

# Cerebral Blood Flow in Pure Dysarthria

## Role of Frontal Cortical Hypoperfusion

Bungo Okuda, MD, PhD; Keita Kawabata, MD, PhD;  
Hisao Tachibana, MD, PhD; Minoru Sugita MD, PhD

**Background and Purpose**—Isolated dysarthria, termed pure dysarthria, develops rarely after stroke, and its pathophysiology remains unclear. To clarify the underlying mechanism of pure dysarthria, we investigated lesion sites and cerebral blood flow in patients with pure dysarthria.

**Methods**—We examined 12 patients with pure dysarthria who underwent MRI and cerebral blood flow study. To visualize cortical blood flow, a three-dimensional display was generated from single-photon emission computed tomography (SPECT). Regional cerebral blood flow of the patients was semiquantitatively measured with SPECT and *N*-isopropyl- $^{123}\text{I}$ iodoamphetamine as a tracer and compared with that of 11 control subjects.

**Results**—On MRI, multiple lacunar infarctions were noted bilaterally in 11 patients, all of whom had lesions involving the internal capsule or corona radiata. The other patient had a unilateral internal capsule–corona radiata infarction. Three-dimensional display showed frontal cortical hypoperfusion in 8 patients. Since interhemispheric differences of blood flow were not significant in any region of the 12 patients, the mean of left and right cortical blood flow was analyzed. Compared with the control subjects, cortical perfusion was significantly reduced in the patients' frontal regions, sparing the sensorimotor, temporal, and parietal cortices and the cerebellum. Reductions of perfusion were rather pronounced in the anterior opercular, medial prefrontal and premotor, and anterior cingulate regions.

**Conclusions**—Pure dysarthria results mainly from multiple lacunar infarctions, which induce frontal cortical hypoperfusion, probably due to interruption of corticosubcortical networks. We conclude that frontal cortical hypoperfusion, particularly in the anterior opercular and medial frontal regions, plays an important role in the development of pure dysarthria. (*Stroke*. 1999;30:109-113.)

**Key Words:** cerebral blood flow ■ cerebrovascular disorders ■ dysarthria ■ frontal cortex

Isolated dysarthria from stroke, termed pure dysarthria (PD), is very rare, because sudden onset of PD is usually associated with other neurological deficits.<sup>1</sup> Fisher<sup>2</sup> defined PD as a variant of lacunar syndromes, caused by a pontine base infarction. However, the boundaries of PD still remain unclear, because clinical features of reported cases of PD have not been uniform, with variations of mild concomitant deficits.<sup>1-5</sup> For instance, there seems to be no definable point of demarcation between PD and dysarthria–clumsy hand syndrome.<sup>5</sup> In addition, lesion sites responsible for PD varied from case to case. In the majority of cases, PD resulted from subcortical lesions, but in some cases cortical lesions produced PD.<sup>4,5</sup> These inconsistent clinical and radiological findings in PD imply the multiplicity of causative conditions. Previous clinicoanatomical studies using CT or MRI have not necessarily clarified the underlying mechanism of PD, because damage to the brain induces a remote effect or compensatory function in the multifarious ways.<sup>6,7</sup> In the present study, we attempted to clarify the pathophysiology of PD by assessment of clinical features, lesion sites, and regional cerebral blood flow (rCBF).

## Subjects and Methods

### Subjects

Twelve right-handed patients with PD participated in this study between July 1988 and February 1997. At the onset, all patients complained of sudden dysarthria but not of any other sensorimotor symptoms. The main characteristics of dysarthria were slurred, indistinct articulation with slow, low-pitched prosody, involving labial, lingual, and palatal consonants. Comprehension of spoken language and ability of writing were intact. Three patients presented with unilateral facial palsy and 2 with unilateral lingual palsy. Mild dysphagia was noted in 2 patients. In all patients muscle strength and limb coordination were preserved, but 7 patients exhibited slight mild neurological signs, including brisk deep-tendon reflexes, arm pronation, or unsteady tandem gait. Their clinical features are summarized in Table 1. All patients underwent MRI and measurement of rCBF between 10 and 54 days after the onset, when dysarthria was still present. Eleven healthy subjects (mean±SD age, 67.6±10.6 years) who had no brain lesions on CT or MRI underwent rCBF measurement as controls. There was no significant difference in age between the patients and controls. Written informed consent was obtained from the control subjects as well as the patients before participation in this study.

