The Age-related Microstructural Changes of the Cortical Gray and White Matter Ratios on T2-, FLAIR and T1- weighted MR Images

Sunseob Choi, Whi-Young Kim, Ki-Nam Lee, Dong-Ho Ha, Myong-Jin Kang, Jin Hwa Lee, Seong Kuk Yoon

Purpose : The purpose of this study was to investigate the microstructural changes according to aging on the thickness and signal intensity (SI) of the cortical gray matter (GM) and white matter (WM) on the T2-, fluid-attenuated inversion recovery (FLAIR) and T1- weighted MR images in normal subjects.

Materials and Methods : The 10, 20, 30, 40, 50, 60, 70, 80 and 90 year age groups of men and women (each 10 individuals) who underwent routine brain MRI, including the T2-, FLAIR and T1- weighted images, were selected for this study. We measured the thickness and the SI of the cortical GM and WM at the postcentral gyrus, which has an even thickness at the level of centrum semiovale, on the axial scans and we calculated the mean values of the thickness ratio of the gray/white matter (TRGW) and the signal intensity ratio of the gray/white matter (SRGW), and we compared the ratios of each age group.

Results : On the T2-weighted images, the TRGWs were 0.81 and 0.79 at the age of 10 and they were 0.73 and 0.71 at the age of 90 in the men and women, respectively. So, the GM thickness was decreased more than the WM thickness was with aging. On the FLAIR images, the TRGWs were 1.09 and 1.00 at the age of 10 and they were 1.11 and 0.95 at the age of 70 in the men and women, respectively. On the T1-weighted images, the TRGWs were 0.66 and 0.80 at the age of 10, and the ratio was changed to 0.90 and 0.78 at the age of 90 in the men and women, respectively. On the T2-weighted image, the SRGWs were 1.53 and 1.43 at the age of 10, and they were 1.23 and 1.27 at the age of 90 in the men and women, respectively. On the FLAIR images, the SRGWs were 1.23 and 1.25 at the age of 10 and they were 1.06 and 1.05 at the age of 90 in the men and women, respectively. On the T1-weighted images, the SRGWs were 0.86 and 0.85 at the age of 10, and they were 0.90 and 0.87 at the age of 90 in the men and women, respectively.

Conclusion : We suggest that the age-related microstructural changes of the thickness and the SI of the cortical GM and WM on the T2-, FLAIR and T1- weighted images are unique, and so this knowledge will be helpful to differentiate neurodegenerative disease from normal aging of the brain.

Index words : Brain, Aging, MRI

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Department of Radiology, College of Medicine, Dong-A University, Busan, Korea
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Corresponding author : Sunseob Choi, M.D., Department of Radiology, Dong-A University Medical Center, 1,3-ga, Dongdaeshin-dong, Seo-gu, Busan 602-715, Korea.
Tel. 82-51-240-5344 Fax. 82-51-253-4931 E-mail: sschoi317@yahoo.co.kr

Introduction

Knowledge of the microstructural changes of the brain cortex would be helpful for differentiating degenerative disease from normal aging. There have been reports that the cortical thickness shows linear changes according to aging (1, 2), and the cortical thickness decreased most significantly with age in the superior frontal area, and it showed a minimal difference in the gray matter (GM)/white matter(WM) ratio between men and women (3). The GM signal intensity(SI) was decreased with strong effects in the medial frontal area and the WM SI decreased in the superior and medial frontal areas, which demonstrated decreased overall contrast with aging in T1 weighted images. These findings may be an important biomarker of the pathologic changes with aging and according to disease (3). The aging effect on brain size may be more apparent in men than in women (4).

We studied the influence of aging on the micro-changes of a gyrus for the thickness and SI of the cortical GM and WM on T2-, fluid-attenuated inversion recovery(FLAIR) and T1-weighted images.

Materials and Methods

One hundred eighty patients (90 men and 90 women) who underwent routine brain MRI because of clinically suspected neurologic diseases, but who were diagnosed as normal on the basis of the MR findings and clinical follow up were selected for this study. The subjects were grouped with 10 individuals of the age of 10, 20, 30, 40, 50, 60, 70, 80 and 90 for the men and women, respectively (a total of 18 groups).

