Changes in Total Cerebral Blood Flow with Aging, Parenchymal Volume Changes, and Vascular Abnormalities: a Two-dimensional Phase-Contrast MRI Study

Sun-Seob Choi[1], Haiying Liu[2], Tae-Beom Shin[1], Seong-Kuk Youn[1], Jong-Yong Oh[1], Young-Il Lee[1]

Purpose : To evaluate changes in total cerebral blood flow (tCBF) with aging, parenchymal volume changes and vascular abnormalities, using 2 dimensional (D) phase-contrast magnetic resonance imaging (PC MRI).

Materials and Methods : Routine brain MRI including T2 weighted image, time-of-flight (TOF) MR Angiography (MRA) and 2D PC MRI were performed in 73 individuals, including 12 volunteers. Normal subjects (12 volunteers, and 21 individuals with normal MRI and normal MRA) were classified into groups according to age (18-29, 30-49 and 50-66 years). For the group with abnormalities in brain MRIs, cerebral parenchymal volume changes were scored according to the T2 weighted images, and atherosclerotic changes were scored according to the MRA findings. Abnormal groups were classified into 4 groups: (i) mild reduction in volume, (ii) marked reduction in volume by parenchymal volume and atherosclerotic changes, and (iii) increased volume and (iv) Moya-moya disease. Volumetric flow was measured at the internal carotid artery (ICA) and vertebral artery bilaterally using the velocity-flow diagrams from PC MRI, and combined 4 vessel flows and tCBF were compared among all the groups.

Results : The age-specific distribution of tCBFs in normal subjects were as follows: 12.0$\pm$2.1 ml/sec in 18-29 years group, 11.8$\pm$1.9 ml/sec in 30-49 years group, 10.9$\pm$2.2 ml/sec in 50-66 years group. The distribution of tCBFs in the different subsets of the abnormal population were as follows: 9.5$\pm$2.5 ml/sec in the group with mild reduction in volume, 7.6$\pm$2.0 ml/sec in the group with marked reduction in volume, and 7.3$\pm$1.2 ml/sec and 7.0$\pm$1.1 ml/sec in the increased parenchymal volume and Moya-moya disease groups respectively.

Conclusion : Total cerebral blood flow decreases with increasing age with a concomitant reduction in parenchymal volumes and increasing atherosclerotic changes. It is also reduced in the presence of increased parenchymal volume and Moya-moya disease. 2D PC MRI can be used as a tool to evaluate tCBF with aging and in the presence of various conditions that can affect parenchymal volume and cerebral vasculature.

Index words : Cerebral blood flow
Aging
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Introduction

Volumetric blood flow is vital for tissue survival in the brain. Cerebral blood flow in turn is affected by the status of the cerebral blood vessels, parenchymal resistance and intracranial pressure. Recently, cerebral blood flow has noninvasively measured by phase contrast (PC) MRI. 2 dimensional (D) PC flow quantification technique is based on flow-induced phase shifts which are proportional to spin velocity, and mapping of these phase differences by subtraction of the flow encoded images from the flow compensated image.

There are some reports about cerebral blood flow in normal individuals (1–3), as well as variations in flow with age (3, 4), height, head size (1, 2) and sex (3). We were unable to find any reports of tCBF changes in relation to parenchymal volume change and vascular abnormalities.

The current study was undertaken to evaluate changes in tCBF with aging, parenchymal volume changes and cerebral vascular abnormalities using 2D PC MRI.

