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Caudate Infarcts

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• **Eighteen patients had caudate nucleus infarcts (10 left-sided; 8 right-sided). Infarcts extended into the anterior limb of the internal capsule in 9 patients, and also the anterior putamen in 5 patients. Thirteen patients had motor signs, most often a slight transient hemiparesis. Dysarthria was common (11 patients). Cognitive and behavioral abnormalities were frequent, and included abulia (10 patients), agitation and hyperactivity (7 patients), contralateral neglect (3 patients, all right caudate), and language abnormalities (2 patients, both left caudate). The majority of patients had risk factors for penetrating artery disease. Branch occlusion of Heubner's artery, or perforators from the proximal anterior or middle cerebral arteries were the posited mechanism of infarction.**

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The caudate is a deep basal gray nucleus commonly affected, along with the other component of the striatum, the putamen, in degenerative brain diseases. In degenerative pathologic conditions, eg, Parkinson's and Huntington's diseases, other central nervous system structures are also involved, making it difficult to know what signs are attributable to the caudate dysfunction. Focal brain lesions, especially strokes, are more useful than diffuse or multifocal disorders in contributing to knowledge of the functions of individual brain structures. Brain tumors are seldom limited to one caudate nucleus, and edema and microscopic tumor spread make anatomicoclinical correlation more difficult than discrete strokes. Caudate hemorrhages[1-4] cause headache, confusion, and agitation, but mass effect and dissection of blood into the lateral ventricles and subarachnoid space, and into the nearby hypothalamus and internal capsule, confound interpretation of the mechanism of the signs and symptoms. Small caudate infarcts are often incidentally found at necropsy though usually there is no clinical history of stroke. Reports and reviews of patients with specific findings such as chorea,[5,6] behavioral abnormalities,[7-11] dysarthria,[12] "subcortical aphasia,"[13-17] depression,[18] and "lacunar" infarcts[19] have included some patients with caudate nucleus infarction, but no previous report analyzed the findings in a series of patients with caudate infarction. We now report clinical and radiographic findings in 18 patients with infarcts in a caudate nucleus and the adjacent anterior putamen and anterior limb of the internal capsule. We also analyze the vascular anatomy and causative stroke mechanisms and discuss the clinical findings in light of what is known about the functions of the caudate nuclei and their connections.

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METHODS

We searched the files of personally examined patients and the Michael Reese (Chicago, Ill) and New England Medical Center (Boston, Mass) stroke registries for patients with acute strokes who had recent computed tomographic (CT)-documented infarcts in a caudate nucleus. Lesions could extend into the adjacent anterior limb of the internal capsule and the anterior putamen. We excluded patients with cortical infarction or known previous strokes. Computed tomographic scans were recorded on standard grids used in the Stroke Data Bank,[20] and were analyzed for the size and location of lesions with each type of neurologic deficit, using a method previously described and illustrated.[21]

RESULTS

Demography and Case Material

There were 12 men and 6 women. The average age at stroke onset was 65.8 years, and the ages ranged from 38 to 83 years. Seven patients were white, 10 were black, and 1 was Chinese. Nine patients were studied in Chicago, Ill—6 at Michael Reese Hospital (J.P.G., L.R.C., D.B.H.) and 3 at the University of Illinois (C.H.). Six patients were studied in Boston, Mass;—4 at the New England Medical Center (L.R.C., E.F.), 1 at Boston City Hospital (J.S.), and 1 at University Hospital (C.K.). One patient was seen in New Hampshire (G.B.) and 2 in New Jersey (J.G.).

CT Findings

A montage of the CT grids is shown in Fig 1. Eight lesions were right-sided, 10 were left-sided. In 4 patients, the infarct was limited to the caudate nucleus; in 9 the infarct included the caudate nucleus and anterior limb of the internal capsule (Fig 2, left), and in 5 the lesion affected the caudate nucleus, anterior limb of the internal capsule, and the anterior putamen (Fig 2, right). Four lesions were small, 9 were moderate sized, and 5 were large. One patient also had magnetic resonance imaging, which showed more capsular extension than CT.