The T2-, FLAIR and T1- weighted images were scanned using a 1.5T MR machine with an 8 channel head coil (Excite HD, GE Medical Systems, Milwaukee, WI). The parameters for the fat saturated spin echo T2-weighted image were 3800/106/2 (TR/TE/excitation), a 320×224 matrix with a 20 cm field of view and a 5 mm thickness with a 2 mm gap. The parameters for the FLAIR image were 8000/134/1(TR/TE/excitation), an inversion time of 2000, a 256×192 matrix with a 20 cm field of view and a 5 mm thickness with a 2 mm gap. The parameters for the spin echo T1-weighted

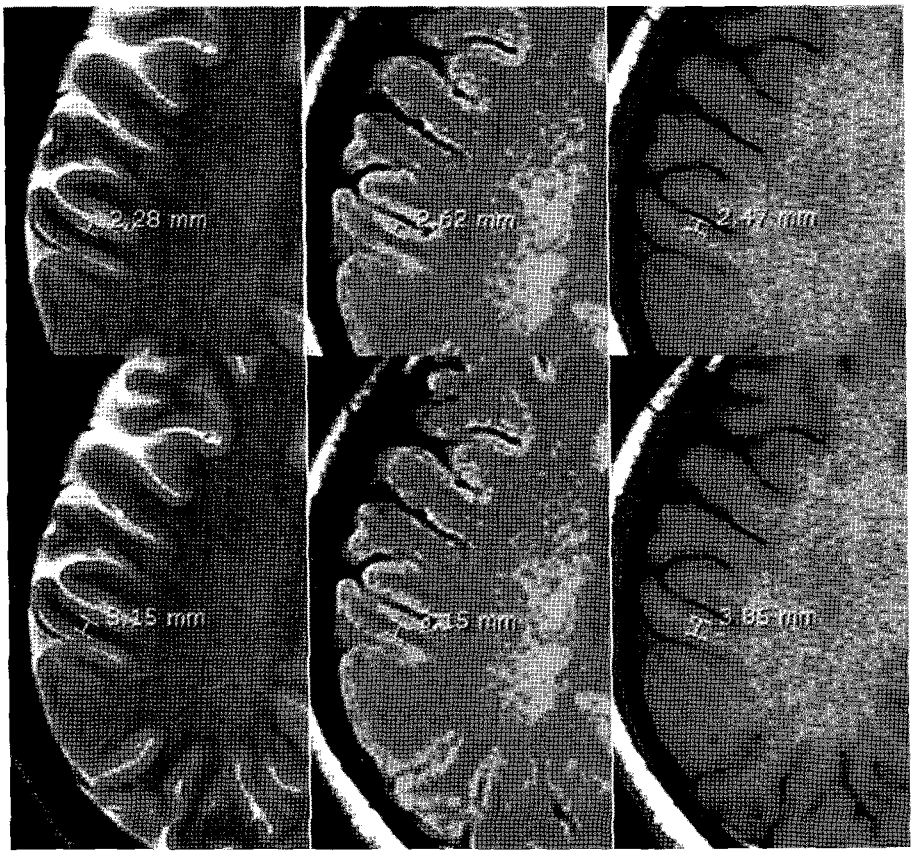

Fig. 1. Example of measuring the thicknesses of the cortical gray matter (upper row) and white matter (bottom row) on the T2-weighted (left), FLAIR (middle) and T1- weighted (right) images.

Table 1. The Thicknesses(mm) of the Gray Matter(GM) and White Matter(WM), and the Ratios of the Cortical Gray/White Matter Thickness of the Brain according to the Age Groups in the Men and Women on the T2-, FLAIR(FL) and T1-Weighted Images

