Legends to the Videotape

Segment **1.** This examination was performed nearly **4** months after her stroke. Rapid alternating movements and fine finger movements were normal. She exhibited mild action tremor in her right upper extremity, most evident during visually guided movements such as fingerto-nose testing, writing, and drawing. Her only other deficit was mild clumsiness of the right lower extremity, most evident when hopping. Her gait was normal.

Segment **2.** This examination was performed 12 months after her stroke, 8 months after the first videotape segment. The right upper extremity action tremor was more severe, but her other neurological deficits had resolved completely.

> Farrukh Qureshi Augusto Morales Rodger J. Elble *Department\$ of Neuro1ogy:and Pediatrics Southern Illihois University School of Medicine\ Springfield, Illinois, U.S.A.*

References

- 1. Deierine J, Roussy G. Le syndrome thalamique. *Rev Neurol* **¹**906; 1 2: 52 1-532.
- 2. Lee MS. Marsden CD. Movement disorders following lesions of the thalamus or subthalamic region. Mov Disord l994;9: 493-507.
- 3. Bastian AJ, Thach WT. Cerebellar outflow lesions: a comparison of movement deficits resulting from lesions at the levels of the cerebellum and thalamus. *Ann Neurol* 1995;38: 881-892.
- 4. Lee MS, Lee SA, Heo JH, Choi IS. A patient with a resting tremor and a lacunar infarction at the border between the thalamus and the internal capsule. *Mov Disord* 1993;8:244 246.
- **5.** Elble RJ, Sinha R, Higgins C. Quantification of tremor with a digitizing tablet. *J Neurosci Methods* 1990;32: 193-198.
- 6. Savitzky A, Golay MJE. Smoothing and differentiation of data by simplified least squares procedures. *Anal Chem* 1964;36: 1627-1639.
- 7. Elble RJ, Koller WC. *Tremor.* Baltimore: Johns Hopkins University Press, 1990: 10-36.
- 8. Elble RJ. Physiologic and essential tremor. *Neurology* 1986; 36:225-23 1.
- 9. Elble RJ, Schieber MH, Thach WT. Activity of muscle spindles, motor cortex and cerebellar nuclei during action tremor. *Brain Res* 1984;323:330-334.
- **10.** Hore J, Vilis T. A cerebellar-dependent efference copy mechanism for generating appropriate muscle responses to limb perturbations. In: Bloedel JR, Dichgans J, Precht W, eds. *Cerebellar functions.* Berlin: Springer-Verlag, 1984:24- 35.
- **11.** Sanes JN, LeWitt PA, Mauritz K-H. Visual and mechanical control of postural and kinetic tremor in cerebellar system disorders. *J Neurol Neurosurg Psychiatry* 1988;51:934-943.
- 12. Thach WT, Goodkin HP, Keating JG. The cerebellum and the adaptive coordination of movement. *Annu Rev Neurosci* 1992; 15:403-442.
- 13. Ferbert A, Gerwig M. Tremor due to stroke. *Mov Disord* 1993;8: 179-1 82.
- 14. Anderson ME, Turner RS. Activity of neurons in cerebellar-

receiving and pallidal-receiving areas of the thalamus in behaving monkey. *J Neurophysiol* 1991 ;66:879-893.

- 15. Hirai T, Jones EG. A new parcellation of the human thalamus on the basis of histochemical staining. *Brain Res Rev* 1989;14: 1-34.
- 16. Shindo **K,** Shimd K, Tanji J. Spatial distribution of thalamic projections to the supplementary motor area and the primary motor cortex: a retrograde multiple labeling study in the macaque monkey. *J Comp Neurol* 1995;357:98-116.
- 17. Mackel R, Iriki A, Brink EE. Spinal input to thalamic VL neurons: evidence for direct spinothalamic effects. *J Neurophysiol* 1992;67: 132-144.
- **18.** Goldman MS, Kelly PJ. The surgical treatment of tremor. In: Findley LJ, Koller WC, eds. *Hundbook of tremor disorders.* New York: Dekker, 1995:521-562.
- 19. Yasui N, Narabayashi H, Kondo T, Ohye C. Slight cerebellar signs in stereotactic thalamotomy and subthalamotomy for parkinsonism. *Appl Neurophysiol* 1976177;39:315-320.
- 20. Caparros-Lefebvre D, Ruchoux MM, Blond S, Petit **H,** Percheron G. Long-term thalamic stimulation in Parkinson's disease. *Neurology* l994;44: 1856-1860.
- 21. Deiber M-P, Pollak P, Passingham R, et al. Thalamic stimulation and suppression of parkinsonian tremor: evidence of a cerebellar deactivation using positron emission tomography. *Bruin* 1993;116:267-279.