Received September 8, 1998; final revision received October 15, 1998; accepted October 15, 1998.

From the Division of Neurology, Fifth Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, Japan.

Reprints requests to B. Okuda, MD, PhD, Fifth Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya 663-8501, Japan.

© 1999 American Heart Association, Inc.

Stroke is available at <http://www.strokeaha.org>

TABLE 1. Clinical Profiles of Patients With Pure Dysarthria

Patient/Age/Sex	VII Palsy	XII Palsy	Dysphagia	Other Signs	Lesion Sites	3-D
1/72/F	...	...	...	Slightly unsteady TG	ML, PI	FH
2/72/M	...	...	+	Brisk JR and DTR	ML	FH
3/78/M	L	...	...	...	ML	...
4/76/M	...	...	...	Slightly unsteady TG, brisk DTR	ML, PI	FH
5/50/M	R	R	...	...	ML	FH
6/81/M	...	...	...	Slight R, AP, brisk DTR	ML	FH
7/49/M	...	...	...	Brisk DTR, R, BR	ML	FH
8/77/M	...	...	...	...	ML	FH
9/57/F	R	R	+	Slight R, AP	ML, PI	...
10/70/M	...	...	...	...	R, IC/CR	...
11/51/M	...	...	...	Slight R, AP	ML	FH
12/81/M	...	...	...	...	ML	...

TG indicates tandem gait; JR, jaw reflex; DTR, deep tendon reflexes; AP, arm pronation; BR, Babinski reflex; ML, multiple lacunar infarcts; PI, pontine infarct; IC, internal capsule; CR, corona radiata; and FH, frontal hypoperfusion.

## Methods

Measurement of rCBF was performed with single-photon emission computed tomography (SPECT) with *N*-isopropyl-*p*-[<sup>123</sup>I]iodoamphetamine (<sup>123</sup>I-IMP). Subjects were injected with 111 MBq of <sup>123</sup>I-IMP into the antecubital vein while sitting with eyes open in a quiet room. Thirty minutes after the injection, SPECT scanning was started. Subjects lay supine on the Starcam 400 AC/T, a single-head rotating gamma camera SPECT system equipped with a low-energy, general purpose collimator. The data acquisition parameters were a 64×64 matrix with use of a ×1.6 zoom (3.75 mm pixel size), 64 views, 30 seconds per view (ie, 35 minutes' scan time). Transaxial tomographic slices 3.75 mm thick were reconstructed with a Hanning prefilter with a 0.8-cycle/cm cut-off frequency and a ramp back-projection filter. Attenuation correction assumed a uniform linear attenuation coefficient (0.064 cm<sup>-1</sup>). Horizontal slices (parallel to the anterior commissure–posterior commissure line) 7.5 mm thick were obtained by interpolation. The resolution of the system in water was 12 mm in the center of the field of view.

To clarify involvement of the cerebral cortex, a three-dimensional surface display was created from the transaxial slices of SPECT early images with use of the STARCAM computer system.<sup>8</sup> The threshold value to define the surface boundary was 55% of the global maximum counts in SPECT images. We adopted the threshold value because the 11 control subjects showed no defect in any cortical area at the 55% or lower threshold. Semiquantitative rCBF values were computed as follows.<sup>9</sup> <sup>123</sup>I-IMP uptake in individual brain areas was quantified by visually placing regular 4×4 pixel regions of interest (ROI), corresponding to 15×15×7.5 mm<sup>3</sup> brain volumes on 28 positions standardized by inspection with reference to a stereotaxic brain atlas.<sup>10</sup> These consisted of the following numbers of ROIs on each brain region: prefrontal, 2 (medial, lateral); anterior operculum, 1; anterior cingulate, 1; medial premotor, 1; sensorimotor, 2 (superior, inferior); parietal, 2 (superior, posterior); temporal, 3 (superior, middle, inferior); occipital, 1; and cerebellum, 1; all bilaterally. Uptake in each region was defined as the mean count per pixel in that region. Since IMP uptake in the occipital cortex is usually highest among these regions, the ratio of uptake in each region was measured relative to the mean uptake in the bilateral occipital region. For each region, an asymmetry index reflecting the degree of perfusion difference between the left and right sides was calculated. The formula used was  $2 \times |L - R| / (L + R)$ . Statistical analysis of rCBF was performed by use of the Wilcoxon signed-rank test, F test, and nonpaired *t* test. The criterion of statistical significance was  $P < 0.05$ .