Neurological Signs

Motor Abnormalities.—The motor abnormalities are listed in Table 1. All

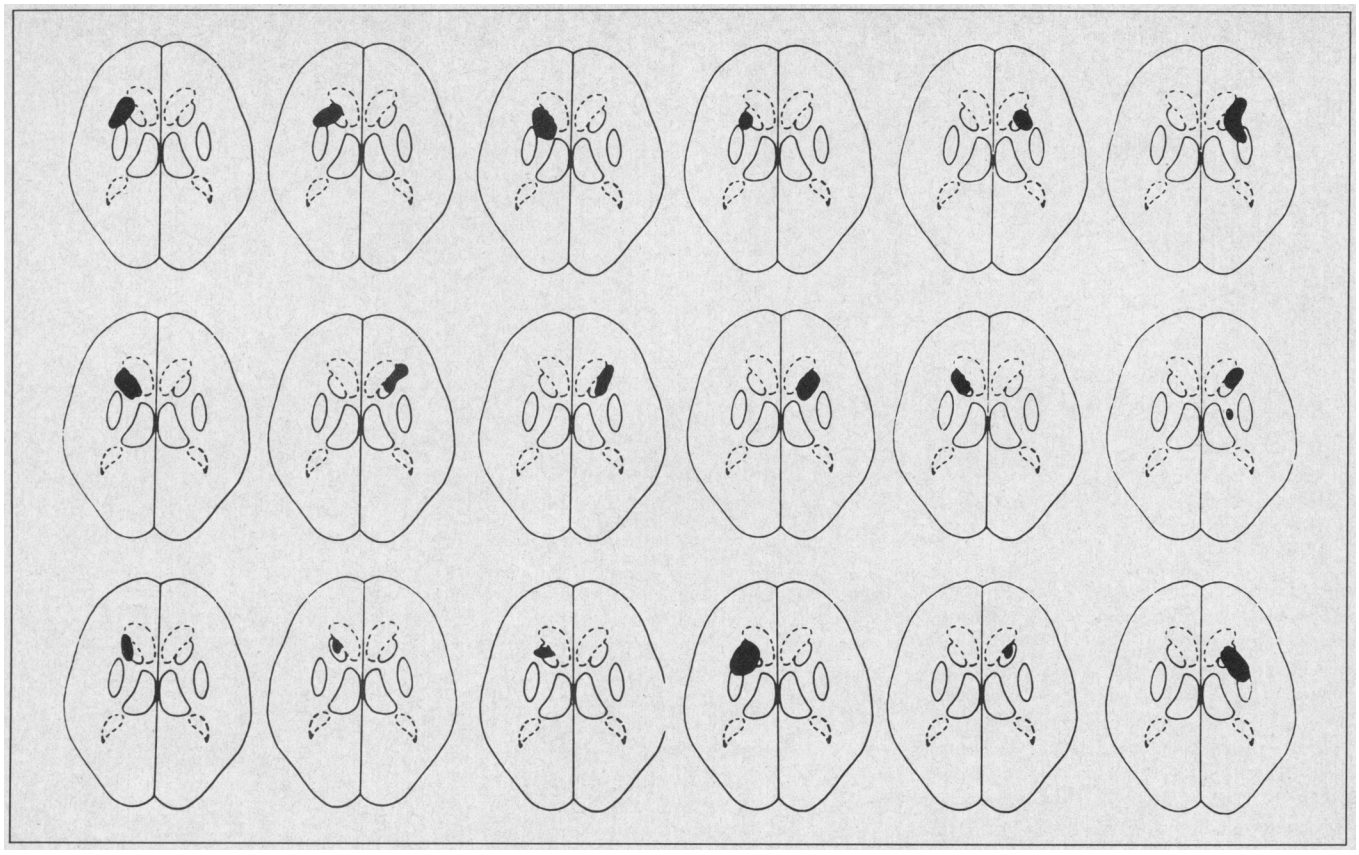

Fig 1.—Montage of computed tomographic lesions at a plane through the superior thalamus charted on Stroke Data Bank grids. Patient 1 is charted at upper left and scans represent patients 1 through 18 from left to right. Patient 18 is at lower right extreme. The left hemisphere is on the viewer's left.

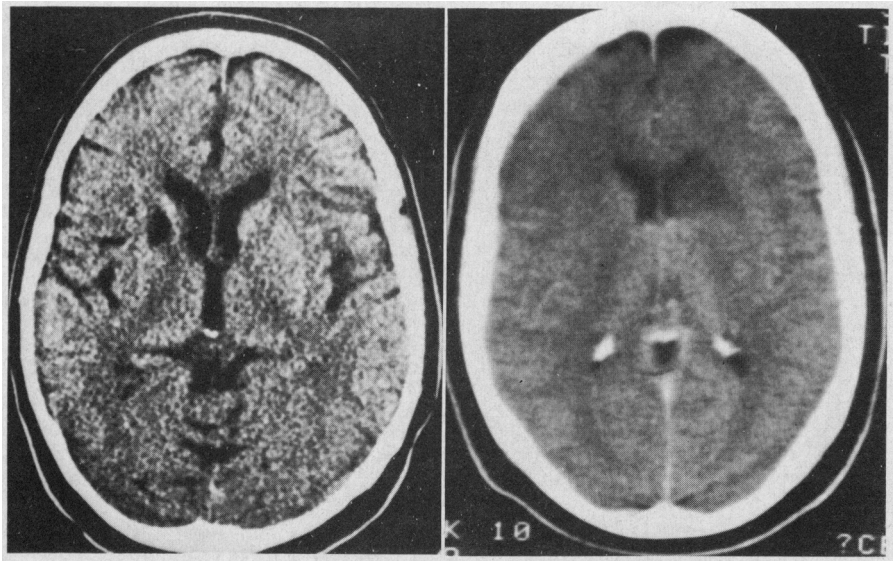

Fig 2.—Left, Infarct in left caudate nucleus extending into adjacent anterior limb of the internal capsule. Right, Right-sided caudate infarct extending to internal capsule and anterior putamen.

Table 1.—Motor Abnormalities

Weakness		
Severity	Location	No. of Patients
None		5
Slight		11
	Face, arm, and leg	7
	Face	2
	Mostly hand	1
	Arm and leg	1
Moderate		2
	Face, arm, and leg	2
Total		18

signs were contralateral to the caudate infarct. Five patients had no motor signs, and two patients had only slight facial weakness or asymmetry. Motor dysfunction, when present, was most often slight, but two patients had a moderately severe hemiparesis. The involved limbs usually showed decreased spontaneous movement and reduced associative movements. Resistance to passive movement was usually increased in both flexion and extension, but there was no spasticity. Often, the motor signs were temporary, improving quickly or after 2 to 3 weeks. No patient had a persistent severe residual hemiparesis.

Among the patients who had no motor abnormality, two had infarcts on CT limited to the caudate and three infarcts extended into the adjacent anterior limb of the capsule, but none extended into the putamen. One patient with moderately severe hemiparesis (patient 9) had two clinically

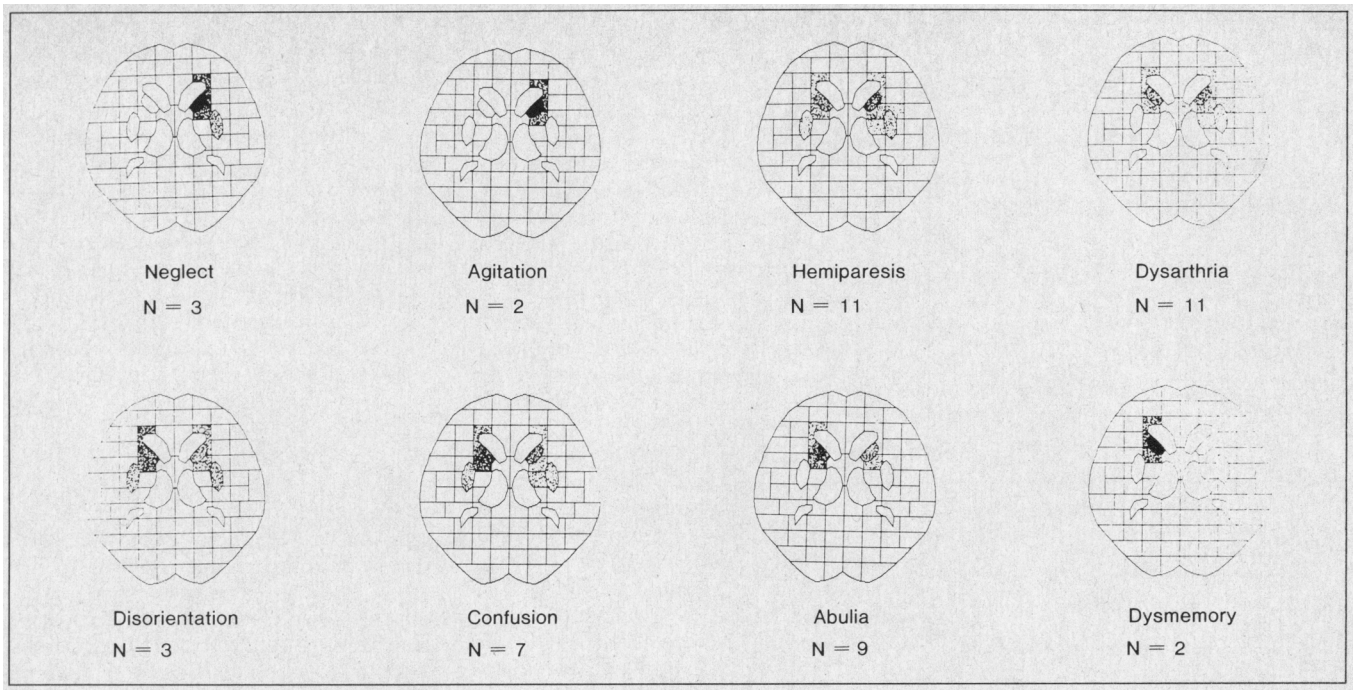

Fig 3.—Composite montages. Computed tomographic grids represent location of all infarcts in patients with the abnormalities cited.

unsuspected old infarcts on CT, one in the posterior limb of the internal capsule on the same side as the caudate infarct, and the other in the cerebellum on the opposite side. Patient 18, with a moderately severe hemiparesis, had a large infarct that extended across the capsule into the anterior putamen.