	Age	10	20	30	40	50	60	70	80	90	Avg	STD
T2, M	GM	2.2	1.8	2.2	1.9	2.0	1.9	1.7	1.7	1.6	1.89	0.21
	WM	2.7	2.7	3.4	2.7	2.8	2.5	2.4	2.5	2.2	2.66	0.34
	Ratio	0.81	0.67	0.65	0.70	0.71	0.76	0.71	0.68	0.73	0.71	0.05
T2, F	GM	2.2	2.2	2.0	2.1	2.0	2.1	1.6	1.7	1.5	1.93	0.26
	WM	2.8	2.9	2.7	3.3	2.9	2.6	2.6	2.7	2.1	2.73	0.32
	Ratio	0.79	0.76	0.74	0.64	0.69	0.81	0.62	0.63	0.71	0.71	0.07
FL, M	GM	2.5	2.0	2.6	2.2	2.0	2.4	2.0	*	*	2.24	0.26
	WM	2.3	2.6	3.5	2.4	2.4	2.3	1.8	*	*	2.47	0.52
	Ratio	1.09	0.77	0.74	0.92	0.84	1.04	1.11	*	*	0.93	0.15
FL, F	GM	2.4	2.3	2.4	2.2	2.3	2.4	2.0	*	*	2.29	0.15
	WM	2.4	2.6	2.6	2.8	2.6	2.0	2.1	*	*	2.44	0.29
	Ratio	1.00	0.88	0.92	0.79	0.88	1.20	0.95	*	*	0.95	0.13
T1, M	GM	2.1	2.2	2.4	2.0	2.1	2.0	1.9	2.0	1.8	2.06	0.17
	WM	3.2	2.7	3.9	2.7	2.7	2.4	2.5	2.4	2.0	2.72	0.55
	Ratio	0.66	0.81	0.62	0.74	0.78	0.83	0.76	0.83	0.90	0.77	0.09
T1, F	GM	2.4	2.1	2.2	2.0	2.3	2.3	1.9	2.0	1.8	2.11	0.20
	WM	3.0	3.0	2.8	3.5	3.1	3.1	2.3	2.9	2.3	2.89	0.39
	Ratio	0.80	0.70	0.79	0.64	0.74	0.74	0.83	0.69	0.78	0.75	0.06

* On the FLAIR images, the measurements of the GM and WM thickness separately were not possible due to indistinct border caused by decreased GM SI and increased WM SI in the aged brain, and so the groups of the 80 and 90 year old age were excluded.

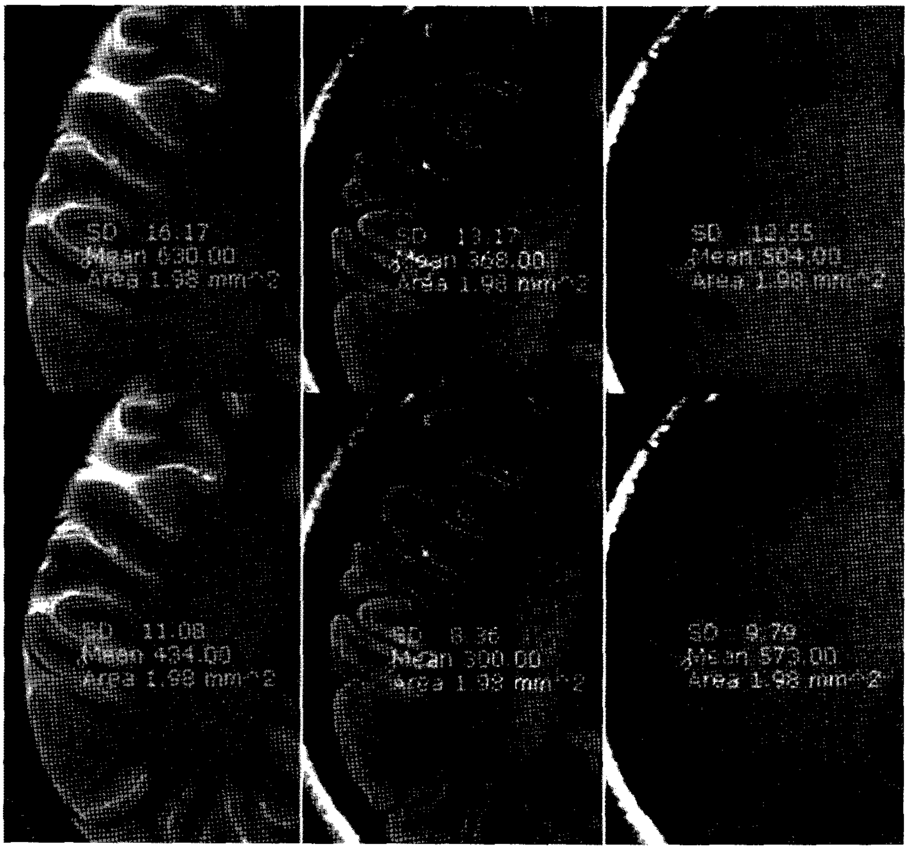

Fig. 2. Example of measuring the signal intensities of the cortical gray matter (upper row) and white matter (bottom row) on the T2-weighted (left), FLAIR (middle) and T1-weighted (right) images.

image were 400/10/1(TR/TE/excitation), a 320×192 matrix with a 20 cm field of view and a 5 mm thickness with a 2 mm gap.