## Results

### Lesion Sites

Eleven of 12 patients showed bilateral multiple lacunar infarctions, and 1 patient (No. 10) had a unilateral internal capsule (IC)–corona radiata (CR) infarction (Table 1). As shown in Figure 1, either the IC or the CR was involved in all patients (unilateral in 3, bilateral in 9). IC infarctions were noted in 8 patients, of whom 6 had lesions in the posterior limb, 3 in the genu, and 1 in the anterior limb. Nine patients had CR infarctions (anterior portion in 3, posterior portion in 2, anterior and posterior portions in 4). The pons was involved in 3 patients, the thalamus in 1, and the basal ganglia in 1. Ten patients showed periventricular high intensity on T2-weighted MRI.

### Cerebral Blood Flow

Three-dimensional surface displays revealed frontal cortical hypoperfusion in 8 of 12 patients. No perfusion defect was detected in other cortical areas. A representative case is shown in Figure 2, in which the frontal cortex was

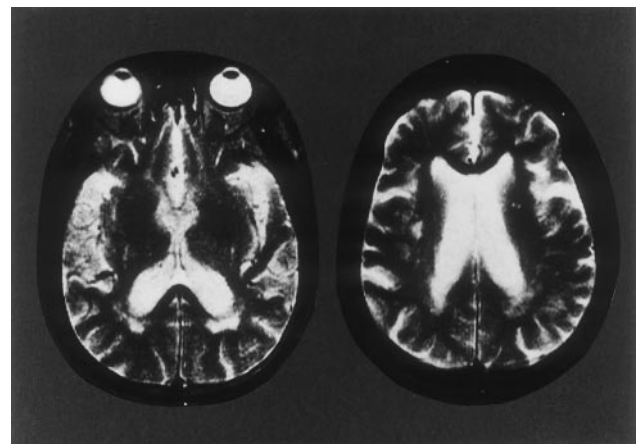
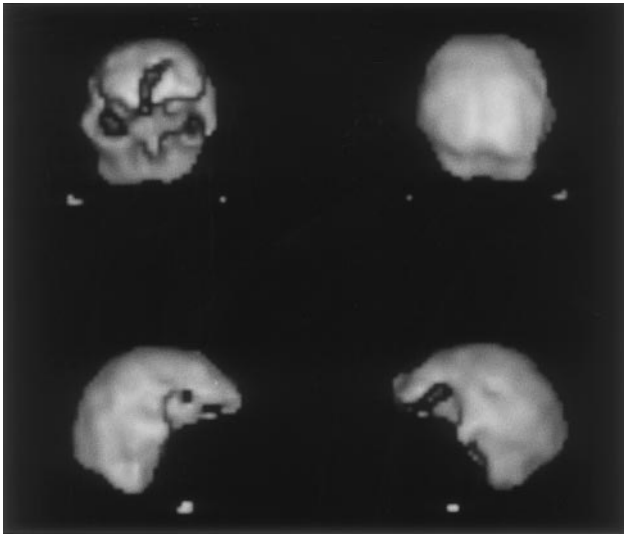


Figure 1. T2-weighted MRI from patient 8 shows lacunar infarctions in the bilateral corona radiata and periventricular high intensity.



**Figure 2.** Three-dimensional surface display from patient 8 shows cortical hypoperfusion in the anterior operculum and medial frontal regions. Four displays indicate anterior (top left), posterior (top right), right lateral (bottom left), and left lateral (bottom right) views.

hypoperfused mainly in the parasagittal and anterior opercular regions. Semiquantitative measurement of rCBF denoted that there was no significant interhemispheric difference (asymmetry index) in any regions in the patients (Wilcoxon signed-rank test). Hence, the mean of left and right rCBFs was analyzed for statistical comparison. Table 2 illustrates the ratio of  $^{123}\text{I}$ -IMP uptake in each region and statistical comparisons. The variances of rCBF values in the patients and control subjects were statistically identical in each region except for the inferior sensorimotor cortex and cerebellum (F test). Cortical blood flow in the patients was significantly reduced in the frontal cortex but not in the parietal and temporal cortices and the cerebellum compared with the control subjects (nonpaired *t* test). Frontal cortical hypoperfusion was rather pronounced in

the anterior opercular, medial prefrontal and premotor, and anterior cingulate regions. Cortical perfusion was not decreased in the superior and inferior portions of the sensorimotor cortex.