Dysarthria.—Eleven patients had dysarthria; 6 dysarthric patients had right-sided caudate infarcts (6 [75%] of 8), while 5 (5 [50%] of 10) had left-sided lesions. Among dysarthric patients, one infarct was limited to the caudate, 8 affected the caudate and anterior limb of the capsule, and 2 extended to include the putamen.

Behavioral and Cognitive Abnormalities.—Abnormalities of behavior, alertness, and speech were even more common than motor dysfunction. Only four patients had no recognized cognitive or behavioral abnormalities.

Abulia.—The most frequent behavioral abnormality was an inactive, slow, apathetic state that we will refer to as abulia, after Fisher.[22] Abulia is defined by three criteria: decreased spontaneous activity and speech; prolonged latency in responding to queries and directions and other stimuli; and reduced ability to persist with a task. Ten patients were abulic (6/10, left; 4/8, right).

Two descriptions illustrate the abnormality. Patient 7 was described by his wife as unusually slow and apathetic. He was content to sit and seemed "disinterested" in doing anything. Speech was slow and labored but "made sense." He had little energy and tired easily. Patient 13 said, "I seem to be able to do things and think things out, but the process has become very slow." This patient would respond to directions or queries, but often only after a 20- to 30-second delay.

Four abulic patients had lesions confined to the caudate nucleus, four had extension to the anterior limb, and only one had spread to the putamen. All of the patients in the series with infarcts limited to the caudate on CT were abulic.

Restlessness and Hyperactivity.—Seven patients were described as confused, restless, or hyperactive at some time during their acute stroke. In three patients, overactivity alternated with abulia. Though these patients were generally apathetic and had reduced spontaneous activity, they were intermittently restless, agitated, and confused. Among these three patients (patients 1, 10, and 17), one had a moderate-sized left caudate infarct, while the other two lesions were right-sided, one moderate sized and the other small. In four patients, hyperactivity was the major abnormality, and features of abulia were absent. Two hyperactive individuals (patients 3 and 16) had large left caudate infarcts, while patients 6 and 9 had large- and moderate-sized right-sided lesions. In two patients (patients 10 and 17) with right-sided caudate infarcts, the behavioral abnormality was severe. These patients are graphed as agitation in Fig 3. Patient 10 was usually apathetic, but intermittently became agitated, moved about incessantly, and frequently called out. Patient 17, with a small infarct limited on CT to the right caudate nucleus, had nearly incessant speech, and was agitated, delirious, and confused.

Contralateral Neglect.—Three patients, all with right-sided infarcts, had neglect of contralateral space. They ignored objects and people on their left and were inattentive to visual and auditory stimuli presented on the left side. One patient with contralateral neglect had a large lesion extending into the anterior limb of the internal capsule and the putamen, while the other two patients had moderate-sized lesions that extended into the internal capsule.

Language Abnormalities.—Two patients with left-sided caudate infarcts had speech abnormalities. Patient 2, with a moderate-sized infarct that extended into the anterior limb of the capsule and the anterior putamen, had spells of "stuttering" accompanied by weakness and clumsiness of the right hand. Later, when he developed persisting hemiparesis, stuttering also persisted and he omitted consonants. Patient 11, with a moderate-sized left-sided caudate infarct extending only

Table 2.—Cognitive and Behavioral Abnormalities

Deficit	No. of Patients	Side of Brain Lesion
None	4	2/10 left; 2/8 right
Abulia	10	6/10 left; 4/8 right
Agitation, hyperactivity	7	3/10 left; 4/8 right
Contralateral neglect	3	3/8 right
Language abnormalities	2	3/10 left

Table 3.—Vascular Investigations*

Angiography, 7
No important diagnostic lesions, 5
Intracranial arterial beading, 1
ICA siphon stenosis (75%), 1
Noninvasive carotid ultrasound, 2
Normal, 2
TCDU, 1; normal, 1
Echocardiography, 7
Normal, 6
Mitral stenosis, 1

* ICA indicates internal carotid artery; TCDU, transcranial Doppler ultrasound.

slightly into the adjacent anterior limb of the capsule, stammered frequently. He also had word-finding difficulty, but did not make paraphasic errors, and comprehension and repetition of speech were normal.

Other Cognitive or Behavioral Abnormalities.—Two patients with left-sided caudate infarcts (patients 1 and 13) had *"poor memory."* Each was also abulic and slow. Memory was improved when the patients were given prolonged time to respond, and when cues or choices were given. Mumbling (patient 10), sleepiness (patient 12), echolalia (patient 17), difficulty dressing (patient 8), poor drawing and copying (patient 17), and visual-spatial abnormalities (patient 6) were occasional findings. The two patients with visual-spatial and constructional abnormalities both had right-sided caudate infarcts. Patient 6, with a large right-sided caudate, capsular, and putaminal infarct, neglected left-sided lines on cancellation tests and recognized only one figure on Poppelreuter's diagram. He ignored people and voices on his left side and had consistent extinction of left-sided tactile and visual stimuli.

The abnormalities found on neurological examination are listed in Tables 1 and 2 and depicted on CT grids in Fig 3.

Vascular Lesions and Stroke Mechanisms.—Patients were not all systematically investigated to determine the causative mechanism of their ischemic strokes. Risk factors for penetrating artery and branch artery disease were prevalent. Fourteen patients (77%) were hypertensive and six patients (33%) had diabetes mellitus. Only five patients had neither hypertension nor diabetes. One elderly man had a very severe autoimmune hemolytic anemia with a hematocrit of 0.16. Four patients had known coronary artery disease, one had mitral stenosis, and one had hyperlipidemia.

Investigations are noted in Table 3. The only important angiographic abnormality was stenosis of an ipsilateral internal carotid artery within the siphon. A Chinese patient had beading of many intracranial arteries, a common finding in our experience in patients from Boston's Chinatown.[23] Carotid ultrasound studies were performed in only two patients, with normal results. Transcranial Doppler ultrasound was normal in one patient. Echocardiography uncovered no unsuspected lesions. Only one patient had an arrhythmia, atrioventricular block. No patient had atrial fibrillation. No necropsy material was available, since no patient died during or after their stroke.

COMMENT

This is the first report, to our knowledge, of a series of patients with caudate infarcts who were studied clinically and with neuroimaging techniques. There are important limitations of this study: *Representativeness of the sample*—This is a retrospective collection of patients referred to neurologists and stroke centers with acute-onset signs. We cannot know if the sample is representative of the universe of caudate infarcts. *Neuroimaging*—We selected patients with CT-documented lesions that we judged to be recent, involving a caudate nucleus and adjacent deep structures. Since magnetic resonance imaging was available in only one patient and we had no necropsy material, we cannot be certain that some individuals did not have confounding cortical ischemia, or even another lesion not seen on CT. *Vascular*—Not all patients had definitive vascular studies that clarified stroke mechanism. Study neurologists performed angiography only when clinically indicated. *Statistical*—The very small sample size and purely descriptive nature of the material do not lend themselves to useful statistically valid interpretation.

