gray matter volume (cm^3)	724.66±68.04
Total white matter volume (cm^3)	496.84±64.68
Total brain volume (cm^3)	1660.43±206.25

RESULTS

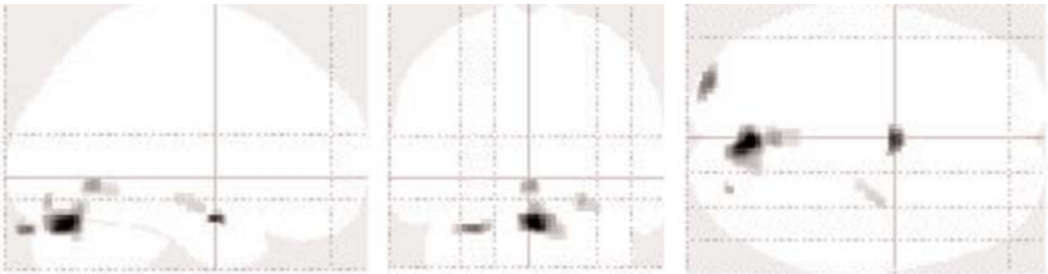
All socio-demographic variables are given in Table 1. When we correlated the education with total gray matter (GM) volume, we observed a positive relationship between two variables (r=0.42 p=0.003). However, when we repeated the analyses after controlling for age and gender, the significant correlation between total GM and

Table 2: The Effects of Formal Education on the Regional of Gray Matter

Region	Cluster size	Z	P	x	y	z*
Positive Correlation						
R Cerebellum (post lobe)	362	4.17	<0.001	3	-68	-14
R Cerebellum (Ant. Lobe)	129	3.59	<0.001	1	-57	0
BA 18 (Right)	48	3.46	<0.001	26	-77	-5
BA 18 (Left)	228	3.81	<0.001	-27	-88	-16
Hypothalamus	118	3.98	<0.001	0	0	-15
Hippocampus	64	3.28	0.001	32	-7	-11
Negative Correlation						
Right Parietal Lobe BA 7	186	4.54	<0.001	28	-64	31
Right Middle Frontal Gyrus BA 8	48	3.58	<0.001	18	31	40

*Talairach Space Coordinates

Positive Correlation



Negative Correlation

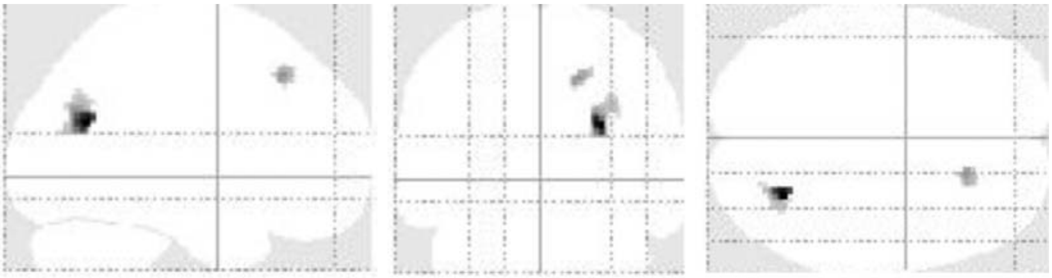


Figure 1: In the glass brain images (the neurological view), number of years in the formal education showed positive correlation with hippocampus, hypothalamus, BA 18 in the occipital lobes and the right cerebellum; but showed negative correlation with the parietal cortex (BA 7) and the middle frontal cortex (BA 8).

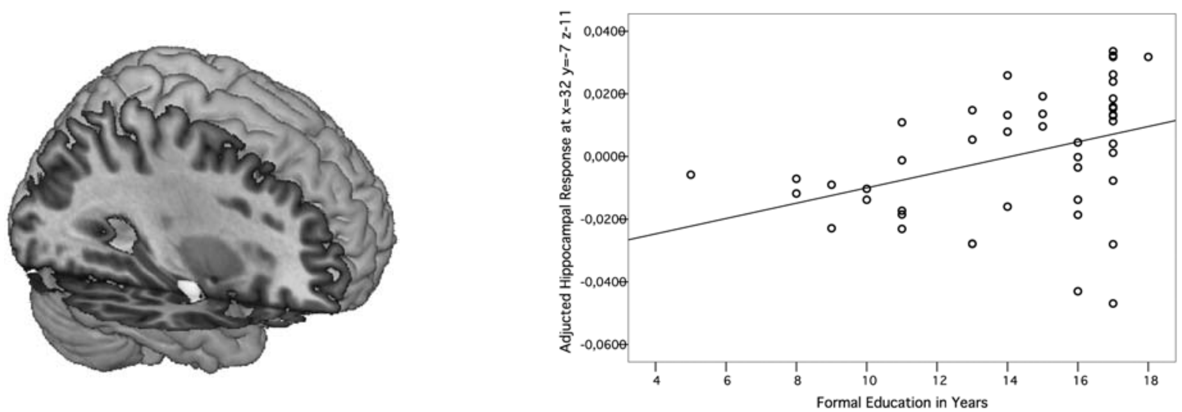


Figure 2: The right anterior hippocampus showed positive correlation with formal education (for visual enhancement p<0.005)

education was lost (r=0.13 df=43 p>0.05). Thus, in our sample, age and sex were better predictors than education for total GM volume (age, ß=-0.36 t=-2.75 p=0.009; sex, ß=0.6 t=4.77 p<0.001; education, ß=0.11 t=0.86 p=0.39).