## Discussion

The status of PD still remains to be conclusively defined, particularly with respect to accompanied neurological deficits.<sup>4,5</sup> Acute onset of dysarthria was the main clinical feature of our patients, and concomitant neurological signs, if present, were very mild. Facial and lingual muscles were affected in 3 and 2 patients, respectively, but other cranial nerves were spared. Although 2 patients showed slight titubation on tandem gait, their gait was not wide based and limb coordination was not clumsy. Six patients presented with mild pyramidal signs, such as brisk deep-tendon reflexes and arm pronation, but their muscle strength was preserved. Thus, clinical manifestations of our patients were compatible with PD and did not border on dysarthria-clumsy hand syndrome or other lacunar syndromes.<sup>2,11</sup> In previous clinicoanatomical studies of PD, lesions responsible for PD were centered in the IC and CR, and IC lesions tended to involve the anterior limb, genu, and anterior parts of the posterior limb.<sup>1,3-5,12,13</sup> Other lesion sites associated with PD have included the basal ganglia, pons, bulbar motor cortex, and cortical regions supplied by the middle cerebral artery.<sup>4,5,13</sup> Some of these cases resulted from bilateral lesions.<sup>13</sup> In agreement with previous studies, all of our patients suffered from IC-CR infarctions. Since our patients showed no limb paresis, the most caudal portion of the IC could be spared in them. While most of previously reported cases with PD resulted from a unilateral IC-CR lesion, 9 of our 12 patients had bilateral IC-CR infarctions and only 1 had a unilateral one. It looks likely that bilateral IC-CR lesions induce PD more frequently than do unilateral ones, provided the pyramidal tract is spared.<sup>12-14</sup>

**TABLE 2. Statistical Comparison of Cerebral Blood Flow Between Patients With Pure Dysarthria and Control Subjects**

Region	Patients	Controls	F	<i>t</i>	<i>P</i>
Medial prefrontal	0.800±0.065	0.875±0.081	0.635*	-2.447	0.023
Lateral prefrontal	0.821±0.064	0.874±0.054	1.393*	-2.125	0.046
Anterior cingulate	0.746±0.092	0.835±0.073	1.604*	-2.560	0.018
Anterior operculum	0.803±0.060	0.881±0.067	0.785*	-2.970	0.007
Medial premotor	0.851±0.093	0.932±0.055	2.836*	-2.499	0.021
Superior sensorimotor	0.818±0.087	0.863±0.051	2.917*	-1.519	0.144
Inferior sensorimotor	0.804±0.100	0.863±0.052	3.779	-1.753	0.094
Superior parietal	0.926±0.090	0.979±0.060	2.269*	-1.641	0.116
Posterior parietal	0.840±0.058	0.887±0.051	1.282*	-2.074	0.051
Superior temporal	0.876±0.065	0.921±0.050	1.655*	-1.887	0.073
Middle temporal	0.850±0.061	0.888±0.054	1.267*	-1.581	0.129
Inferior temporal	0.806±0.060	0.845±0.056	1.175*	-1.578	0.129
Cerebellum	0.962±0.120	0.986±0.058	4.273	-0.616	0.545

For F values, the significance of variance ratios was tested by the F test (\**P*>0.05); for *P* values, the significance of differences was compared by nonpaired *t* test.

