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High-field magnetic resonance imaging in patients with moyamoya disease

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Object. The purpose of this study was to assess the utility of high-field magnetic resonance (MR) imaging as a quantitative tool for estimating cerebral circulation in patients with moyamoya disease.

Methods. Eighteen patients with moyamoya disease who were scheduled to undergo revascularization surgery and 100 healthy volunteers were examined using T_2-reversed MR imaging performed using a 3-tesla system. Ten of the 18 patients underwent a second study between 1 year and 3 years after revascularization. Magnetic resonance images obtained in the patients with moyamoya disease were statistically analyzed and compared with those obtained in healthy volunteers. The MR imaging findings were also correlated with results of single-photon emission computerized tomography and conventional cerebral angiography studies.

Transverse lines in the white matter (medullary streaks) were observed in almost all persons. In healthy volunteers, the diameter sizes of the medullary streaks increased significantly with age ($p < 0.001$). Multiple logistic regression analysis revealed that age-adjusted medullary streak diameters were significantly larger in patients with moyamoya disease ($p < 0.001$). Diameter sizes also increased significantly with the increased severity of cerebral hypoperfusion ($p < 0.001$) and a higher angiographically determined stage of the disease ($p < 0.001$). Diameter sizes decreased significantly after surgery ($p < 0.001$).

Conclusions. The increases in medullary streak diameters observed in patients with moyamoya disease appear to represent vessels dilated due to cerebral hypoperfusion. High-field T_2-reversed MR imaging is useful in estimating cerebral circulation in patients with moyamoya disease.

KEY WORDS • moyamoya disease • magnetic resonance imaging • T_2-reversed imaging • cerebral circulation

MOYAMOYA disease is a cerebrovascular disease characterized by slowly progressive occlusion of major cerebral arteries and prominent collateral artery formation (moyamoya vessels).[12] The disease is prevalent among young children of east Asian ethnicity. Most cases occur sporadically, although approximately 10% of the disease is familial.[3] Indeed, recently the familial form of moyamoya disease has been linked to genetic markers located at chromosome 3p24.2–26.[4]

Using high-resolution T2R MR images obtained on a high-field (3-tesla) system, we previously reported that direct visualization of the pathological findings in moyamoya disease, that is, stenosis or occlusion of the major arteries and moyamoya vessel formation, can now be readily obtained without resorting to conventional cerebral angiography.[2] We have additionally noted that medullary streaks—linear structures crossing the white matter of the brain—are consistently observed in patients with moyamoya disease and are more prominent in the more severely affected hemisphere (Figs. 1 and 2). We propose that the medullary streaks observed in patients with moyamoya disease reflect abnormal conditions of cerebral circulation and may be used to develop a quantitative index of the disease process. Considering the fact that young children represent the majority of the patient population with moyamoya disease, it would be beneficial to develop a single noninvasive diagnostic test that yields both anatomical and quantitative information. Accordingly, we performed the current correlation studies.

Clinical Material and Methods

Patient Population

Eighteen patients with moyamoya disease and 100 healthy volunteers participated in the study. The mean age of healthy volunteers was 37.7 years (14 patients in the second decade, 24 in the third, 16 in the fourth, 15 in the fifth, 16 in the sixth, and 15 in the seventh decade of life). In none of the volunteers was there a diagnosis of cerebrovascular ischemic stroke, hypertension, or congestive heart failure. The patients' clinical profiles are summarized in Table 1. All 18 patients underwent conventional

Abbreviations used in this paper: ANOVA = analysis of variance; MR = magnetic resonance; SPECT = single-photon emission computerized tomography; T2R = T_2-reversed.