Materials and Methods

Brain MRIs (including T2 weighted images), TOF

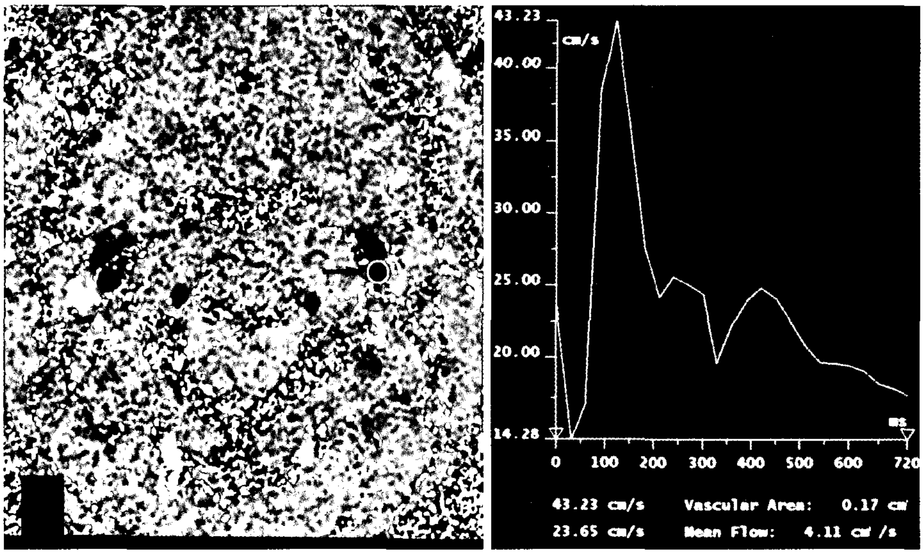

Fig. 1. Phase-contrast image (left) at the level of C2-3 intervertebral disc space shows region of interest (arrow) at the left internal carotid artery for flow measurement. The Velocity-flow diagram (right) shows mean flow as 4.11 cm^3/sec. Vertical axis is flow velocity and horizontal axis is one cardiac cycle.

Fig. 2. An example of mild reduction in volume group: T2 weighted images show mild ischemic changes at the deep white matter and mild dilation of the cortical sulci and the lateral ventricles (Evans index 33%).

MRA and 2D PC MRI were performed on 73 subjects (49 male and 24 female) using Magnetom vision (Siemens, Erlangen, Germany). Imaging parameters of T2 weighted image were as follows: TR/TE 5100/132 msec, FOV 17×23 cm, matrix number 315×512, slice thickness 6 mm, distance factor 0.2 and one acquisition number. 3D TOF MRA was done at the level of Circle of Willis with the following parameters: TR/TE/flip angle 27/7.2/20, FOV 15×20 cm, matrix number 200×512 and 10 cm slab thickness. 2D PC MRI was performed with EKG gating at the C2-3 disc level in the plane perpendicular to all four vessels. TR/TE/flip angle was 29/7/30 msec, velocity encoding value was 150 cm, phase numbers were 24–30, FOV was 15×15 cm, matrix was 192×256, slice thickness was 6 mm, excitations were 1 or 2, and scan time was 2–4.5 minutes. After getting localizer image and phase difference image with directional and velocity information, volumetric flows were measured from velocity-flow diagram according to the cardiac cycle by drawing circular regions of interest (ROI) at the four vessels on the phase difference image (Fig. 1).

Normal subjects (12 volunteers, and 21 individuals with normal MRI and normal MRA) were classified according to age into three groups: 18-29 years (N = 13, mean 25.7 years), 30–49 years (N = 9, mean 38.4 years), 50–66 years (N = 11, mean 57.3 years).

Parenchymal volume changes were scored subjectively, as mild (score 1, Fig. 2) or marked (score 2, Fig. 3) according to the degree of atrophy and the amount of high signal intensities in areas with chronic ischemic changes or old infarctions on T2 weighted

Fig. 3. An example of marked reduction in volume group: T2 weighted images show mild ischemic changes at the deep white matter and marked dilation of the cortical sulci and the lateral ventricles (Evans index 36%).