Hemichorea After a Striatal Ischemic Lesion: Evidence of Thalamic Disinhibition Using Single-Photon Emission Computed Tomography: A Case Report

Recently, Bathia and Mardsen (1) reported that motor disorders may occur in about half of patients with cerebrovascular lesions of the basal ganglia. Hemichorea is, however, relatively rare—it is seen in only 8% of patients with striatal lesions. The mechanism responsible for chorea following a vascular lesion is not yet completely understood. **A** widely accepted hypothesis to explain hyperkinetic disorders underlines the role of the loss of subthalamic nucleus (STN) control on the internal segment of the nucleus pallidus (GPi), followed by the disinhibition of thalamic neurons *(2).*

Emission tomography studies have repeatedly reported a decrease in striatal metabolic activity in Huntington's disease (3-7) as well as in less common choreiform syndromes, such as neuroacanthocytosis and Lesh-Nyan disease (8,9). The glucose metabolism has, instead, been found to be increased in the lentiform nucleus of two patients with Sydenham's chorea during the active phase of their disease (10). Functional abnormalities of the thalamus have been reported in a group of patients with Huntington's disease only by Young et al. (5).

We describe the modifications of cerebral blood flow (CBF) observed in a patient who developed right-sided hemichorea after a lacunar lesion of the left internal capsule marginally affecting both the caudate and lentiform nuclei. An 80-year-old right-handed man was admitted to our hospital after the sudden onset of right-sided involuntary movements 2 days earlier. His medical and family histories were unremarkable, except for a surgical operation for a bladder papilloma at age **60.**

Neurological examination found choreiform movements of the right side affecting the face, arm, and leg. The involuntary movements were present at rest and increased during voluntary actions. There was a slight decrease in muscle strength in the right arm and in muscle tone in the right limbs. Stretch reflexes were normal, and plantar reflexes were flexor. The neuropsychological examination showed a normal overall cognitive state (Mini-Mental State Exam score $= 26$) with a mild decline in abstractive and constructive abilities and verbal fluency.

His blood pressure was 190/100 mm Hg; an electrocardiogram revealed hypertrophy of the left ventriculum. His blood tests were normal. A plaque at the origin of both the internal carotid arteries, with stenosis of 60% on the right and **305'0** on the left, was demonstrated by echo Doppler examination. The magnetic resonance study was performed with *ii* 1.5-Tesla superconductive unit (Magnetom; Siemens). TI-weighted spin-echo sequences (TR 560, TE 15) on the axial plane and T2-weighted spin-echo sequences (TR 2300, TE 90) and PD (TR **2400,** TE 15) on the sagittal, axial, and coronal planes were obtained. A small area (longitudinal axis = 0.83 cm) of altered signal (hyperintense in T2-weighted images and hypointense in T1-weighted images) was observed in the left internal capsule between the head of the caudate nucleus and the upper part of the border zone between the putamen and external pallidum. These structures of the left basal ganglia, i.e., the head of the caudate nucleus, putamen, and external pallidum were marginally affected by the necrotic lesion (Fig. 1). The left subthalamic nucleus was normal. In the right hemisphere there was another small lesion (longitudinal axis $= 0.98$ cm) with the same characteristics of signal alteration, affecting the anteroexternal part of the putamen.

The single-photon emission computed tomography (SPECT) study uas performed in the postacute phase, on day 18 after clinical onset, at a time when the involuntary movements were still present. Brain radioactivity was recorded by a brain-dedicated high-resolution apparatus (Tomomatic 564; Medimatic) following an i.v. injection of 20 mCi of 99mTc hexamethylpropylenamine oxide (HM-PAO). The patient's head was positioned with the orbitomeatal line perpendicular to the floor by using a laser beam reference system and ink dots on the skin; the head was then fixed to the head holder by tape. The study was performed at rest in a dimly lit room with external stimuli reduced to a minimum.

