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SUMMARY: The caudatoputamen (CP) and globus pallidus (GP) are supplied by vessels often involved with stroke in both rat and human. The pattern of vascular supply to the CP and GP in rat has, in contrast to humans, been only partially described. The vascular pattern to the rat CP and GP is described utilizing vascular endocasts and scanning electronmicroscopy in aging, normotensive rats. Endocasts were produced by intra-cardiac infusion of Batson's Corrosion Compound. The vascular pattern is complex, involving 1) recurrent vessels from the anterior cerebral artery, 2) branches from the arterial circle rostral or caudal to the origin of the middle cerebral artery (MCA), 3) up to 6 branches from the MCA, and 4) 2 major branches from the caudal part of the arterial circle. The vessels in groups 1-3 were serpentine, their luminal diameters abruptly reduced at branch points, and the angle of departure from the parent vessels approximated 90°. These vessels supplied much of the CP and GP, while group 4 supplied the caudal CP with vessels arranged in a lattice-like fashion from the 2 penetrating parental arteries.

THE VASCULAR SUPPLY to the basal ganglia (caudate, putamen and globus pallidus) is involved in a large percentage of the cerebrovascular accidents that occur in man. Patients with infarction or hemorrhage into the basal ganglia may show movement disorders and postural abnormalities. Although hypertension is a significant factor in cerebral vascular diseases, the effects of hypertension on the structure and histochemistry of extracerebral vessels is better understood than the pathophysiology of stroke prone vessels.

The rat is one of the principal models in the study of vascular pathophysiology associated with hypertension, and, most important, stroke mechanisms in rats and humans may be similar. The vascular supply to the rat basal ganglia has been only partially described. The endocast data reported here are in accord with the microangiographical observations of Yamori et al.; however, endocasts provide a more definitive picture of the vascular patterns in the basal ganglia. A detailed description of the vascular patterns in the basal ganglia is a prerequisite to an evaluation of ultrastructural and histochemical changes in the walls of these stroke prone vessels and their relation to the pathophysiology of hypertension. The vascular patterns in the caudatoputamen (CP) and globus pallidus (GP) are described utilizing vascular endocasts and scanning electron microscopy in aging, normotensive male rats.

Methods
Two techniques were used to gather the data for the present report. These techniques are described under headings I) Production of Endocast for Scanning Microscopy and II) Dissection of Fixed Brain with Endocast in situ.

I. Production of Endocast for Scanning Microscopy
Thirteen male rats (13-20 months old) with normotensive blood pressures (systolic pressure range of 92-128 mm Hg, Narco Bio-systems, indirect blood pressure measurement system) were anesthetized with sodium pentobarbital (40 mg/kg i.p.). The thorax was opened and each animal was infused through the heart with heparinized physiological saline. The descending aorta was clamped with a hemostat and 70-100 ml of freshly prepared Batson’s Corrosion Compound (Polysciences, Inc.) were slowly injected into the left ventricle. The mixture of methacrylate monomer (100 ml), catalyst (15 drops) and promotor (24 ml) was contained in a 60 ml syringe. This mixture was delivered through a 16 G needle (cut to 1.5 cm in length) into the left ventricle. When injection of the methacrylate solution was completed, the animal’s head was removed and kept in cold water for at least 6 hours while the methacrylate resin cured. The brain and associated blood vessels were exposed by careful removal of the skull. A Zeiss operating microscope was used when the brain and vascular tree were removed from the cranial vault. The brain was placed in a solution of potassium hydroxide (85 g KOH in 250 ml water) maintained at 50°C and the nerve tissue and bone fragments were eroded from the cured endocast. The solution of KOH was renewed every 24 hours and the endocast was washed with a thin stream of water to facilitate removal of eroded tissue. The endocast was soaked in tap water for at least 24 hours and then inspected, using the Zeiss operating microscope, to determine if the endocast was free of bone and brain tissue and also whether the arteries of the base of the brain had filled with resin. The major arteries on the base of the brain were identified with the aid of Greene’s figure 219. The endocast was

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allowed to air dry 3 to 5 days and then divided into left and right half. The casts were divided to provide a clearer view of the vessels supplying the caudatoputamen and globus pallidus. Frequently, the distal cortical branches of the middle cerebral artery were also trimmed to permit a clear view of the penetrating vessels in the basal ganglia. Each half was positioned on a narrow strip of adhesive copper tape and attached to a stub with silver conducting paint. Specimens were coated with gold palladium in a Technics Hummer II sputter coater and examined with an ISI Super 3A scanning electron microscope with an accelerating voltage of 15 kV.