Using PACS tool, we measured whole thickness of the gyrus, and measured the thickness and the SI of the cortical GM and WM at the postcentral gyrus, where it has an even thickness at the level of centrum semiovale, on the axial scans (Figs. 1, 2), and we calculated the mean values of the thickness ratio of gray/white matter(TRGW) and the signal intensity ratio of gray/white matter(SRGW) in each age group, and we compared the ratios according to the age of the men and women (Tables 1, 2). Statistical analysis was performed using *t*-test.

Results

On the T2-weighted images, the thicknesses of the gyrus were 7.1 mm and 7.2 mm at the age of 10, and 5.4 mm and 5.1 mm at the age of 90 in men and women, respectively, and so the whole thickness was decreased 24% and 29%, with a 27% and 32% decrease of the GM and a 19% and 25% decrease of the WM in the men and women, respectively. The TRGWs were 0.81 and 0.79 at the age of 10, and 0.73 and 0.71 at the age of 90 in the men and women, respectively (Fig. 3). On the FLAIR images, the thickness of the gyrus was 7.3 mm and 7.2 mm at the age of 10, and 5.8 mm and 6.1 mm at the age of 70, and so it was decreased 21% and 15% for the whole thickness, with a 20% and 17% decrease of the GM, and a 22% and 13% decrease of the WM in the men and women, respectively. The TRGWs were 1.09 and 1.00 at the age of 10, and 1.11 and 0.95 at the age of 70 in the men and women, respectively. The ratios showed the lowest value at the age of 30 in the men and at the age of 40 in the women due to decreased GM thickness (Fig. 4), but eventually the thicknesses of the GM and WM were decreased to a similar degree. The border between the GM and WM

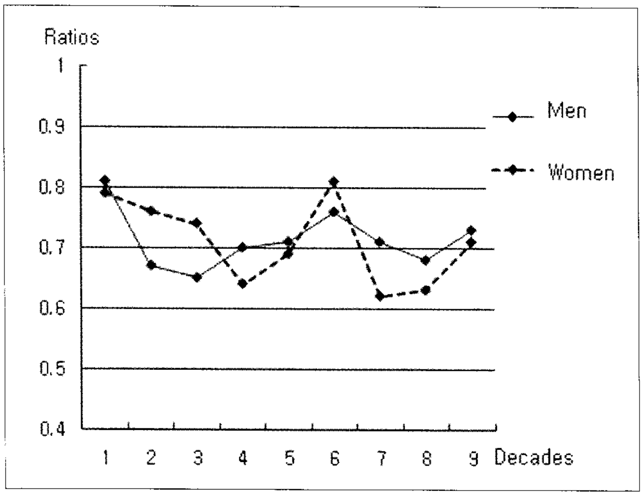

Fig. 3. The slopes of the thickness ratios on the T2-weighted images. The ratios decreased slightly with aging.

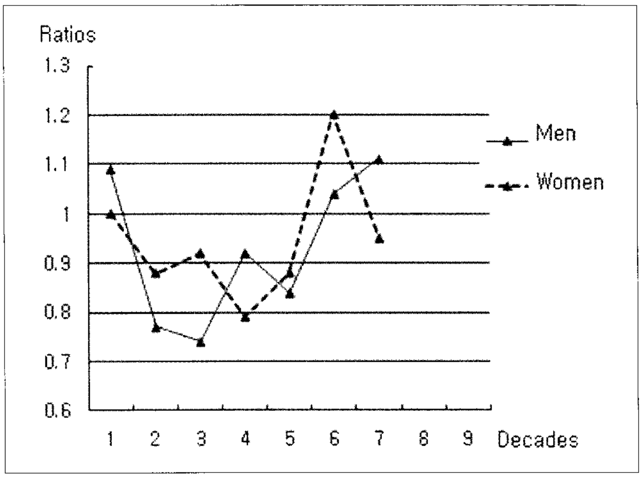

Fig. 4. The slopes of the thickness ratios on the FLAIR images. The ratios showed the lowest value at the age of 30 in men and at the age of 40 in women. The measurements of the GM and WM thickness separately were not possible in the aged brain, and so the 80 and 90 year old age groups were excluded.