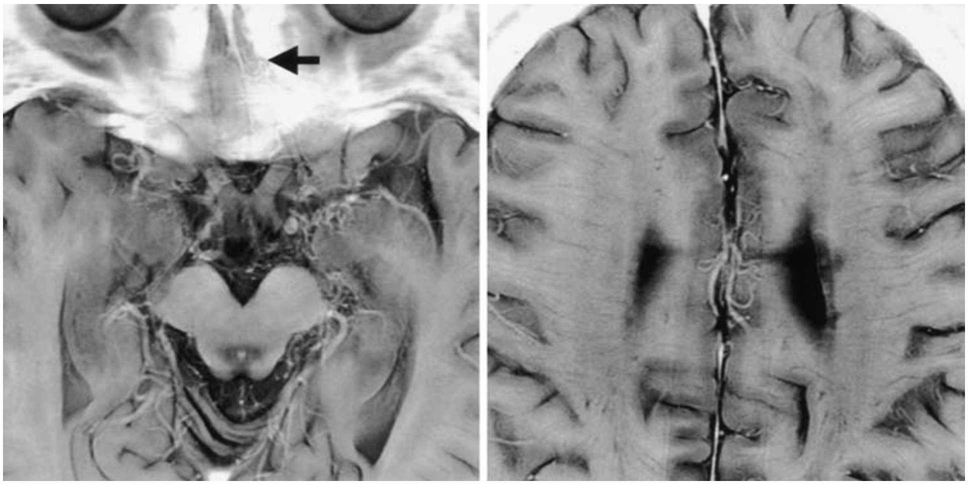

FIG. 1. Axial MR images obtained in a 37-year-old woman with moyamoya disease. Note visualization of linear structures throughout the white matter (medullary streaks) as well as fine moyamoya vessels (*arrow* identifies ethmoid moyamoya vessels).

cerebral angiography, SPECT scanning, and high-field MR imaging as part of their preoperative evaluation for revascularization surgery. Twelve of the 18 patients displayed neurological symptoms and SPECT-confirmed hemispheric hypoperfusion, thereby meeting our institution's criteria for revascularization surgery. Our standard postoperative follow-up protocol included interval clinical evaluation, as well as conventional cerebral angiography, SPECT scanning, and high-field MR imaging performed at least 1 year after the revascularization procedure. At the time of writing, 10 of the patients who underwent revascularization have passed the 1-year postoperative point. None of the patients has been lost to follow up.

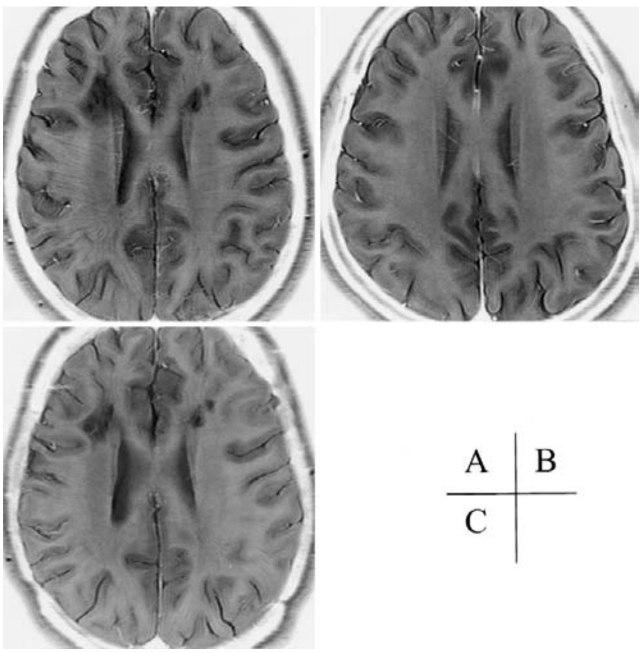

FIG. 2. Axial MR images obtained in a 17-year-old woman with moyamoya disease before treatment (A) and after revascularization surgery (C). Note the high density of medullary streaks, which is more marked in the right hemisphere. An axial MR image obtained in a 19-year-old healthy volunteer is shown for comparison (B).