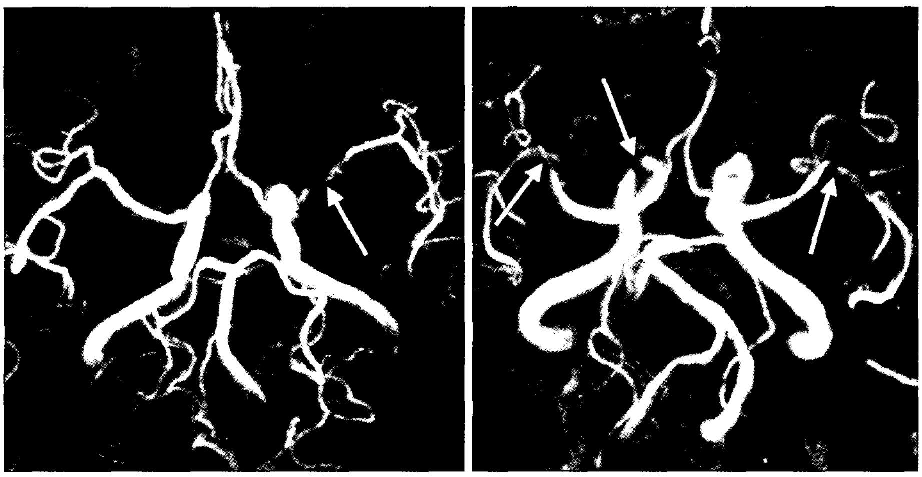

Fig. 4. An example of mild atherosclerotic change (left) and an example of marked atherosclerotic changes (right): MRA shows narrowing of one vessel (left, arrow) and show narrowing of multiple vessels (right, arrows).

images. Atherosclerotic narrowing of 50% or more of the major intracranial vessels were scored as mild (one vessel involvement, score 1) or marked (more than two vessels involvement, score 2) according to the findings of MR angiography (MRA) (Fig. 4).

Subjects with abnormalities on MRI and/or MRA were classified by combining the parenchymal volume and atherosclerosis scores: a score of 1–2 represented a mild reduction in volume (N = 17) whereas a score of 3-4 represented a marked reduction in volume (N = 12). Brain swelling, as evidenced by small ventricles and small cortical sulci or the presence of large brain tumors was classified as increased volume group (N = 6), and Moya-moya disease (N = 5) without parenchymal volume change was grouped separately.

The tCBF was calculated by adding the volumetric flow of the four vessels, and inter-group comparisons were made using the Student t-test.

Results

The age-specific distribution of tCBFs in normal subjects were as follows: 12.0±2.1 ml/sec in 18–29 years group, 11.8±1.9 ml/sec in 30–49 years group, 10.9±2.2 ml/sec in 50–66 years group. The differences were not significant ($p < 0.0001$) between these groups.

The distribution of tCBFs in the different subsets of the abnormal population were as follows: 9.5±2.5 ml/sec in the group with mild reduction in volume, 7.6 ±2.0 ml/sec in the group with marked reduction in

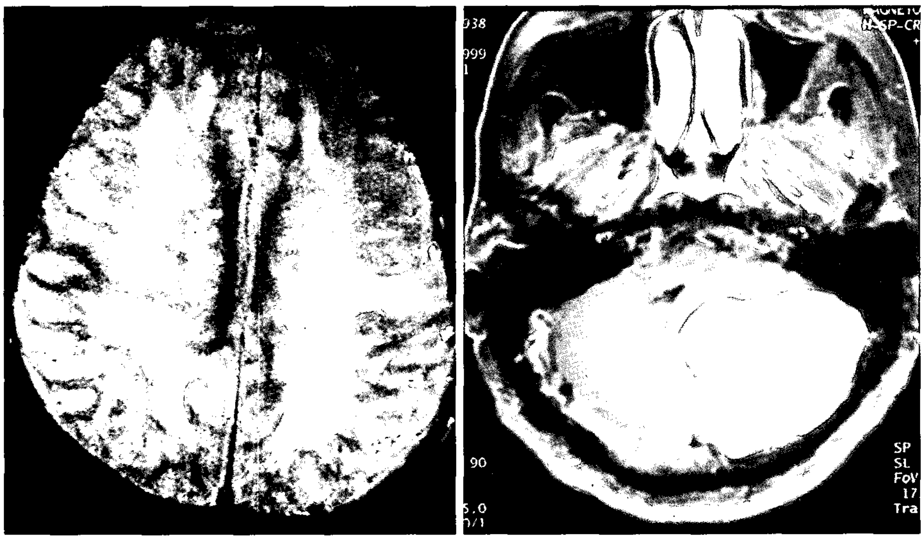

Fig. 5. Examples of increased volume group: T2 weighted image (left) shows diffuse high signal intensity at the white matter and obliterated cortical sulci due to the brain swelling caused by meningo-encephalitis. Post contrast T1 weighted image (right) shows densely enhancing large meningioma at the posterior fossa and markedly compressed fourth ventricle.