Table 2. The Signal Intensity Ratios of the Cortical Gray/White Matter (SRGW) of the Brain according to the Age Groups in the Men and Women on the T2-, FLAIR and T1-Weighted Images

Age	10	20	30	40	50	60	70	80	90	Avg	STD
T2, M	1.53	1.39	1.44	1.36	1.39	1.38	1.29	1.28	1.23	1.37	0.09
T2, F	1.43	1.48	1.38	1.35	1.36	1.35	1.36	1.27	1.27	1.36	0.07
FL, M	1.23	1.27	1.25	1.23	1.19	1.11	1.12	1.07	1.06	1.16	0.07
FL, F	1.25	1.26	1.23	1.15	1.17	1.16	1.10	1.06	1.05	1.16	0.08
T1, M	0.86	0.87	0.84	0.87	0.88	0.95	0.90	0.91	0.90	0.89	0.03
T1, F	0.85	0.88	0.86	0.89	0.90	0.87	0.87	0.89	0.87	0.88	0.02

become indistinct with aging due to the decreased GM SI and the increased WM SI. So, it was not possible to measure the thickness of the GM and WM separately in some subjects after the age of 60 (6 and 5 subjects for the men and women. respectively) and 70 (1 and 2 subjects, respectively), and in most subjects at the age of 80 (9 and 7 subjects, respectively) and 90 (6 and 9 subjects in men and women, respectively), and so the 80 and 90 age groups were excluded from comparison with the results of the other images.

On the T1- weighted image, the thickness of the gyrus was 7.4 mm and 7.8 mm at the age of 10, and 5.6 mm and 5.9 mm at the age of 90, and so it decreased 24% and 24% for the whole thickness, with a 14% and 25% decrease of the GM and a 38% and 23% decrease of the WM in the men and women, respectively. The whole thickness of the gyrus was measured as 8% thicker on the T1-weighted images than that on the T2-weighted images. The TRGWs were 0.66 and 0.80 at the age of 10, and the ratios were changed to 0.90 and 0.78 at the age of 90 for the men and women, respectively (Fig. 5). The border between the GM and WM became somewhat unclear according to aging because of the decreased difference of SI between the GM and WM, and so the TRGW is less reliable in the aged brain on T1-weighted images. The changes of the TRGWs with age were significant on the FLAIR and T1-weighted images ($p < 0.05$).

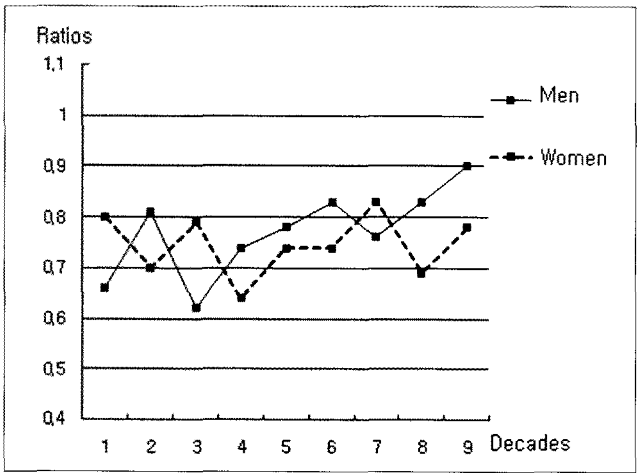

Fig. 5. The slopes of the thickness ratios on the T1-weighted images. The ratios increased slightly with aging.

On the T2-weighted image, as compared with the age of 10, the SIs at the age of 90 were decreased 11% and 6% in the GM, and the Sis were increased 9% and 5% in the WM in the men and women, respectively. The SRGWs were 1.53 and 1.43 at the age of 10 and they progressively decreased to 1.23 and 1.27 at the age of 90, and so they were decreased 20% and 11% in the men and women, respectively (Fig. 6).

On the FLAIR image, compared with the age of 10, the SIs at the age of 90 were decreased 9% and 10% in the GM and they were increased 7% and 8% in the WM in the men and women respectively. The SRGWs were 1.23 and 1.25 at the age of 10, they were 1.06 and 1.05, respectively, at the age of 90, and so the ratios are decreased 14% and 16% in the men and women, respectively (Fig. 7). The border between the GM and

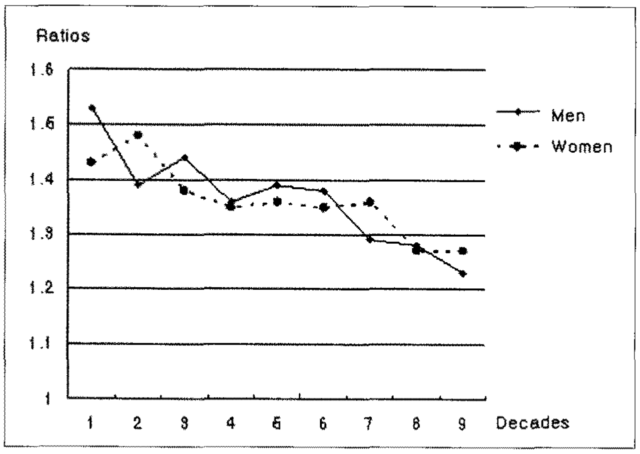

Fig. 6. The slopes of the signal intensity ratios on the T2-weighted images. The contrast between the GM and WM was decreased with aging.