After tomographic image reconstruction that provided a set of nine slices (10 mm of thickness, **9** mm of spatial resolution in the transverse plane), we observed a 15% CBF increase in the left thalamus (Fig. 2). The percentage of perfusional asymmetry, calculated as the ratio between mean counts in the left and right thalami, was significantly above the upper limit of the 95% confidence interval calculated in six normal volunteers (mean \pm SD of the left to right asymmetry in controls = $2.05 \pm 3.8\%$; range = $-3.5-7.6\%$). No other CBF abnormalities were detected except for a significant CBF decline (-12%) in the right cerebellar hemisphere (mean \pm SD of the left to right cerebellar asymmetry in controls = 3.08 ± 1.7 ; range = $0.99 - 5.57\%$).

When the patient was discharged on day 28, the involuntary movements were still present, though to a lesser extent. The diagnosis of right hemichorea caused by a lacunar stroke was made. In this case, two findings are of particular interest: (a) the crucial location of the striatal structural damage, which induced contralateral hemichorea probably by disrupting connecting fibers between the striatum and the globus pallidus, and (b) the remote left thalamus functional alteration, which followed the striatal fiber disruption and represented the evidence of the basal ganglia-cortical circuit derangement considered to be responsible for the appearance of the hemichorea (2).

Contralateral hemichorea has been described following

 $A-C$

FIG. 1. Magnetic resonance images of a patient with right hemichorea in the transverse **(A: T1** weighted, B: T2 weighted) and coronal (C: T2 weighted) planes show two small areas of altered signal: one in the left internal capsule between the head **of** the caudate nucleus and the border zone between the putamen and the external pallidum and another in the antero-external portion of the right putamen.

lesions that selectively involve the caudate nucleus **(1** 1- 13), the putamen **(14),** and the globus pallidus (15) and also, in association with ballism, following larger lesions that involve both the caudate and lentiform nuclei **(16-** 20). However, the location of the lesion within the basal ganglia seems to be of crucial importance in inducing hemichorea. The association between basal ganglia lesions and choreic movements in humans is, in fact, relatively rare **(1).** Furthermore, ablative lesions of the striatum in experimental animals do not produce choreiform movements (21). It is noteworthy that the two small basal ganglia lesions in our patient also had different clinical expressions. While the left lesion, strategically located between the caudate nucleus, the putamen, and the globus pallidus, caused contralateral hemichorea, the right lesion, involving the antero-external portion of the putamen, was asymptomatic.

Additional information was obtained from functional neuroimaging. A hypoperfusion in the regions corresponding to the ischemic lesions was not detected because they were too small for the spatial resolution power of our camera. SPECT did, however, highlight remote effects of the left lacuna in structurally intact brain areas, which is quite common in cerebrovascular patients. Areas of reduced CBF and metabolism far from the site of the infarct stemming from loss of excitatory input are often observed after a stroke and termed diaschisis (22).

In our study functional findings were obtained by using SPECT and 59m Tc HMPAO. The distribution of 99m Tc HMPAO within the brain is proportional to the CBF (23). When cerebral autoregulation is preserved, CBF is directly related to the metabolic needs, which in turn depend on neuronal functional activity **(24).** The CBF increase observed in the left thalamus of our patient probably reflects an increased neuronal activity of thalamic cell bodies, free from inhibitory pallidal control. The contralateral cerebellar hypoperfusion, on the other hand, probably indicates decreased functional activity of both granule and Purkinje cells due to the interruption of the multisynapatic excitatory pathway originating in the cerebral cortex. This latter finding, termed crossed cerebellar diaschisis (25), is frequently seen after supratentorial lesions (26).

The finding of a CBF increase in the left thalamus was of particular interest because it probably represents the functional result of the loss of pallidal inhibitory input to the thalamus. A similar mechanism was considered to explain the thalamic metabolic increase observed in patients with chronic intractable pain after loss of sensory input following laterocervical cordotomy (27).

Our interpretation of the observed thalamic hyperperfusion is in accordance with the pathogenetic mechanism proposed to explain the occurrence of hemichorea in humans. Choreiform movements have been experimentally produced in monkeys either by damage to the STN (28) or by functional block of STN neurons by injection of gamma-aminobutyric acid (GABA) antagonist either into the STN (29) or into the lateral segment of the pallidum (30). Therefore it was hypothesized that damage to the striatum causes a contralateral hemichorea when striatal neurons that project through the external segment of the globus pallidus (GPe) to the STN are selectively affected **(30).**

The interruption of GABAergic transmission from the striatum to the GPe would lead to an abnormally increased activity of GPe neurons, which exert an inhibitory action upon the STN (31). Increased inhibition of the STN would result in the loss of its control upon the GPi neurons. Besides excitatory STN inputs (32), the GPi neurons also receive inhibitory afferent signals directly from the striatum. The imbalance between the indirect excitatory and the direct inhibitory pathways would ultimately lead to a disinhibition of the motor thalamus.