High-Field MR Imaging

A 3-tesla MR system (Signa; General Electric Medical Systems, Waukesha, WI) equipped with a superconductive magnet operated at 3 teslas (Magnex; Abingdon, Oxon, UK) was used to perform all MR imaging studies. The studies were performed according to the human research guidelines of the Internal Review Board of the University of Niigata. Informed consent to undergo high-field MR imaging studies was obtained from all participants.

Data were obtained using a standard fast spin–echo sequence with the following parameters: TR 4000 msec; TE 17 msec; two acquisitions; field of view 20×20 cm; matrix size 512×512; and a 12-echo train. Due to the specific absorption rate, the number of slices obtained during a single session was limited to 16 slices. Raw data were obtained using 256 phase-encoding steps (eight experiments) and were zero-filled into 512 data points. The total imaging time necessary to obtain 16 slices was approximately 6 minutes. After conventional two-dimensional Fourier transformation, the gray scale of the images was inverted and given an expanded window range (T2R).[2]

Medullary streaks were defined as linear structures that could be observed crossing the frontal aspect of the semioval center on axial images. The diameters of the medullary streaks were determined by counting the number of pixels (390×390 μm) covering the width of the streaks. The mean of the largest five diameters was used for statistical analysis.

Cerebral Angiography

Conventional radiographical angiography was performed in all patients. The findings were classified according to the criteria of Suzuki and Takaku[12] as follows: Stage 1, narrowing of the carotid siphon; Stage 2, initiation of moyamoya vessels; Stage 3, intensification of moyamoya vessels; Stage 4, reduction of moyamoya vessels; and Stage 5, minimization of moyamoya vessels.

TABLE 1
*Summary of clinical data in 18 patients with moyamoya disease**

							Laterality in Hypoperfusion		Angiographic Stage		Angiographic Patency†		Diameter of Medullary Streak			
													Preop		Postop	
Case No.	Age (yrs), Sex	Type of Moyamoya Disease	RS	Side of RS	Type of RS	Postop Symptom Recurrence	Preop	Postop	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt
1‡	14, F	ischemic	yes	bilat	A & M	no	lt	lt§	2	3	good	good	2.2	3.6	1.6	1.8
2‡	42, M	ischemic	yes	bilat	A & M	no	rt	none	4	2	good	good	3.6	1.4	1.8	1.6
3‡	50, M	ischemic	yes	lt	A & M & G	no	lt	none	3	4	NA	good	1.8	4.0	1.8	1.8
4‡	17, F	ischemic	yes	bilat	A & M & G	no	rt	rt	4	3	good	good	3.0	0.8	1.4	0.4
5‡	42, F	ischemic	yes	bilat	A & M	no	lt	none	3	4	good	good	0.6	2.0	0.8	1.8
6‡	37, F	ischemic	yes	lt	A & M	no	lt	none	1	3	NA	good	1.0	3.4	1.4	1.2
7‡	23, M	ischemic	yes	bilat	A & M & G	no	none	none	3	3	poor	good	3.0	2.4	2.4	1.0
8‡	22, F	ischemic	yes	rt	A & M & G	no	rt	none	4	3	good	NA	3.0	1.4	2.0	1.4
9‡	15, M	ischemic	yes	lt	A & M	no	lt	none	1	3	NA	good	0.4	2.8	0.8	1.8
10‡	28, F	ischemic	yes	bilat	A & M & G	no	lt	none	3	3	good	good	3.0	4.0	1.8	1.6
11	26, F	ischemic	yes	bilat	A & M	no	rt	NA	3	3	NA	NA	3.8	2.4	NA	NA
12	36, F	ischemic	no	NA	NA	NA	lt	NA	3	4	NA	NA	1.8	2.8	NA	NA
13	35, F	ischemic	no	NA	NA	NA	none	NA	5	5	NA	NA	2.6	2.8	NA	NA
14	29, F	ischemic	no	NA	NA	NA	none	NA	4	4	NA	NA	1.2	1.6	NA	NA
15	61, F	ischemic	no	NA	NA	NA	none	NA	4	2	NA	NA	2.4	2.0	NA	NA
16	40, F	neither	no	NA	NA	NA	rt	NA	5	1	NA	NA	4.0	1.4	NA	NA
17	21, F	hemorrhagic	yes	bilat	A & M	no	none	NA	3	3	NA	NA	2.2	2.6	NA	NA
18	24, F	hemorrhagic	no	NA	NA	NA	none	NA	3	3	NA	NA	0.6	0.6	NA	NA