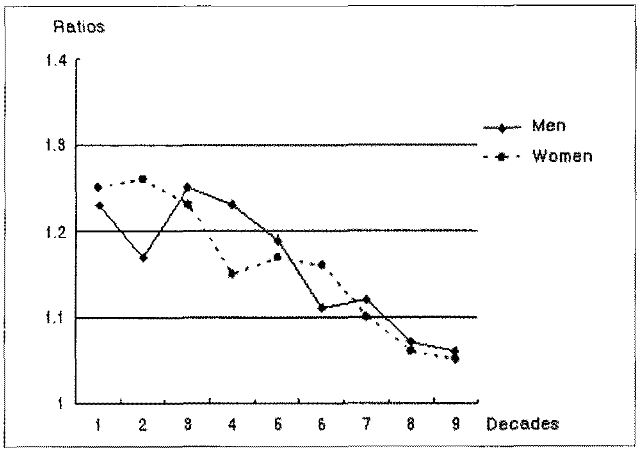

Fig. 7. The slopes of the signal intensity ratios on the FLAIR images. The ratios were decreased to 1 with aging, which means the contrast between the GM and WM had almost disappeared.

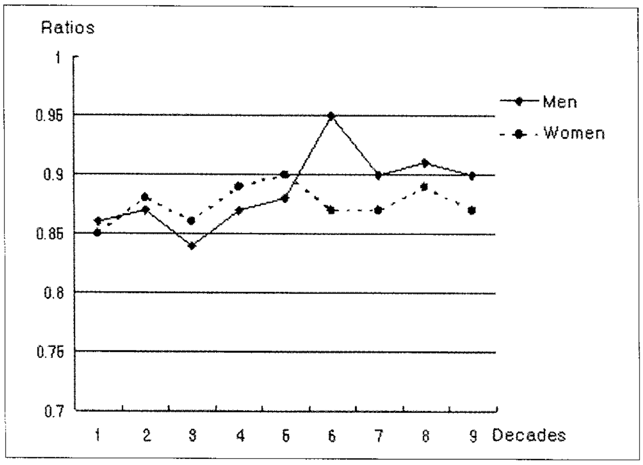

Fig. 8. The slopes of the signal intensity ratios on the T1-weighted images. The ratios were slightly increased with aging due to the decreased contrast between the GM and WM.

WM became unclear after the age of 40, and the measurement of the GM and WM SI separately was not possible after the age of 80 in most cases.

On the T1-weighted images, the SIs of the GM are increased 6% in the men and they were decreased 2% in the women, and the WM was increased 1% in the men and they were decreased 4% in the women, respectively. The SRGWs were 0.86 and 0.85 at the age of 10, and they were 0.90 and 0.8 at the age of 90, and so they were increased 5% and 2% in the men and women, respectively, which means this was the minimal contrast change between the GM and WM according to aging (Fig. 8). The changes of the SRGWs with age were significant on the T2-, FLAIR and T1-weighted images ($p < 0.05$).

Any gender differences in the TRGW and SRGW were not evident ($p > 0.05$).

Discussion

Normal aging is associated with substantial macrostructural changes of the brain such as enlargement of the ventricles and cortical sulci, and this all reflects brain atrophy. Those changes are the results of microstructural changes of the whole brain tissue, and the knowledge of the microstructural changes of the brain cortex would be quite helpful to differentiate degenerative diseases from normal aging of the brain (1, 2), but the microstructural changes of the GM and WM on MRI have not yet been fully clarified. There are strong regional changes in the properties of neural tissue with aging, and the GM and WM have different vulnerabilities to aging, and the SI itself could serve as an important biomarker of degeneration(3). Yet little is known on which tissue parameters are altered in the aging brain.

This type of analysis was previously difficult to perform due to the need for precise representations of the GM/WM and the GM/cerebrospinal fluid (CSF) borders. Microstructural imaging is important to achieve a complete picture of the complex changes that occur in the brain aging (5). There is a report that T2-weighted MRI and diffusion tensor MRI can demonstrate the microstructural age-related brain tissue changes (6). We thought that routine MRI also could provide information about the underlying subtle microstructural changes that occur with aging. So, we used the routine brain T2-, FLAIR, and T1- weighted images from a 1.5T MR scanner.