The most important findings in this series are as follows: (1) the frequency of prominent dysarthria, (2) the nature of the motor abnormalities, (3) the striking prevalence and nature of the frequent cognitive and behavioral abnormalities and their relationship to the laterality of the lesions, and (4) the most likely stroke mechanism was branch arterial occlusive disease of Heubner's artery or medial lenticulostriate branches of the proximal middle cerebral artery, or direct penetrators from the proximal portion of the anterior cerebral artery.

Motor Findings

Motor abnormalities contralateral to the infarcts were common in our series, and occurred in more than two thirds of the patients. Weakness was more likely to be present when the caudate lesion extended into the anterior limb, especially when the putamen was involved. Usually, the weakness was slight and most often affected the face, arm, and leg. The most frequent motor abnormalities were decreased spontaneous use, clumsiness, decreased associative movements such as reduced arm swing and decreased excursion of leg movement on walking, and increased tone. Some patients used the arm "en bloc," showing difficulty in rapid, precise, or alternating movements. Paralysis, grossly exaggerated deep tendon reflexes, and extensor plantar signs were not often noted. No patient had "cerebellar" type incoordination or ataxia of the affected limbs. We call the motor findings described a "non-pyramidal hemimotor syndrome" to distinguish them from the abnormalities in patients with lesions of the precentral gyrus, posterior limb of the internal capsule, and more distal corticospinal projections in whom Babinski signs, hyperreflexia, paralysis, and "pyramidal distribution" weakness and altered tone are found.[24]

In the monkey, the motor and somatosensory cortical areas and the supplementary motor area project to the striatum (mostly putamen but some caudate),[25] and then by way of the pallidonigral pathways to the ventrolateral thalamus and back to the cortex in a "motor circuit."[26] Unilateral ablation of Brodman areas 4 and 6 in the monkey lead to prominent but temporary decrease in metabolic activity in the caudate nucleus ipsilateral to the lesion, providing further evidence for inclusion of the caudate in the motor system.[27] The anterior limb of the internal capsule carries frontopontine motor fibers. Abnormal motor signs

such as akinesia, increased tone, and decreased associative and automatic movements are prominent features in patients with degenerative diseases of the basal ganglia.

In prior reports of humans with focal vascular lesions in the caudate nucleus or adjacent structures, hemiparesis has been noted, but usually not further characterized. In a series of 12 patients with hypertensive hemorrhages in the caudate nucleus, 7 had a contralateral hemiparesis.[1] In the hemiparetic patients, hematomas extended into or across the internal capsule and often caused mass affect while, in patients without hemiparesis, the hematomas were limited to the caudate and adjacent lateral ventricle.[1] In another series of patients with caudate hemorrhages, 4 out of 8 had hemiparesis, but 3 of 4 hemiparetic patients had carotid aneurysms associated with meningocerebral hemorrhage and ischemia outside the caudate nucleus.[2] Others have also noted hemiparesis in patients with caudate hemorrhage.[3,4] Among 30 patients with pure motor hemiplegia, Rascol and colleagues[19] found two with "anterocapsulocaudate" infarcts, which were comma or halfmoon-shaped lesions extending from the caudate, passing laterally and posteriorly, forming a medial concavity across the anterior limb of the internal capsule into the anterior putamen. These two patients had predominantly faciobrachial weakness and the CT lesions were identical to patients in our series whose lesions extended into the anterior limb and putamen. Hemichorea has also been described in patients with caudate infarcts,[5,6] but was not found in any of the patients in the present series. Denny-Brown[28] and Denny-Brown and Yanagisuma[29] did not find important sensory-motor abnormalities in monkeys with bilateral caudate-putamenal lesions, but others have noted slight transient contralateral "paresis" and persistent absence of contralateral placing reactions in cats with unilateral caudate lesions.[30]

Dysarthria

Abnormalities of the articulation of speech were very common in our series, especially in patients with right-sided caudate infarcts. The responsible lesions nearly always involved the anterior limb of the internal capsule; only one patient had an infarct limited to the caudate nucleus on CT. Van Buren[31] stimulated the head of the caudate nucleus and the anterior limb of the internal capsule and the adjacent deep white matter, and only rarely was able to produce "garbled speech." Critchley,[32] in a review of the findings in patients with anterior cerebral artery territory infarction, correlated dysarthria with lesions of the centrum semiovale and the anterior part of the anterior limb of the internal capsule. When affected alone, left-sided caudate lesions did not cause dysarthria.[33] Most authors have emphasized the importance of lesions of the motor cortex or white matter in the production of abnormal speech articulation and dysarthria. Fisher and Curry[34] and Fisher[35] described dysarthria in their patients with pure motor stroke and pontine or capsular infarction. In patients with capsular infarction, the lesion involved corticobulbar fibers in the genu of the internal capsule, and left-sided lesions predominated. The patient with the most severe dysarthria had a large lacune involving the genu and anterior limb of the superior part of the left internal capsule.[34] Schiff and colleagues[36] studied the anatomical basis of severe dysarthria in patients with left frontal lobe infarcts. Two had infarcts in the lower half of the precentral gyrus and subjacent white matter, while two had infarcts in the anterior limb of the internal capsule between the caudate head and the putamen, closely resembling our patients. One subcortical lesion extended into the head of the caudate nucleus. Alexander et al[37] studied 19 patients with aphasia and left-sided subcortical lesions. Striatal involvement was not important for the production of articulatory dysfunction; dysarthria correlated best with lesions in the periventricular white matter, particularly in the region of the junction between the anterior limb and genu of the internal capsule. Ozaki et al[38] described 5 hypertensive patients who had the sudden onset of dysarthria, but no limb weakness or other important neurological signs. All had lesions in the anterior limb of the internal capsule or the adjacent corona radiata, 4 on the left side, and 1 on the right side. In all of the above-cited studies, dysarthria could be explained by lesions of the motor cortex or underlying white matter innervating bulbar muscles, or by interruption of the anteriorly placed white matter fibers connecting motor association cortex with the contralateral cerebellum. Corticobulbar fibers and thalamocortical fibers travel in the anterior limb and genu of the internal capsule. Fisher and Curry[34] and Fisher[35] and Ozaki et al[38] had a predominance of left-hemisphere lesions among their patients with dysarthria, and others[36,37] studied only left-hemisphere-dominant lesions in order to analyze aphasia profiles. Ropper,[39] in contrast, emphasized the importance of right-hemisphere lesions in the production of dysarthria. All of his 10 patients had infarction of the right frontal lobe or underlying white matter. Lechtenberg and Gilman[40] and Gilman et al[41] had noted a preponderance of left-sided compared with right-sided cerebellar lesions in patients with dysarthria. The left cerebellum connects mostly to the right cerebral hemisphere via thalamocortical fibers passing through the anterior limb of the internal capsule. Our series of dysarthric patients also shows a slight right-sided predominance.