* A = superior temporal artery–middle cerebral artery anastomosis; G = encephalogaleosynangiosis; M = encephalomyosynangiosis; NA = not applicable; RS = revascularization surgery.
† Refers to patency of revascularization bypass.
‡ Patient was followed for longer than 1 year postsurgery and completed study protocol.
§ Patient had left frontoparietal lobe infarction.

Single-Photon Emission Computerized Tomography

The SPECT studies were obtained using *N*-isopropyl-p-[^{123}I]iodoamphetamine) on a triple-headed system (GCA-93A/HG; Toshiba, Tokyo, Japan). The presence of asymmetry in perfusion between the right and left frontal lobes was judged according to the following criteria: 1) decrease in radioactivity within one frontal lobe demonstrated on the early image; and 2) improvement revealed on the late image (3 hours after the injection).

Statistical Analysis

The T2R images were examined by neuroimaging specialists who were blinded to the patients' clinical parameters and angiography and SPECT findings. In cases in which there was a difference in the diameter sizes of medullary streaks between the two hemispheres, the larger value was used for statistical analyses. Analysis of variance in linear regression was used to assess correlations between the medullary streak diameter and the patient's age and findings on angiograms and SPECT scans. Simple and multiple linear regression analyses were used to examine the correlation between diameters of medullary streaks and patient age. A paired t-test was used to test the significance of changes in diameter sizes of medullary streaks in patients with moyamoya disease after surgery. Multiple logistic regression analysis was used to assess factors independently associated with moyamoya disease. Values are expressed as the means ± standard errors of the means. For all tests, probability values less than 0.05 were considered to indicate statistical significance.

Results

Figure 3 summarizes our findings on medullary streak diameters in patients with moyamoya disease and in healthy volunteers. The statistical values are summarized in Tables 2 and 3. The mean diameter size in healthy volunteers increased with age: 0.6 ± 0.1 pixels in the second decade, 0.7 ± 0.1 pixels in the third, 1.1 ± 0.1 pixels in

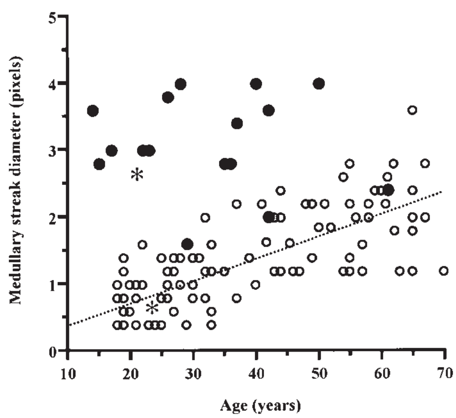

FIG. 3. Graph representing the distribution of medullary streak diameter size against age. *Dotted line* indicates the correlation between diameter size and age in 100 healthy volunteers (simple linear regression analysis: r = 0.713, p < 0.001). *Open circles* = healthy volunteers; *closed circles* = patients with moyamoya disease and ischemia; *asterisks* = patients with moyamoya disease and hemorrhage.

TABLE 2

*Relationship of diameter of medullary streaks to age and moyamoya disease in 18 affected patients and 100 healthy volunteers**

Parameter	Standard β Coefficient	t Value	p Value
age (yr)	0.456	7.921	<0.001
moyamoya disease (yes or no)	0.735	12.76	<0.001

* Parameters were significantly associated with the diameter of medullary streaks according to multiple linear regression analysis.

the fourth, 1.4 ± 0.1 pixels in the fifth, 1.8 ± 0.1 pixels in the sixth, and 2.1 ± 0.2 pixels in the seventh decade of life. The diameters of medullary streaks in patients with moyamoya disease were significantly larger than those found in healthy age-matched volunteers ($p < 0.001$).