When we explored the regional effect of education over GM, as we expected, the anterior hippocampal GM volume was correlated with education (Table 2, Fig. 1 and 2). Furthermore, we also observed that education showed positive correlations with gray matter volume in the Brodmann area (BA) 18 in the occipital lobes and with the right cerebellum. The parietal cortex (BA 7) and the middle frontal cortex (BA 8) showed negative correlations with education.

DISCUSSION

The results of this study showed that the number of years in the formal education has a significant correlation with specific brain regions like hippocampus, cerebellum, occipital, frontal and parietal cortex. These findings support the idea that duration of environmental stimuli during school years might affect the brain structure; hence brain is a plastic organ.

Education is a complex process including learning knowledge, information and developing skills on problem solving. During education, one of the main processes is to encode new information and later retrieve the already learned information and extend it with the new one. This process, both implicit and explicit memories are actively used in the formation of long-term memory (10). Among many brain structures, hippocampus plays a unique role in the long-term memory formation (11). Beyond its functional role as a gateway to our long-term memory, the human hippocampus has a capacity to generate neurons derived from local stem cells (12). Physical activity and enriched environment, i.e., more opportunity for social interacting and learning have been shown to improve the rate of neurogenesis and maintenance of these new cells (13,14). It is proposed that hippocampus is also functionally segregated. Functional neuroimaging studies have linked anterior hippocampal activity with the detection of stimulus novelty and encoding, while posterior hippocampus has been associated with memory retrieval (15,16). Hemispheric asymmetry has been reported with the right hippocampus often assumed to be especially important for spatial memory, whereas the left hippocampus has been more involved in context-dependent episodic memory (17,18). However, there are reports showing this kind of strict dissociation may not be valid (19,20). The finding of increased GM in the right anterior hippocampus in this study might be related to novel stimuli and encoding during formal years of education as functional studies suggested, and the local neurogenesis with new synapses formation might be responsible for this enlargement. This idea might be supported by a study of Maguire et al. (1998) who reported that London taxi drivers had more GM in their posterior hippocampus but less GM in their anterior hippocampus as they gain more experience in navigation in years and need to learn less (21). This effect might be due to necessity of the recalling function is greater than the encoding function of the hippocampus in experienced taxi drivers (22). This finding was later supported by a functional study showing decreased anterior hippocampal activity after initial learning (23). Draganski et al. (2) focused on short term effects of extensive learning and reported increased right posterior hippocampal volume enlargement even after three months of the learning period. However, one should be cautious about comparing the studies, because each study explored the different aspects of learning. While we were focused on the number years in education, Draganski et al focused on the short-term effects of intense learning. Thus, our finding on hippocampus might represent long-term adaptation to continuous learning rather term short term learning.

Both spatial and semantic memories are used extensively during education. Semantic memory is widely outspread in the neocortex, but spatial memory is formed in a restricted network including hippocampal complex, retrosplenial, occipitotemporal, frontal and parietal cortices (24-26). Our findings of GM changes in the parietal and frontal cortices might be related to both spatial and semantic memory formation. In support of this idea, Springer et al (27) reported education and memory were correlated in the medial temporal, parietal, and frontal cortices in the young age in a functional MRI study. It is remarkable that the recent study (27) reported functional loci in BA 7 in parietal cortex and BA 8 in prefrontal cortex, close to GM changes in our report. It is known that posterior and inferior parietal cortices are associated with information represented in the long-term memory (28). Recently, Draganski et al (2) reported GM changes in posterior parietal regions during extensive learning. On the other hand, BA 8 is best known with its function of controlling eye movements; however, it is also active in many cognitive processes especially during formation of spatial memory (26). Moreover, visual information processing is an important step of learning and memory. It was reported that complicated perceptual-motor skills like juggling or practice needed activity like mirror reading had increased GM in the visual system (3,6). Our findings in the occipital cortex and BA 8 should be evaluated in this context and might be related to long-term visual stimulation during education related activities.

Bonnet et al. (29) explored the effect of education on cerebral and cerebellar function at various attentional loads. They observed that in healthy young adults; increased load of attention is associated with higher activation of cerebellum and a lower activation of the cortical areas including medial prefrontal and inferior parietal cortices; in subjects with higher education level compared to subjects with lower education level. They proposed that during higher cognitive performance lower cerebral activity was balanced by higher cerebellar activity which might be related to automatized strategies that might decrease the work load of cortical regions in educated brains. This idea is partially supported by our findings of increased GM in cerebellum and decreased GM in parietal cortex and prefrontal cortex. Although functional loci of Bonnet et al.'s study (29) and GM structural changes in our study are not exactly on the same coordinates, as reported by Ilg et al (3), functional and anatomical changes may not be observed on the same coordinates but structural changes may modulate the functions of the neighboring areas.

The current study has several limitations. First, we did not measure the IQ scores of subjects involved in the study. Our sample had a mean of 14 years of education with a minimal education year of 5 years. It is very unlikely that we included anybody with mental retardation in our sample. All subjects had SCID-NP before the MRI scan by a psychiatrist and no mental retardation was reported for any of the subjects. It is reported that general intelligence is correlated with the lateral prefrontal cortex, cingulate, cerebellum, thalamus, and parietal cortex (30,31). Therefore, it is not possible to say that our findings for the cortical regions are independent from IQ scores of subjects. Another limitation is that our sample was mostly consisted of young adult subjects. Thus, our results might only represent the population of this age group. It has been reported that the highly educated older population use their frontal cortex more extensively compared to the highly educated younger population (27). Thus, structural pattern of the younger population may follow or lead this functional difference in our study.

To our knowledge, this is the first study specifically explored the effect of the duration of formal education on GM in adults and showed that formal education in school has produced significant changes in structures that are related to the detection of novel stimuli, semantic and spatial memory, and visual system.

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