Cognitive and Behavioral Abnormalities

The basal ganglia and caudate nucleus have long been generally accepted as having important roles in motor function.[42] Only more recently have clinicians and investigators begun to explore involvement of basal gray structures and their connections in relation to abnormalities of cognition and behavior. The term *subcortical dementia*[43] implies that lesions of deep structures might cause decreased intellectual abilities either by anatomical disruption of cortical connections or by involvement of the basal gray nuclei and their neurotransmitters in the physiology of higher cortical function. Experimental and clinical studies document abnormalities of language, attention, learning, memory, and behavior in humans and experimental animals, with a variety of basal ganglia diseases and lesions. Strokes and other focal lesions that involve white matter fibers disrupt cortical-subcortical connections. However, degenerative diseases with pathologic findings limited to loss of basal ganglia cells could cause neuropsychological impairment only by disrupting the function of the gray nuclei themselves.[44] In the series reported herein, the most striking finding was the prevalence, nature, and variety of cognitive and behavioral abnormalities.

The caudate nucleus is an essential component of basal ganglia-thalamocortical circuitry. Anatomical and physiological studies in animals by Alexander et al[26] and Alexander and DeLong,[45] and others,[26,46-49] have defined connections between cortical areas in the frontal, parietal, and temporal lobes usually considered to be so-called associative cortex with deeper structures in a number of corticostriatopallidonigralthalamocortical circuits. A current schema of this cir-

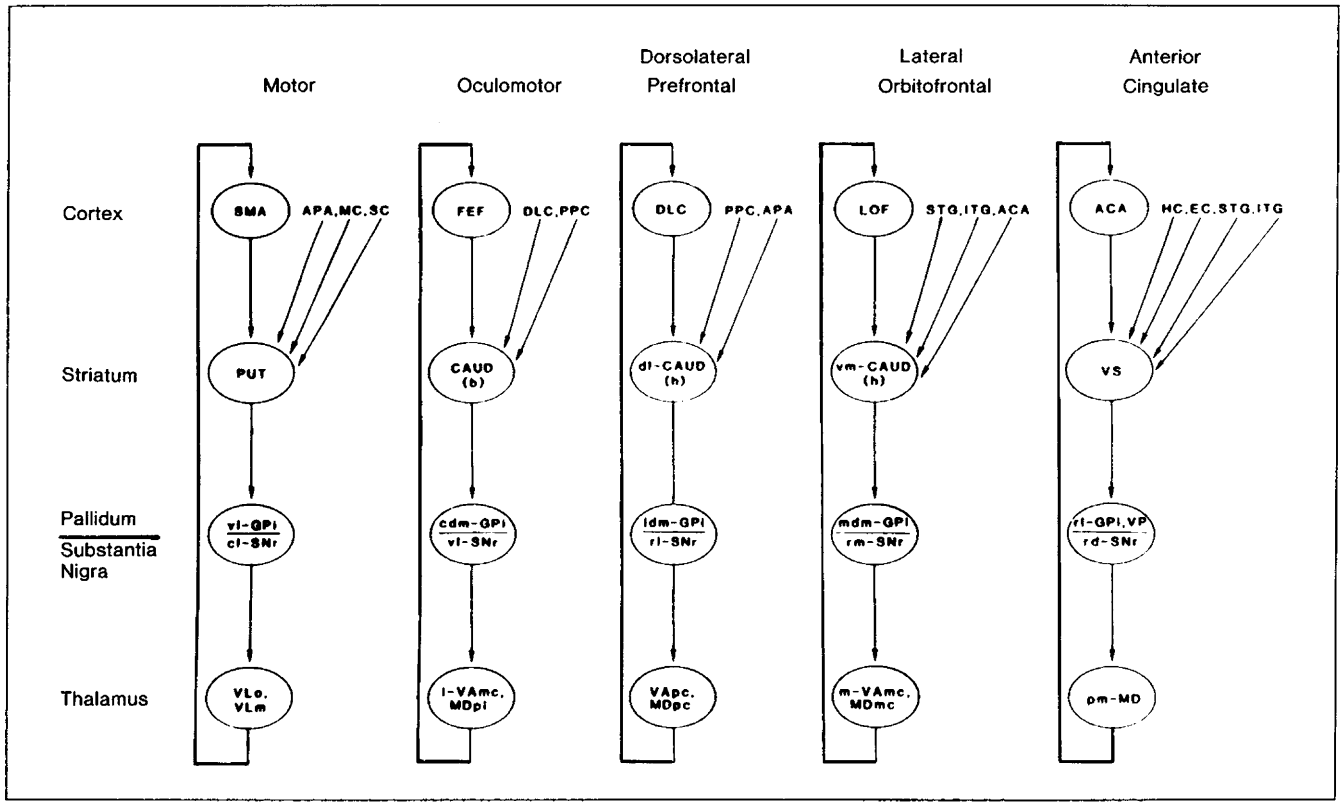

Fig 4.—Tabular description of basal ganglion-thalamic-cortical circuits. From Alexander et al.[26] Abbreviations are as follows: ACA, anterior cingulate area; APA, arcuate premotor area; CAUD, caudate, (b) body (h) head; DLC, dorsolateral prefrontal cortex; EC, entorhinal cortex; FEF, frontal eye fields; GPi, internal segment of globus pallidus; HC, hippocampal cortex; ITG, inferior temporal gyrus; LOF, lateral orbitofrontal cortex; MC, motor cortex; MDpl, medialis dorsalis pars paralamellaris; MDmc, medialis dorsalis pars magnocellularis; MDpc, medialis dorsalis pars parvocellularis; PPC, posterior parietal cortex; PUT, putamen; SC, somatosensory cortex; SMA, supplementary motor area; SNr, substantia nigra pars reticulata; STG, superior temporaL gyrus; VAmc, ventralis anterior pars magnocellularis; Vapc, ventralis anterior pars parvocellularis; VLm, ventralis lateralis pars medialis; VLo, ventralis lateralis pars oralis; VP, ventral pallidum; VS, ventral striatum; cl-, caudolateral; cdm-, caudal dorsomedial; dl-, dorsolateral; l-, lateral; ldm-, lateral dorsomedial; m-, medial; mdm-, medial dorsomedial; pm, posteromedial; rd-, rostrodorsal; rl-, rostrolateral; rm-, rostromedial; vm-, ventromedial; and vl-; ventrolateral.

cuitry suggests that there are multiple, discrete, but partially overlapping, corticostriate inputs.[26] These inputs are progressively integrated in their passage through the pallidum and substantia nigra to restricted portions of the thalamus and, from there, they are funneled back to the cortical area.[26] The behavioral functions of these circuits has not been as well defined as similar motor and oculomotor pathways so, at present, it seems best to simply describe what is known about the anatomy of these circuits without prematurely designating functions for each.