Every single cerebral gyrus is different for its thickness and SI due to the partial volume effect caused by its tortuosity. So, to compare the thickness and SIs, it is mandatory to measure the gyrus where it has even thickness with a straight shape. Thanks to advanced technology, conventional MRI can provide information on subtle microstructural changes, and conventional MRI offers a somewhat constant SI level, although the SI is not an absolute value.

Cerebral gyri have different thicknesses by the location, and on an axial scan the gyrus itself is usually scanned as an oblique section because of its tortuosity, and so it is mandatory to measure a place where the gyrus that has a typical shape and typical location to compare the thickness and SI. We chosen the postcentral gyrus as a representative gyrus as it is straight and it has an even thickness at the centrum semiovale level on an axial scan to minimize the partial volume effect when measuring the thickness or SI of the GM and WM. We measured the cortical GM thickness as the distance between the outer cortical surface and the GM/WM border. Because the SI itself is not an absolute value and it is affected by many factors, we adopted the TRGW and SRGW to exclude the effect of external factors.

In the previous studies, reductions of the cerebral cortex and subcortical volume were seen in the healthy aging brain, and cross-sectional studies of cortical thickness have reported linear changes over the adult life (1, 2). The mean thicknesses of the cerebral cortex in middle age were 2.21 mm and 2.18 mm in the men and women, respectively, and both genders showed a similar degree of global thinning, and this mean thickness did not differ in the younger or older group (2). The brain volume was decreased on the order of 0.2–0.5% annually, and the annual decline of the temporal and prefrontal volume was approximately 0.5% (4). Brain atrophy was reported to be accelerated with increasing age and this is due to preclinical Alzheimer dementia (1). The majority of the cortical mantle showed a thinning rate of at least 0.01 mm/decade and the greatest rate was found in the primary motor cortex as up to 0.07 mm/decade(2). The cortical thickness decreased most significantly with age in the superior frontal area (3).

In our study, on the T2-weighted image, the GM thickness was decreased more than the WM thickness was with aging, and the thickness of the GM was observed as the lowest value on the T2-weighted image due to the partial volume effect of the bright CSF SI of the cortical sulci. On the FLAIR image, the border become indistinct with aging because of the decreased GM SI and the increased WM SI, and so it was not possible to measure the thickness of the GM and WM separately in some subjects, and so the groups of the age of 80 and 90 were excluded when comparing the results of the other images. On the T1- weighted images, the border between the GM and WM became somewhat unclear according to aging because of the decreased difference of SI between the GM and WM, and so the TRGW is less reliable in the aged brain on the T1-weighted image. The thicknesses of the cortical GM and WM were measured differently on the different pulse sequences, and the ratios showed the highest value on FLAIR and the lowest value on the T2-weighted images.

The SI of the MRI depends on many factors such as main magnet homogeneity, coil sensitivity, pulse sequences, TR/TE, flip angle, slice thickness, the number of matrixes, the number of acquisitions etc. Because of a limitation for quantifying the SI, we adopted the SI ratio in the images with same scan parameters for comparing the SI of the GM and WM. There is a report that measurement of the SRGW is a practical way to evaluate delayed myelination (7). The SI changes of the WM in the infants and early children show dramatic changes and especially on FLAIR images due to myelination (8, 9). We excluded the images of the young children and the elderly subjects who had obvious high WM SI on the FLAIR images. The GM SI was decreased in the medial frontal area, and the WM SI was decreased in the superior and medial frontal areas, demonstrating decreased overall contrast with aging, and the GM/WM ratio was changed in the superior and inferior frontal areas (3).

In our study, on the T2-weighted images, the contrast between the GM and WM was decreased in the aged brain due to decreased GM SI and increased WM SI. FLAIR is an inversion-recovery pulse sequence designed to nullify or greatly reduce the SI from CSF and brain parenchyma, but it can more clearly show parenchyma. On the FLAIR images in our study, the SI of the GM was decreased and the SI of the adjacent WM was increased, and so the border between the GM and WM became unclear, and so the SI was less reliable on the FLAIR image in the old age subjects. In a previous study, the GM and WM SI was decreased with age, and the GM/WM ratio was increased with age due to the decreased WM SI on the T1-weighted image(3). In the present study, the border became unclear after the age of 40, and the measurements of the GM and WM SI separately were not possible on the T1-weighted images in 2 cases of the 80 and 90 year age groups, respectively. The patterns of change of the SI ratio on the T2-weighted and FLAIR images look similar with advancing age, and the ratios showed the highest value on the T2-weighted images and the lowest value on the T1-weighted images. The causes of the SI change are considered to be decreased water content, an increased iron concentration etc.