The observed CBF increase in the left thalamus observed in our case might be the result of the abovementioned cascade of events. A similar finding was described by Young et al. (5), although in patients with chorea of different origin and by using a different methodology. In fact, they found a glucose metabolic increase in the thalamus of a group of 15 patients with Huntington's disease only when they considered the thalamus-to-cortex ratio. This ratio was, however, correlated with dystonia. A different part of this mechanism of action might be represented by the increased striatal glucose consumption reported in two cases of Sydenham's chorea by Weindl et al. (10), likely due to increased activity of GPe deprived of inhibitory striatal control. On

A.B

FIG. 2. SPECT with ^{99m}Tc HM-**PA0** images of a patient with right hemichorea shows CBF modifications in structurally intact areas. CBF decrease in the right cerebellum **(A)** and CBF increase in the left thalamus **(B)** are evident.

the other hand, in patients who do not show involuntary movements following a striatocapsular lesion, thalamic perfusion is normal or decreased (33). The thalamic CBF increase observed in our patient may represent the first in viva evidence that thalamic disinhibition caused by a striatal lesion is the pathogenetic mechanism responsible for choreic movements after stroke.

> tStefania'Di Cesare Monica Ricci#
Gian Franco Gualdi‡ *Umberto §abatini tVittorio Di Piero **First Chair of Neuroradiology* 1 f *Fifth Chair of Neurology Department of Neurological Sciences KTIMR Service* 51-54. *First Chair of Infernal Medicine University of Rome "La Sapienza" Rome, Italy*

Acknowledgment: Work was supported by CNR grant 1428-1429. CT **93.04577.04.** We thank Prof. *G.* L. Lenzi and Dr. **A.** Berardelli for their useful comments and Mr. B. Di Pofi for technical assistance. 492.

References

- 1. Bathia KP, Mardsen CD. The behavioural and motor consequences of tbcal lesions of the basal ganglia in man. *Brain* 1994; 117: 859-876.
- 2. De Long MR. Primate models of movement disorders of basal ganglia origin. *Trends Neurosci* 1990;13:281-285.
- 3. Kuhl DE, Phelps ME, Markham CH, Metter EJ, Riege WH, Winter J. Cercbral metabolism and atrophy in Huntington's disease determined by "FDG and computed tomographic scan. *Ann Neurol* 1982;12:425-434.
- 4. Leenders **KL.** Frackowiak RSJ, Quinn N, Mardsen CD. Brain energy metabolism and dopaminergic function in Huntington's disease measured in vivo using positron emission tomography. *Mov Disord* 1986;1:69-77.
- *5.* Young AH, Penney JB, Starosta-Rubinstein **S,** et al. PET scan investigations of Huntington's disease: cerebral metabolic correlates of neurological features and functional decline. *Ann Ncurol* 1986;20:296-303.
- 6. Mazziotta JC, Phelps ME, Pahl JJ, et al. Reduced cerebral glucose metabolism in asymptomatic subjects at risk for Huntington's disease. *N Engl* J *Med* 1987;316:357-362.
- 7. Garnett ES. Firnau G, Nahmias C, Carbotte R, Bartolucci G. Reduced srriatal glucose consumption and prolonged reaction time are early features in Huntington's disease. *J Neurol Sci* 19X7;65:231-237.
- 8. Dubinsky RM, Hallett M, Levey R, Di Chiro G. Regional brain glucose metabolism in neuroacanthocytosis. *Neurology* 1989;39:1353-1255.
- 9. Palella TD, Hichwa RD, Ehrenkaufer RC, et al. 18- Fluorodeoxyglucose PET scanning in HPRT deficiency. *Am J Hum Genet* 1981;37:A70.
- 10. Weindl A, Kuwert T, Leenders KL, et al. Increased striatal glucose consumption in Sydenham's chorea. *Mov Disord* 1993;8:437-444.
- 11. Kawamura M. Takahashi N, Nirayama K. Hemichorea and its denial in a case of caudate infarction diagnosed by magnetic resonanie imaging. *J Neurol Neurosurg Psychiarry* 1988;51:590-591.
- 12. Dewey RB, Jankovic **J.** Hemiballism-hemichorea: clinical

and pharmacologic findings in 21 patients. *Arch Neurol* 1989;46: 862-867.