The mean diameters of medullary streaks in patients increased significantly with the severity of the angiographically determined stage of the disease ($p < 0.001$; Fig. 4). Increased medullary streak diameter size was found to lateralize to the hemisphere with the higher degree of hypoperfusion, as determined by SPECT findings (Fig. 5); that is, diameter size increased significantly with increased severity on cerebral hypoperfusion ($p < 0.001$).

In patients with moyamoya disease the mean medullary streak diameter before surgery, 3.6 ± 0.6 pixels, decreased significantly after revascularization surgery to 1.8 ± 0.3 pixels ($p < 0.001$; Fig. 6).

Discussion

Moyamoya disease is a unique vasoocclusive disease that affects the internal carotid arteries bilaterally, with attendant rich collateral arteries located at the base of the brain. Efforts to elucidate its pathogenesis and to establish medical treatment for moyamoya disease have been unfruitful, although recently the familial form of moyamoya disease has been linked to genetic markers located at Chromosome 3p24.2–26.[4] The mainstay of treatment for symptomatic moyamoya disease remains surgical revascularization procedures, such as superficial temporal artery–middle cerebral artery anastomosis and encephaloduroarteriosynangiosis.[3] However, no randomized studies have been performed to assess surgical efficacy in the prevention of ischemic events or intracranial bleeding. Such studies would be greatly facilitated by the availability of a convenient assessment tool capable of providing structural and functional information.

In this report we have demonstrated the utility of high-field high-resolution T2R MR imaging as a single noninvasive neuroimaging procedure capable of providing quantitative information about cerebral perfusion and anatomical structures present in moyamoya disease. Medullary streaks observed on high-resolution T2R MR images correlated quantitatively with perfusion-related parameters obtained by SPECT and cerebral angiography. Reassessment of the diameter sizes of medullary streaks following revascularization surgery further demonstrated that quantitative assessment of the medullary streaks can serve as a sensitive indicator of cerebral circulation and a valuable tool for assessing treatment effect.

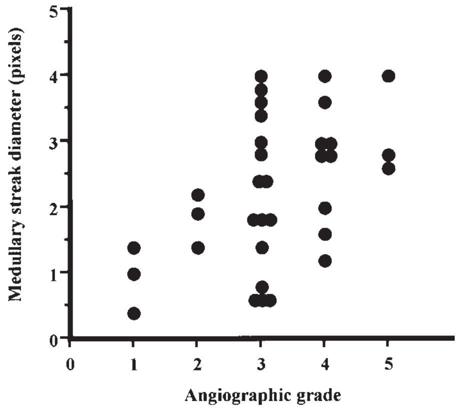

FIG. 4. Graph depicting correlation between the medullary streak diameter and angiographically determined stage of the disease. The diameters of the medullary streaks increased significantly with the severity of the disease ($p < 0.001$; ANOVA in linear regression).

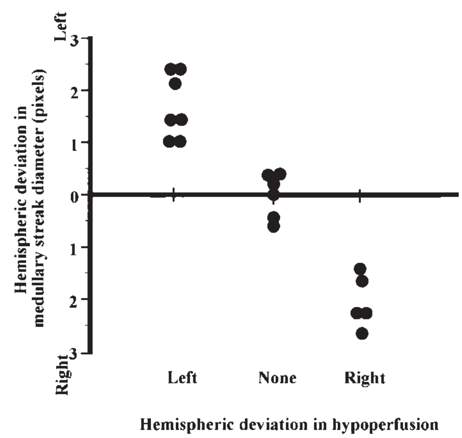

FIG. 5. Graph depicting the correlation between medullary streak diameter, expressed as a hemispheric deviation in medullary streak diameter (left hemisphere diameter − right hemisphere) and the hemisphere with the more severe hypoperfusion. Hemispheric deviation in streak diameter correlated inversely and significantly with hemispheric deviation in hypoperfusion severity ($p < 0.001$) defined by SPECT scanning (ANOVA in linear regression).