A *dorsolateral prefrontal circuit* in primates connects cortex within and around the principal sulcus and the dorsal prefrontal convexity cortex, including Brodman areas 9 and 10, with caudate nucleus neurons extending from the dorsolateral regions of the head to the tail of the nucleus.[27,28,48] These caudate regions, in turn, project to the dorsomedial globus pallidus and the rostral portions of the substantia nigra, which, in turn, project to the ventral anterior and medial dorsal nuclei of the thalamus. Thalamocortical fibers then project back to the dorsolateral prefrontal originating cortex to complete the circuit.[26] Projections from the posterior parietal cortex, Brodman area 7, and the arcuate premotor area also have projections to the same caudate regions.[25,26]

A separate *lateral orbitofrontal circuit* projects from orbitofrontal cortex (Brodman area 10) to the ventromedial caudate nucleus, extending from the head to the tail.[26] This portion of the caudate also receives input from the temporal lobe visual and auditory association cortex.[47] The ventromedian caudate projects to the internal segment of the globus pallidus and the rostromedial substantia nigra, which, in turn, also project to the ventral anterior and dorsomedial thalamic nuclei that complete the circuit by projecting back to lateral orbitofrontal cortex.

A final pathway usually referred to as the *anterior cingulate circuit* originates in the anterior cingulum (Brodman area 24) and from "limbic" temporal lobe structures, including the hippocampus, amygdala, and entorhinal and perirhinal cortex, and from orbitofrontal cortex, which all project to the ventral striatum (nucleus accumbens septi and olfactory tubercle) called the *limbic striatum* by Nauta and Domesick.[50] The ventral striatum projects to the ventral pallidum and substantia nigra, and then to the mediodorsal nucleus of the thalamus and back to the originating cortical regions.

Projections from these striatal circuits can be interrupted by lesions undercutting the caudate within the anterior limb of the internal capsule. These circuits are depicted in tabular

form in Fig 4, taken from the work of Alexander et al.[26] The striatum receives input from all major sensory, multimodal association regions, and limbic regions of the cortex. The cortical projections are highly patterned and cortical areas that are reciprocally connected by corticocortical connections project in turn to similar regions within the caudate nucleus.[47] Thus, there is an anatomical substrate for the contribution of the caudate nucleus to cognitive function and behavior.[48,51] The caudate nucleus may be part of a mechanism whereby cortical regions involved in higher functions, including motivation, may gain access to motor output areas.[52]

Abulia

Reduced activity and slowness were the most common and important behavioral abnormalities identified in our patients. The quantitative and temporal features of behavior have received less attention than the qualitative aspects. The initiation of spontaneous behavior, the latency of responses after stimulation, the speed of responses, and the duration and completeness of responses are variables readily assessed in motor units, but more difficult to measure when responses are complex or cognitive. A variety of descriptive terms have been used to describe clinical disorders of the amount, speed, and thoroughness of behavior, including intermittent interruption of behavior,[53] bradykinesia and bradyphrenia, abulia, akinesia, and akinetic mutism. These terms describe a continuum from minor or transient reduction to complete absence of observable behavior (akinetic mutism), despite retained ability to move and speak normally under some circumstances. We prefer and use herein the term *abulia*, popularized by Fisher[22] to describe the full spectrum of abnormalities. Fisher characterized abulic patients as lacking in spontaneity of action and speech, deficient in initiative, apathetic, inert, mentally slow, slow to move, having reduced excursion of motion, and poorly attentive and yet easily distractable.[22] Verbal responses are late, terse, incomplete, and emotionally flat, but the intellectual content is normal if patients are prodded repeatedly. Our abulic patients conformed in every detail with Fisher's description.[23]

The anatomy of abulia in man has not been systematically studied. Fisher's abulic patients most often had lesions in the anterior cerebrum (frontal lobes and underlying structures) or in the thalamus and upper brain stem.[22] When focal lesions were present, lesions in front of the central sulcus tended to produce reduced behavior, abulia, while posterior lesions were more often associated with a hyperactive, restless, agitated state.[22] Akinetic mutism has been reported in bilateral pallidal lesions,[28,54] bilateral frontal lobe infarcts,[55-57] and lesions of the thalami and upper brain stem.[58,59] Frontal lobe tumors[60,61] and patients with advanced Huntington's, Picks, or Alzheimer's disease (disorders that prominently affect frontal lobe structures) often have abulia. Recently cognitive and behavioral deficits have been noted in parkinsonian patients comparable to those found in patients with lesions of the prefrontal and frontal cortex.[50,62,63] A young woman with bilateral hypodense caudate lesions on CT had dramatic personality and behavioral changes, but no motor abnormalities.[7] She was indifferent, inattentive, and uninterested in her surroundings or examiners, but could be encouraged to concentrate well for short periods of time. Among 12 patients with neurobehavioral abnormalities and caudate lesions there were four who were apathetic and had decreased spontaneous verbal and motor activity.[11]

Animal and human experiments provide some insights into the role of caudate nucleus lesions in causing reduced behavior. Certain neurons in the caudate and putamen of monkeys can be shown by microelectrode recordings to be activated during presentation of signals that prepare the animal for movement; these neurons are activated up to 3 seconds before self-initiated or automatic and purposeful arm movements.[64] Similar neuronal activity is found in the supplementary motor area, premotor cortex, and substantia nigra[64] regions involved in the circuits described above.[26] The striatum and cortex are closely linked so that in animals selective caudate lesions lead to behavioral deficits equivalent to those found with lesions of the areas of the cerebral cortex that project to that region of the striatum.[42] In adult monkeys, bilateral electrical lesions in the caudate nuclei and anterior putamen lead to hypokinesia, slowness, poor attention, and a tendency to stand and stare for periods as long as 7 weeks.[29] Anterior caudate lesions in cats impair delayed response and attention tasks.[65] In epileptic patients, unilateral electrical stimulation of the head of either caudate nucleus causes partial cessation of voluntary movements and speech similar to stimulation in the white matter of the posterior frontal lobes.[66] "Psychic" effects such as amnesia, euphoria, and decreased responsiveness to visual and auditory areas were also found after caudate stimulation.[66] Supplementary motor area lesions[67] and stimulation[68] in man produce similar behavioral and speech arrests.

Abulia in our patients and others with caudate lesions could be due to interruption of frontalstriatalthalamiccortical circuits described. Alternatively dysfunction of circuits arising from the brain-stem reticular activating system-stimulating cortex might be implicated also. Ascending biogenic amine pathways originate in the brain stem and project through the median forebrain bundles, disperse into the caudate nuclei, and pass to the frontal cortex.[69,70] The presence of akinetic mutism in patients with brain-stem lesions[58] and improvement in a patient with akinetic mutism due to rostral brain-stem disease after treatment with dopamine agonists,[59] all support involvement of these afferent systems in some abulic patients. Afferent aminergic systems are distributed asymmetrically.[71] Starkstein et al[18] postulated that these asymmetries might explain the preponderance of depression in left anterior hemisphere-damaged stroke patients over those with right-hemisphere comparable lesions, and Fisher[22] has wondered if abulia was more common in patients with left anterior cerebral lesions. We found a slight, but nonsignificant, preponderance of left caudate lesions among our abulic patients. Lesions of the anterior limb of the capsule were not necessary, since the four patients with lesions limited to the caudate nucleus all had abulia.