- 13. Saris **S.** Chorea caused by caudate infarction. *Arch Neurol* 1983;40:590-591.
- 14. Rum1 **V,** Nardocci N, Combi M, Savoiardo M, Angelini L. Transient hemichorea symptomatic of a vascular lesion in the contralateral putamen: case report of a child [Abstract]. *Mov Disord* 1992;7(suppl 1):30.
- corpus Luysii. *Bruin* 1957;80: 1-10, *Patrizia Pantano 15. Martin JP. Hemichorea (hemiballism) without lesions in the
	- 16. Fragnito 0, Scarpini **V.** Report anatomo-patologico in un caso di emicorea sintomatica. *Riv Pafol Nerv Menf* 1926;31:
	- 17. Austregesilo **A,** Borges-Fortes A. Sur un case d'hemichoree avec lésion du noyau caudé. Rev Neurol (Paris) 1937;67: 477-488.
	- 18. Goldblatt D, Markesbery W, Reeves AG. Recurrent hemichorea following striatal lesions. *Arch Neurol* 1974;31:
	- 19. Kase CS, Maulsby GO, DeJuan N, Mohr JP. Hemichoreahemiballism and lacunar infarction in the basal ganglia. *Neurology* 1981,31.452-455.
	- 20. Srinivas K, Rao VM, Subbulakshmi N, Bhaskaran J. Hemiballism after striatal hemorrhage. *Neurology* 1987;37:
	- 21. Wilson SAK. An experimental research into the anatomy and physiology of the corpus striatum. *Brain* 1914;36:427-
	- 22. Feeney DM, Baron JC. Diaschisis. *Stroke* 1986;17:817-830.
	- 23. Sharp PF, Smith FW, Gemmell HG, et al. Technetium-99m HM-PAO stereoisomers as potential agents for imaging regional cerebral blood flow: human volunteer studies. *J Nucl Med* 1986;27: 171-177.
	- 24. Raichle ME, Grubb RL, Gado MH, Eichling JO, Ter-Pogossian MM. Correlations between regional cerebral blood flow and oxidative metabolism. *Arch Neurol* 1976;33: 523-526.
	- 25. Baron JC, Bousser MG, Comar D, Castaigne P. "Crossed cerebellar diaschisis" in human supratentorial brain infarction [Abstract]. *Ann Neurol* 1980;8:128.
	- 26. Pantano P, Baron JC, Samson Y, Bousser MG. Crossed cerebellar diaschisis: further studies. *Brain* 1986;109:677-694.
	- 27. Di Piero V, Jones AKP, lannotti F, et al. Chronic pain: a PET study of the central effect of the percutaneous high cervical cordotomy. *Pain* 1991;46:9-12.
	- 28. Whittier JR, Mettler FA. Studies on the subthalamus of the rhesus monkeys. 11. Hyperkinesia and other physiological effects of subthalamic lesions, with special reference to the subthalamic nucleus of Luys. *J Comp Neurol* 1949;90:319- 372.
	- 29. Crossman AR, Sambrook MA, Jackson A. Experimental hemichorea/hemiballismus in the monkey: studies on the intracerebral site of action in a drug-induced dyskinesia. *Brain* 1984;107:579-596.
	- 30. Crossman AR, Mitchell IJ, Sambrook MA, Jackson A. Chorea and myoclonus in the monkey induced by gammaaminobutyric acid antagonism in the lentiform complex. *Brain* 1988;111:1211-1233.
	- 31. Ohye C, Le Guyader C, Feger J. Responses of subthalamic and pallidal neurons to striatal stimulation: an extracellular study on awake monkeys. *Brain Res* 1976;111:241-252.
	- 32. Hamada I, DeLong MR. Excitotossic acid lesions of the primate subthalamic nucleus result in reduced pallidal neuronal activity during active holding. J *Neurophysiol* 1992;68: 1859-1866.
	- 33. Pantano P, Formisano R, Ricci M, et al. Prolonged muscular flaccidity after stroke: morphological and functional brain alterations. *Brain* 1995:118:1329-1338.