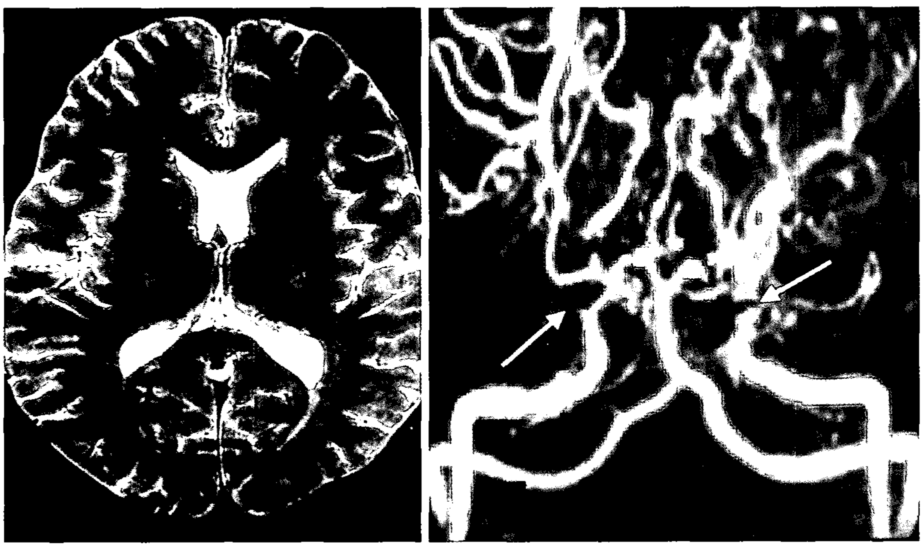

Fig. 6. An example of Moya-moya disease: T2 weighted image (left) shows no abnormality except some signal void of the salt and pepper pattern at the basal ganglia, and MRA (right) show obliteration of the terminal ICA (arrows) and marked telangiectatic collateral vessels.

volume, and 7.3±1.2 ml/sec and 7.0±1.1 ml/sec in the increased volume (Fig. 5) and Moya-moya disease groups (Fig. 6) respectively. The differences were significant ($p < 0.0001$), between normal and each abnormal groups by Student t-test.

Discussion

PC MRI provides a noninvasive tool to measure volumetric cerebral blood flow (1). PC MRI uses flow-induced phase shifts of moving spins that are proportional to spin velocity. Application of a flow compensation gradient is used to generate a flow compensated image. A flow-encoded image is then obtained by modifying the gradient system for flow rephasing. Subtraction of a flow-encoded image from a flow compensated image provides the phase difference image. The flow-velocity diagram depicting the flow pattern and volumetric flow is obtained by drawing the ROI at each vessel.

The level of scan is important for the exact quantification of tCBF. Most authors have reported scanning for tCBF measurement at the level of the cavernous portion of the internal carotid artery (ICA) and the basilar artery (the posterior inferior cerebellar arteries are not included) (2, 3, 5–7), the petrous portion of ICA (8), or in the upper cervical region (4, 9, 10).

PC MRI can be performed either as a 1 dimensional (11) or a 2 dimensional (3) technique. It can also be done with (6, 13, 14) or without (3, 5, 11, 12) cardiac gating. The scan time is about 30 sec without cardiac gating and about 3 min with cardiac gating. The measured tCBF values were 5.7% higher in the absence of cardiac gating (15). Flow quantification by PC MRI has a 3–5% error rate (3, 5), shows small inter- and intra-observer variability (4, 16), and is therefore, quite reproducible (8, 15). The blood flows were 142 ml/ min in the basilar artery, 229 ml/min in the left, 223 ml/min in the right ICA (1,2). However, tCBF measurement is much more significant compared to the blood flow in individual vessels, since the flow and pressure in each of the 4 vessels is rapidly compensated by the collateral circulation through the Circle of Willis.