TABLE 3

*Evaluation of independent factors associated with the ratio of 18 patients with moyamoya disease to 100 healthy volunteers**

Parameter	SD	t Value	Odds Ratio†	95% CI	p Value
age (yr)	15.8	−2.713	0.122	0.268–0.558	0.008
diameter of medullary streaks (pixel)	0.98	3.859	28.88	5.233–159.3	<0.001

* Parameters were independently and significantly associated with the ratio of patients with moyamoya disease to healthy volunteers according to multiple logistic regression analysis. Abbreviations: CI = confidence interval; SD = standard deviation.

† Odds ratio indicates changes (ratio) in the probability of the ratio of patients with moyamoya disease to healthy volunteers when explanatory variables increased by one standard deviation.

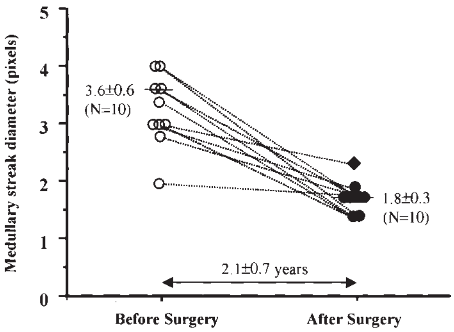

FIG. 6. Graph representing changes in medullary streak diameter after revascularization surgery. Streak diameter decreased significantly after surgery ($p < 0.001$; paired t-test). *Solid diamond* represents the single patient in whom patency of the revascularization bypass on conventional angiography was not demonstrated.

Although this study was not specifically designed to elucidate the pathogenetic mechanisms underlying medullary streak formation in moyamoya disease and aging, the results nevertheless provide insight concerning their significance. The MR relaxation properties indicate that medullary streaks represent spaces occupied by stagnant fluid. The increases in medullary streak diameter that accompany advancing age, which we observed in this study, coincide with the histopathological findings of age-related enlargement of fluid-filled perivascular spaces that accompany senile brain atrophy;[9] we can infer from this that the perivascular spaces are the basis for the increased diameter size of medullary streaks in the aging brain. Several lines of evidence indicate that there is a different pathogenetic mechanism leading to the increased medullary streak diameter size observed in moyamoya disease. Positron emission tomography studies of patients with moyamoya disease have shown cerebral blood flow to be decreased and cerebral blood volume increased compared with findings in healthy volunteers. These hemodynamic abnormalities were found to improve after revascularization surgery.[5,7,13] Similarly, our results clearly demonstrated that medullary streak diameters in patients with moyamoya disease were increased commensurate with the degrees of hypoperfusion, and were normalized following revascularization surgery. Certain pathological vascular conditions associated with increased cerebral blood volume, such as sinus thrombosis and venous angioma, result in dilation of medullary vessels, which indeed can be identified using conventional MR imaging and during postmortem examination.[1,6,8,10,11] It is plausible, therefore, that the medullary streak enlargement associated with moyamoya disease is attributable primarily to dilation of medullary vessels rather than expansion of perivascular spaces. Although speculative, medullary streaks in moyamoya disease likely represent dilated medullary vessels with stagnant flow. Further studies are warranted to delineate the identity of medullary streaks in moyamoya disease.

Conclusions

The accentuated medullary streaks in patients with moyamoya disease appear to represent medullary vessels that are dilated due to cerebral hypoperfusion. High-field T2R MR imaging represents a useful single noninvasive clinical tool for use in patients with moyamoya disease because it provides both structural and quantitative information regarding cerebral perfusion.

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