In addition to MRI features, the present results revealed a characteristic pattern of brain perfusion in patients with PD. Although the patients had subcortical lesions without cortical involvement, cortical blood flow was decreased mainly in the frontal cortex. Vascular mechanism is a possible cause to account for such cortical hypoperfusion. However, the regional distribution of cortical hypoperfusion is not necessarily in favor of the vascular theory. In our cases there was a predilection of frontal perfusion defects in which the anterior operculum and medial frontal cortex were considerably affected. Since the former is supplied by the middle cerebral artery and the latter by the anterior cerebral artery, it seems unlikely that a disorder of each major vessel results in such a regional distribution of cortical hypoperfusion. Besides, no watershed pattern of hypoperfusion indicative of a major vessel disorder was seen on SPECT. An alternative explanation concerns the remote effect termed "diaschisis," in which interruption of neural networks from a focal lesion induces depression of neural activities in a distant area of the brain.<sup>8</sup> In line with this theory, multiple white matter lesions can disrupt corticosubcortical connections indispensable for speech output. Frontal cortical hypoperfusion results usually from white matter disease such as Binswanger's disease. In our previous study, patients with Binswanger's disease showed widespread hypoperfused regions, including the sensorimotor cortex and cerebellum as well as the frontal cortex.<sup>15</sup> This indicates that Binswanger's disease involves more extensive corticosubcortical connections than PD. Because extensive white matter lesions produce sensorimotor deficits other than dysarthria, PD necessitates restricted damage to neural circuits. It appears likely that PD is attributable to IC-CR lesions resulting in cortical hypoperfusion mainly in the anterior opercular and medial frontal regions.

The anterior operculum is a candidate for dysarthria of cortical origin, since this area controls voluntary movements necessary for vocalization and articulation.<sup>16,17</sup> Bilateral anterior opercular lesions cause facio-pharyngoglossomasticatory palsy with dysarthria and dysphagia (Foix-Cavany-Marie syndrome), and a mild form of this syndrome can be produced by unilateral anterior operculum damage.<sup>13,16,18</sup> The frontopontine and frontobulbar tracts, including descending fibers from the anterior operculum, pass through the genu and anterior and posterior limbs of the IC,<sup>3,4,18</sup> while the corticospinal tract occupies the most posterior part of the IC posterior limb. These clinicoanatomical facts favor the idea that multiple lacunar infarctions involving the IC-CR can disrupt neural connections with the anterior operculum. In fact, subcortical lesions in the IC-CR produce dysarthria with facial, velar, or lingual palsy without hemiparesis.<sup>4,5</sup> Clinical and experimental studies suggest that the medial frontal cortex is relevant to speech expression. Stimulation of the parasagittal prefrontal cortex induces vocalization and utterances, and medial frontal infarction from the anterior cerebral artery occlusion has been reported to cause motor aphasia.<sup>19</sup> The medial premotor cortex, probably corresponding to the supplementary motor area (SMA), appears to play a

role in vocalization, because damage to the SMA lead to speech expression disorders.<sup>20</sup> The SMA receives a fair amount of information from the cingulate gyrus. The anterior cinguli works as a center for controlling phonation, and mutism can result from damage to the anterior cingulate cortex.<sup>21</sup> Corticocortical connections between these frontal cortices and other language areas are crucial for generating complicated utterances.<sup>22</sup> Hence, dysfunction of the anterior operculum and medial frontal cortex is a likely cause of PD. In our cases frontal cortical hypoperfusion reflected dysfunction of these regions, possibly due to interruption of thalamocortical and corticothalamic fibers as well as frontopontine and frontobulbar tracts.<sup>3,8,17</sup>

A problem remaining to be solved is whether PD is a distinct lacunar syndrome. Some authors regarded PD as a variant of dysarthria-clumsy hand syndrome.<sup>1,5</sup> Although clinical features of PD are variable among cases, the pure form of PD, without cranial nerve palsies or sensorimotor deficits, differs from dysarthria-clumsy hand and other lacunar syndromes if rigid clinical criteria are used.<sup>2,11</sup> Besides, typical lesion sites differ between patients with PD and dysarthria-clumsy hand syndrome. Most cases of PD result from IC-CR lesions, whereas those of dysarthria-clumsy hand syndrome are caused by pontine base lesions.<sup>11</sup> PD can arise from either lacunar or cortical infarction without clinically evident differences.<sup>4,5</sup> As is the case for PD, however, other lacunar syndromes can result from cortical lesions as well.<sup>1</sup> In this regard, PD is considered a distinct lacunar syndrome, because cortical lesions are a much less frequent cause than lacunar infarctions. It is conceivable that PD originates mainly in lacunar infarctions and that disruption of frontal corticosubcortical networks is crucial for the development of PD.