Restlessness and Hyperactivity

Restlessness, increased motor activity, and even delirium characterized the behavioral abnormalities of seven of our patients with caudate infarction. In some, the hyperactivity and agitation alternated with abulia and periods of apathy, but in others hyperactivity was the predominant abnormality. Anxiety, agitation, and talkativeness were also common among a series of patients with caudate lesions and neurobehavioral abnormalities.[11]

Fisher[22] noted that behavioral hyperactivity with restlessness, excitement, agitation, talkativeness, and shouting was sometimes associated with aggressiveness and striking out at others. Patients with these findings usually had posterior hemispheral lesions in contrast to abulic patients who had anterior lesions. In a series of pa-

tients with right middle cerebral artery inferior division infarcts, restlessness and agitation correlated with lesions in the temporal lobe on CT.[72] In another series of patients with right-sided middle cerebral artery infarction, extreme agitation, irritability, and "autonomic overactivity," also correlated with temporal lobe infarction, especially involving the middle temporal gyrus.[9] Among 41 of these patients, 34 had infarction involving the basal ganglia, 4 of whom had extreme agitation and 30 of whom did not. Others have also emphasized the importance of temporal lobe lesions in patients with agitation.[73,74] Hyperactivity and agitation can also be found in patients with left middle cerebral artery inferior division infarcts,[75] and bilateral temporal lobe lesions, eg, herpes simplex encephalitis.

Infarction within the posterior cerebral artery territories (PCA) affecting the occipital and temporal lobes inferior to the calcarine fissure, including the lingual and fusiform gyri, also has been associated with agitated delirium.[76-80] Most reported examples have been bilateral infarcts, but unilateral PCA territory infarction, especially affecting the left occipital and posteromedial left temporal lobe, has also been accompanied by restlessness, distractibility, irritability, and disorientation.[80]

Lesions of limbic cortex or the brain-stem reticular activating system underlie these reported instances of restlessness and agitation. We have already noted that these regions have input into the caudate nucleus and projection fibers from these regions and from the thalami traverse the anterior limb of the internal capsule adjacent to the caudate nucleus. Nauta[81] reviewed the connections of the caudate nucleus, the basal ganglia, and the ventral striatum with the frontal and temporal lobe components of the limbic system.

Neglect of Contralateral Space

Contralateral neglect was a prominent feature in three of our patients all with right caudate infarction. In animals[82-85] and man,[21,86-93] a variety of right brain-stem and cerebral lesions have been associated with inattention or neglect of left-sided visual, auditory, and tactile stimuli. Hemispatial neglect has been described in humans with lesions of the right frontal lobe,[21,86-88] inferior parietal lobule,[21,89,90] cingulate gyrus,[87] thalamus,[91,92] and the superior colliculus.[93] The putamen[94] and caudate nucleus[95-98] have also been implicated, but the described lesions have all been large, extending beyond the confines of the striatum. Ferro et al[8] described 15 patients with lesions limited to the striatum, internal capsule, and adjacent white matter in the right cerebrum who had contralateral "subcortical" neglect. Six had involvement of the caudate nucleus and 1 patient with a "caudateputamenocapsular" infarct similar to the largest infarcts in patients in our report had severe hemispheral neglect. Most patients with subcortical neglect had slight abnormalities that were often transient.[8]

In the rhesus monkey, the caudate nucleus receives projections from all areas of the cerebral cortex that have been implicated in hemi-inattention—[70,99] the polymodal regions of association cortex,[26,100,101] the frontal lobes,[26,47,102] and the cingulate gyrus.[26] Hemi-inattention may follow lesions of the caudate nucleus because of disruption of the parietal, frontal, limbic, or reticular components of the circuitry subserving attention. The hemi-inattention syndrome following caudate infarction is usually transient because the remaining intact structures are able to compensate.

The anterior limb of the internal capsule was involved in all three of our patients with hemi-inattention, and one also had extension to the putamen. A lesion of the anterior limb itself could cause neglect even when the striatum is spared by interfering with afferent projections from the thalamus.[103] One of the authors (J.D.S.) has observed a patient with hemi-inattention following infarction of the genu of the right internal capsule.

Hemi-inattention presumably results from predominantly right-sided subcortical lesions because of the recognized dominance of that hemisphere for attention and visual-spatial orientation.[70,104-106] Visual-spatial abnormalities were also occasionally found in patients with right-sided caudate infarction.

Language Abnormalities

Abnormalities of the production and comprehension of written and spoken language have been noted in patients with subcortical lesions that do not involve traditional perisylvian-dominant hemisphere cerebral cortex. Patients with left-sided putaminal hemorrhage often have an initial global aphasia and later show elements of transcortical aphasia. Broca's-type aphasia can be found in patients with anteriorly placed putaminal hemorrhages, while hemorrhages located far posteriorly in the putamen have been associated with fluent Wernicke-type aphasia. None of the patients with caudate hemorrhage was described as aphasic.[1-4] Subcortical infarcts have also been noted to cause dysphasia. Naeser et al[13] and Damasio et al[14] each reported series of patients with aphasia and predominantly subcortical lesion sites on CT. The aphasic syndromes varied greatly depending on the size, anteroposterior location, and extent of the lesion. Patients were invariably hemiparetic and had prominent dysarthria; recovery of language function was usually rapid. Paraphasic errors and abnormal naming and repetition of spoken language were common. No patients in either series had a lesion limited to the caudate nucleus or the structures included in our series. A single patient with aphasia and left-sided caudate infarction has been reported in abstract form.[16] This patient had preserved comprehension and repetition of language, but made semantic errors and had many intrusions and perseverations. Among 19 aphasic patients with subcortical lesion sites studied by Alexander and colleagues,[37] several had lesions of the caudate nucleus, anterior limb of the internal capsule, and putamen similar to our patients. These patients had slight word-finding difficulty or hesitancy, but none had severe aphasic abnormalities. Projections from the auditory cortex to the head of the caudate nucleus travel in the anterior limb of the internal capsule[107] and could have been affected in patients with aphasia and left-sided caudate infarction. Stuttering and stammering were prominent features of our two aphasic patients with left-sided caudate infarction. Stuttering can occasionally be acquired and develop after stroke and has been associated with lesions affecting the extrapyramidal system.[108]

Other cognitive and behavioral abnormalities frequently noted in patients with hemispheral cortical lesions were occasionally found in our series. These abnormalities included memory abnormalities, poor drawing and copying, and visual-spatial abnormalities. Depression has also been noted in patients with subcortical infarcts, especially those located in the caudate nucleus and adjacent white matter,[109,110] and in Parkinson's disease.[111,112] We did not detect depression in the patients in our series, but one patient in the series of Mendez et al.[11] had "crying spells." One of the authors (L.R.C.) has seen a patient with a CT-documented caudate infarct of uncertain chronicity, whose major symptom

was acute depression responding to tricyclic antidepressants.