There are reports that the aging effect on brain size may be more apparent in men than in women (4), and the prefrontal WM volume was decreased during late adolescence, and particularly among female (10). The cortical thickness showed a minimal difference in the GM/WM ratio between the men and women in each age group (3). The effect of gender on the age-related changes of the brain structure was negligible on the age slope of the brain volumes both in healthy individuals and in individuals with Alzheimer dementia (11). In our study, any gender differences in the TRGW and SRGW were not evident. In this study, there is basic limitation in the measurement of the thickness of the GM and WM because of large voxel size compared with the object thickness itself, and it also has possibility of intraobserver variance according to the manual measurements.

To summary, in this study on the age-related microstructural changes of the cortical GM and WM, the border between the GM and WM became somewhat indistinct according to the aging. The GM thickness was decreased more than the WM thickness on the T2- weighted images. The GM thickness was decreased more in the middle age groups and the WM thickness was decreased more in the old age groups on the FLAIR images. The contrast between the GM and WM was decreased in the aged brain because of decreased GM SI and increased WM SI on the T2-weighted images. The contrast between the GM and WM almost disappeared according to aging on the FLAIR images. The contrast between the GM and WM was slightly decreased due to a mild increase of the GM SI according to aging on the T1-weighted images.

Conclusion

We suggest that the age-related microstructural changes of the thickness and the SI of the cortical GM and WM on the T2-, FLAIR and T1-weighted images are unique, and so this knowledge will be helpful for differentiating between neurodegenerative disease and normal aging of the brain.

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T2, FLAIR, T1 강조 MR영상에서 나이에 따른 뇌피질의 회질과 백질의 미세구조 변화

동아대학교 의과대학 영상의학교실

최순섭 · 김휘영 · 이기남 · 하동호 · 강명진 · 이진화 · 윤성국

목적: 정상인의 나이에 따른 뇌피질의 회질과 백질의 T2 강조, FLAIR, T1 강조 영상에서의 두께와 신호강도의 미세구조 변화 양상을 알고자 한다.

대상 및 방법: 남녀 각각 10 명씩의 10세, 20세, 30세, 40세, 50세, 60세, 70세, 80세, 90세 군의 T2, FLAIR, T1 강조 MR영상을 이용하였다. 뇌의 난형중심 부위의 축상영상에서 일정한 두께를 보이는 후중심뇌회 부위에서 피질의 회질과 백질의 두께와 신호강도를 측정하여, 각 군의 평균값을 구하여 나이 증가에 따른 회질/백질 두께 비와 회질/백질의 신호강도 비의 변화 양상을 비교 관찰하였다.

결과: T2 강조영상에서 회질/백질 두께 비는 남녀 각각 10세에는 0.81과 0.79, 90세에는 0.73과 0.71로써 회질이 백질의 두께보다 더 감소하였으며, 회질/백질 신호 비는 10세에는 1.53과 1.43, 90세에는 1.23과 1.27로써 남녀 각각 20%와 11% 감소하였다. FLAIR 영상에서 회질/백질 두께 비는 남녀 각각 10세에는 1.09와 1.00, 70세에는 1.11과 0.95였으며, 회질/백질 신호 비는 10세에는 1.23과 1.25, 90세에는 1.06과 1.05로써 남녀 각각 14%와 16% 감소하였다. T1 강조영상에서 회질/백질 두께 비는 남녀 각각 10세에는 0.66과 0.80이었고, 90세에는 0.90과 0.78로 변화하였으며, 회질/백질 신호 비는 10세에는 0.86과 0.85, 90세에는 0.90과 0.87로써 남녀 각각 5%와 2% 증가하였다.

결론: T2, FLAIR, T1 강조영상에서 뇌피질의 회질과 백질의 나이증가에 따른 두께와 미세신호강도의 변화 양상은 특징적이며, 이 양상을 이해하는 것은 뇌의 정상 노화와 퇴행성 질환을 구별하는데 도움을 줄 것으로 생각된다.

통신저자 : 최순섭, (602-715) 부산시 서구 동대신동3가 1, 동아대학교 의과대학 영상의학교실
Tel. 82-51-240-5344 Fax. 82-51-253-4931 E-mail: sschoi317@yahoo.co.kr