Although the differences between the age groups were not significant in this study, Rempp et al have observed age-related reductions in rCBF with noninvasive dynamic susceptibility contrast-enhanced imaging (17), and Marks et al have observed a significant decline of volume flow with age in the basilar artery, but not in the carotid artery (7). The tCBF was 617 (1, 2) to 628 ml/min in a young adult (14), 748 ml/min between the ages of 19–29 years and 474 ml/min in the 80-89 years age group (3). This data suggests an age-related reduction in tCBF of the order of 4.8 ml/min/year. The volume of the brain parenchyma was 1363 ml (29 years group), and it dropped to 1025 ml (59 years group) after 30 years, thereby implying a loss of 11 ml per year (18). The latter reduction might be related to the decreased cerebral blood flow with aging. The tCBF did not show variability between sexes (3). It was noted to be influenced by height in contrast to basilar artery flow which was influenced by head size (1, 2). Mean vertebral flow was 165 ml/min in patients with vertigo and was similar to normal subjects (16). The tCBF increased to 157% after the injection of acetazolamide (4). PC MRI has been used to measure the reduction in cerebral blood flow following the inhalation of 100% oxygen (19), and hypoxia-induced cerebral vasodilation (20). Flow quantification using PC MRI has been used to evaluate intracranial pressure by measuring cerebral blood flow and CSF flow (10). Aqueduct flow mesasurement can assist in the diagnosis of normal pressure hydrocephalus (NPH) (21) and to predict a response to shunt operation in patients with NPH (22).

Our results suggest the reduction in cerebral blood flow have a possible direct relationship with the development of chronic ischemic changes or old infarctions. Conversely, the reduction in brain volume as a result of aging or previous ischemic damages may have resulted in a decreased demand for cerebral blood flow. Additionally, vascular narrowing may have a direct relationship with the reduced cerebral blood flow seen in atherosclerosis and Moya-moya disease. In the increased brain volume group, the reduction in cerebral blood flow may be caused by increased ICP and decreased elasticity due to swelling or compression of the brain that eventually results in decreased neural function.

In summary, we report a variety of age-related and disease-specific tCBF changes using the 2D PC MRI technique. This technique can be used to estimate and monitor the amount of loss of the functioning brain volume using serial measurements.

Conclusion

Total cerebral blood flow decreases with increasing age with a concomitant reduction in parenchymal volumes and increasing atherosclerotic changes. It is also reduced in the presence of increased parenchymal volume and Moya-moya disease.

2D PC MRI can be used as a tool to evaluate tCBF with aging and in the presence of various conditions that can affect parenchymal volume and cerebral vasculature.

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나이와 뇌실질부피 변화 및 혈관이상에 따른 총뇌혈류량 변화: 이차원 위상대조 자기공명영상을 이용한 연구

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목적 : 이차원 위상대조 자기공명영상을 이용하여 나이변화와 뇌실질 부피변화 및 혈관이상의 정도에 따른 총뇌혈류량의 변화를 알고자 하였다.

대상 및 방법 : 12명의 지원자를 포함한 73명을 대상으로 T2강조 영상과 Time-of-flight 방법의 자기공명혈관촬영과 이차원 위상대조 자기공명영상을 얻었다. 정상군은 지원자 12명과 자기공명영상 및 자기공명혈관촬영에서 정상소견을 보인 21 명으로서 이들은 18-29세, 30-49세, 50-66세 군으로 나누었다. 비정상군은 T2강조영상의 뇌실질부피 변화정도와 자기공명 혈관촬영의 동맥경화 정도에 따라 mild reduction군(17명), marked reduction군(12명)으로 나누었고, 뇌실질이 증가한 increased volume군(6명)과 Moya-moya군(5명)으로 분류하였다. 뇌혈류는 위상대조 자기공명영상의 속도-혈류 곡선으로부터 양쪽 내경동맥과 추골동맥에서 측정하고 합하여 뇌의 총뇌혈류량으로 하였으며, 각군 사이의 혈류량을 비교 관찰하였다.

결과 : 정상군의 총뇌혈류량은 18-29세군은12.0±2.1 ml/sec, 30-49세군은 11.8±1.9ml/sec, 50-66세군은 10.9±2.2 ml/sec였다. 비정상군 중에서 mild reduction 군은 9.5±2.5 ml/sec, marked reduction 군은 7.6±2.0 ml/sec, increased volume군은 7.3±1.2 ml/sec, Moya-moya군은 7.0±1.1 ml/sec였다.

결론 : 총뇌혈류량은 나이 증가에 따라 감소하였고, 뇌실질부피 감소와 동맥경화 정도에 따라 감소하였으며, increased volume군과 Moya-moya군에서도 감소하였다. 이차원 위상대조 자기공명영상은 나이변화나 뇌실질의 부피변화와 혈관이상을 초래하는 다양한 뇌질환에서 총뇌혈류량을 관찰할 수 있는 유용한 방법이라고 생각된다.

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