### Acknowledgment

We would like to thank H. Tanaka for her assistance with the assessment of language function.

### References

1. Arboix A, Massons J, Oliveres M, Titus F. Isolated dysarthria. *Stroke*. 1991;22:531. Letter.
2. Fisher CM. Lacunar strokes and infarcts: a review. *Neurology*. 1982;32:871-876.
3. Ozaki I, Baba M, Narita S, Matsunaga M, Takebe K. Pure dysarthria due to anterior internal capsule and/or corona radiata infarction: a report of five cases. *J Neurol Neurosurg Psychiatry*. 1986;49:1435-1437.
4. Ichikawa K, Kageyama Y. Clinical anatomic study of pure dysarthria. *Stroke*. 1991;22:809-812.
5. Kim JS. Pure dysarthria, isolated facial paresis, or dysarthria-facial paresis syndrome. *Stroke*. 1994;25:1994-1998.
6. Okuda B, Kawaguchi S, Yamamoto T, Samejima A. Changes in the cerebello-cerebral response in the parietal cortex following ablation of the motor cortex in the cat: early occurrence and persistence. *Neurosci Res*. 1990;8:1-11.
7. Weiller C, Ramsay SC, Wise RJS, Friston KJ, Frackowiak RSJ. Individual patterns of functional reorganization in the human cerebral cortex after capsular infarction. *Ann Neurol*. 1993;33:181-189.
8. Okuda B, Tanaka H, Tachibana H, Kawabata K, Sugita M. Cerebral blood flow in subcortical global aphasia: perisylvian cortical hypoperfusion as a crucial role. *Stroke*. 1994;25:1495-1499.
9. Okuda B, Tanaka H, Tomino Y, Kawabata K, Tachibana H, Sugita M. The role of the left somatosensory cortex in human hand movement. *Exp Brain Res*. 1995;106:493-498.

10. Talairach J, Tournoux P. *Co-Planar Stereotaxic Atlas of the Human Brain*. New York, NY: Thieme Medical Publishers Inc; 1988.
11. Glass JD, Levey AI, Rothstein JD. The dysarthria-clumsy hand syndrome: a distinct clinical entity related to pontine infarction. *Ann Neurol*. 1990;27:487–494.
12. Bogousslavsky J, Regli F. Capsular genu syndrome. *Neurology*. 1990;40:1499–1502.
13. Besson G, Bogousslavsky J, Regli F, Maeder P. Acute pseudobulbar or suprabulbar palsy. *Arch Neurol*. 1991;48:501–507.
14. Loeb C, Gandolfo C, Caponnetto C, Del Sette M. Pseudobulbar palsy: a clinical computed tomography study. *Eur Neurol*. 1990;30:42–46.
15. Tomino Y, Tachibana H, Sugita M. Three-dimensional surface display with 123I-IMP brain perfusion imaging in patients with dementia [in Japanese]. *Rinsho Shinkeigaku*. 1994;34:318–325.
16. Mao C-C, Coull BM, Golper LAC, Rau MT. Anterior operculum syndrome. *Neurology*. 1989;39:1169–1172.
17. Schiff HB, Alexander MP, Naeser MA, Galaburda AM. Aphemia: clinical-anatomic correlations. *Arch Neurol*. 1983;40:720–727.
18. Rousseaux M, Lesoin F, Quint S. Unilateral pseudobulbar syndrome with limited capsulothalamic infarction. *Eur Neurol*. 1987;27:227–230.
19. Racy A, Jannotta FS, Lehner LH. Aphasia resulting from occlusion of the left anterior cerebral artery: report of a case with an old infarct in the left rolandic region. *Arch Neurol*. 1979;36:221–224.
20. Gelmers HJ. Non-paralytic motor disturbance and speech disorders: the role of the supplementary motor area. *J Neurol Neurosurg Psychiatry*. 1983;46:1052–1054.
21. Starkstein SE, Berthier M, Leiguarda R. Bilateral opercular syndrome and crossed aphemia due to a right insular lesion: a clinicopathological study. *Brain Lang*. 1988;34:253–261.
22. Aboitiz F, García VR. The evolutionary origin of the language areas in the human brain: a neuroanatomical perspective. *Brain Res Rev*. 1997;25:381–396.