Vascular Anatomy and Mechanisms of Stroke

The infarcts in this series were limited anatomically to the head of the caudate nucleus, the rostral putamen, and the anterior limb of the internal capsule. These structures receive their blood supply from three major sources: Heubner's artery, direct penetrating arteries from the proximal anterior cerebral artery, especially the short central artery, and medial striate branches from the proximal middle cerebral artery. Heubner described his artery over 100 years ago,[113] yet descriptions of the anatomy of this vessel vary widely.[114-119] The recurrent artery of Heubner usually (>75%) arises from the beginning of the A2 segment of the anterior cerebral artery near the anterior communicating artery junction.[114,117] The artery then loops and usually courses parallel to the A1 segment of the anterior cerebral artery. In only one fourth of patients is the recurrent artery a single vessel; more often, there are two, three, or even four recurrent arteries.[117] The multiplicity of major penetrating arteries is similar to the situation in the lateral lenticulostriate and thalamostriate arteries. Heubner's artery nearly always supplies the head of the caudate and the anterior limb of the internal capsule,[117] but has little supply posterior to the anterior commissure.[118] Figure 5 from Gorczyca and Mohr[117] shows the distribution of supply of the recurrent artery of Heubner from injection techniques.

The very far medial lenticulostriate arteries also can supply the anterior limb of the internal capsule, the putamen, and the most lateral border of the caudate nucleus. Anastomoses are sometimes present between these medial striate arteries and the recurrent artery of Heubner.[117,119] Figure 6 depicts a lesion in the anterior limb of the internal capsule caused by a proximal occlusion of the middle cerebral artery before the medial lenticulostriate branches. Most observers have identified arteries that penetrate directly into the anterior perforating substance and more laterally from the proximal anterior cerebral artery. One artery, the short central artery, is more consistent than others and may in some individuals supply a portion of the caudate nucleus and anterior limb of the internal capsule.[120] All the arteries that supply the caudate nucleus, anterior limb of the capsule, and anterior putamen are penetrating arteries

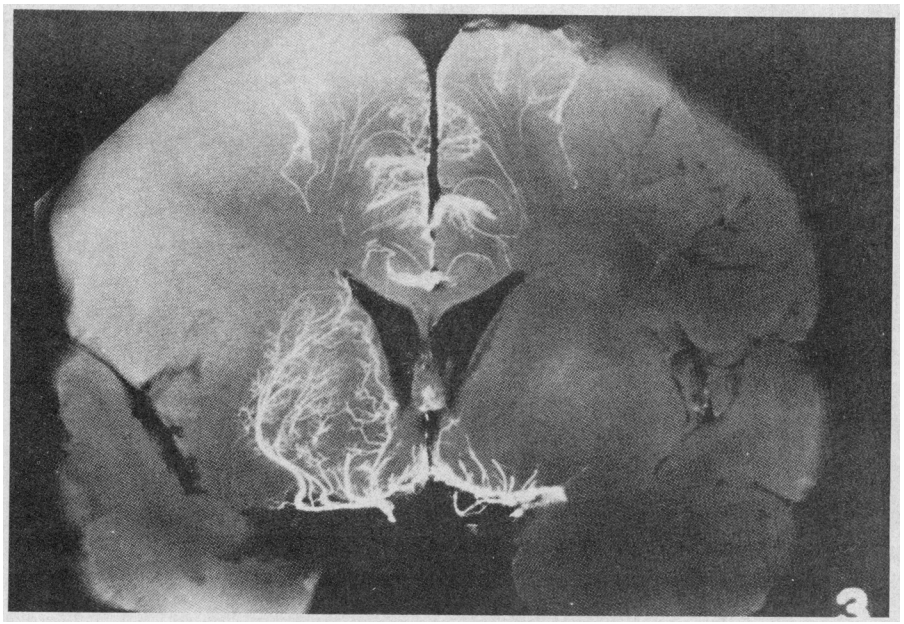

Fig 5.—Supply of Heubner's artery at the level of the anterior commissure. On the left of the figure, the arterial supply is shown in white. From Gorczyca and Mohr.[117]

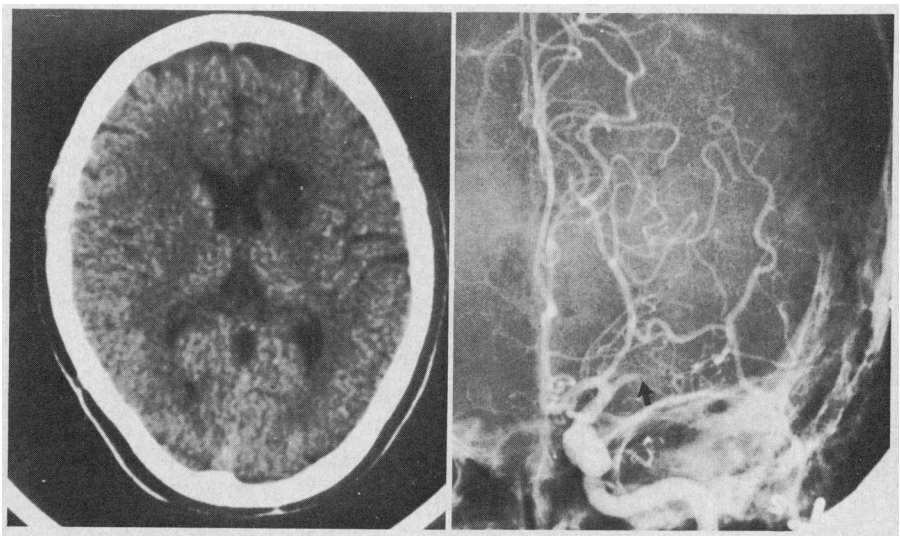

Fig 6.—Left, Computed tomographic scan without contrast showing infarct in the anterior limb of the internal capsule and white matter adjacent to the caudate nucleus. Right, Carotid angiogram, anteroposterior view. Occlusion of proximal middle cerebral artery (black area) before medial lenticulostriate branches. The posterior cerebral artery fills from the internal carotid artery directly.

subject to the same pathologic conditions as the lenticulostriate, thalamostriate, and thalamoperforating arteries. These vessels could theoretically be compromised by occlusion of the parent artery[112,122] (as in Fig 6, right) or by microatheroma or lipohyalinosis at the origin of the penetrating branch.[35]

Most patients were not systematically evaluated to establish stroke mechanism. The overwhelming majority of patients had well-established risk factors for primary penetrating artery disease; hypertension was very common (77%) and diabetes mellitus was present in one third of patients. Five patients had both hypertension and diabetes, and only three patients (16%) had neither hypertension nor diabetes. Only one patient had confirmed larger artery occlusive disease (angiographically demonstrated carotid artery syphon stenosis) that could have been incidental. Only one patient had a documented cardioembolic source, mitral stenosis. These demographic data, and the fact that in-

farcts were limited to penetrating artery territory favors the hypothesis that the causative mechanism was penetrating branch disease caused by microatheroma or lipohyalinosis. Without necropsy, this hypothesis must remain speculative. Unfortunately, the literature contains no examples of infarction limited to the caudate nucleus and anterior limb of the internal capsule in which pathological data establishes the stroke mechanism.

Caudate and anterior capsular infarction probably represents another stroke syndrome usually caused by penetrating branch disease. The most common features are dysarthria and behavioral abnormalities, especially abulia and restless agitation. Analysis of future cases may help define the vascular mechanism and spectrum of usual clinical findings and may yield further insight into the function and connections of the striatum and anterior limb of the internal capsule.

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