II. Dissection of Fixed Brain with Endocast In Situ

Fixed brains were dissected following the injection and curing of the colored (red) methacrylate resin to determine the vascular pattern in the various regions of the caudatoputamen and globus pallidus. Three brains were carefully removed from the cranial vault after injection of the colored resin and then placed in a 10% formalin solution for 2 to 3 days. The brains were then cut into 1 mm coronal slabs. The initial cut was made at the caudal end of the olfactory tubercle, and the coronal section produced corresponds to level A:7.8 of the stereotaxic atlas for the rat by Pellegrino and Cushman. The anterior commissure, corpus callosum, lateral ventricle and lateral olfactory tract were used as landmarks while dissecting the caudatoputamen (A:7.4 to A:10.5) (fig. 1B). The internal capsule, corpus callosum, optic tract and lateral ventricle and the fornix served as landmarks for the dissection of the globus pallidus and the caudatoputamen (A:7.6–A:3.6). The neural tissue was teased from the injected blood vessels. The location of the vessels supplying the caudatoputamen and globus pallidus were plotted on line drawings of the appropriate coronal sections. The origin of each penetrating vessel that supplied the caudatoputamen or globus pallidus was marked on the coronal sections. The vascular supply was then serially reconstructed and correlated with the scanning micrographs of the tissue free endocasts.

**Figure 1.** A. A photograph of the base of the rat brain showing the arterial circle and the major vascular branches from the circle. The arterial vessels have been filled with polymerized methacrylate resin (Batson's Corrosion Compound). The major vessels include the internal carotid (ICA), the middle cerebral (MCA) and anterior cerebral (ACA) and posterior cerebral arteries (PCA). B. A line drawing of a coronal section of a rat brain demonstrating the relationships between the caudatoputamen (CP), globus pallidus (GP), and the corpus callosum (CC), the ventricle (v) and the anterior commissure (CA). The latter 3 structures form the boundaries around the CP and GP.
Results

The observations reported in this study are presented under 3 headings: I) Pattern of arterial supply to caudatoputamen and globus pallidus, II) Variations in vascular patterns and III) Morphology of vessels drawn from the endocasts.

I. Pattern of Arterial Supply to the Caudatoputamen and Globus Pallidus

The arterial supply to the caudatoputamen and globus pallidus is complex, involving branches from 1) "recurrent arteries" from the anterior cerebral artery, 2) the arterial circle just rostral to the middle cerebral artery, 3) the middle cerebral artery and an arterial branch running along the medial aspect of the lateral olfactory tract, and 4) 2 major branches from the arterial circle between the middle cerebral and posterior cerebral arteries (fig. 1A). These 4 groups of vessels supply, with some overlap, regions of the caudatoputamen and globus pallidus.

The rostral area of the caudatoputamen (CP) extending from A:10.5 to A:8.2 is supplied by penetrating branches from the anterior cerebral and a vessel coursing along the medial aspect of the lateral olfactory tract (TOL vessel) (fig. 2A). Recurrent arteries (RA, 4–6) that arise from the anterior cerebral artery supply the rostro-medial aspect of the CP. The rostro-lateral portion of the CP is supplied by several penetrating vessels from the TOL vessel. An occasional anastomosis between branches from the TOL vessel is present; however, no evidence of vascular overlap or anastomosis between medial and lateral arterial branches was observed (fig. 2A). The more caudally arising branches from the arterial circle (rostral to the origin of the middle cerebral artery) supplying the CP at approximately A:8.2 are distributed to the middle and infero-lateral aspect of the CP. The infero-lateral branch penetrates to the depth of the posterior limb of the anterior commissure (CA) and then arborizes (fig. 2B).

The area of the CP between A:8.2 and A:6.8 is supplied by branches from the middle cerebral artery and branches from the arterial circle at the origin of the middle cerebral. The globus pallidus appears at A:7.6 and is supplied by penetrating branches from the arterial circle posterior to the origin of the middle cerebral (fig. 2B). The vessels generally do not arise as medial or lateral clusters; rather they emerge individually from points distributed along the middle cerebral artery. More specifically, the initial 2.5 mm of the middle cerebral, particularly as it courses around the caudal end of the olfactory tubercle, provides up to 6 penetrating branches that supply principally the CP. One of the more medial branches forms a fan-like arbor that is distributed to the medial and basal portion of the CP in association with the posterior limb of the anterior commissure. The intermediate branches penetrate into the CP, passing caudal to the posterior limb of the commissure. The more lateral and rostral branches enter the CP close to the medial surface of the corpus callosum.

The globus pallidus appears at approximately A:7.6 and the rostral part of this nucleus receives

![Figure 2](http://stroke.ahajournals.org/)

**Figure 2.** A composite reconstruction of the vascular patterns to the caudatoputamen and globus pallidus. Part A reveals the vascular pattern to the anterior portion of the CP. This region is supplied by "recurrent arteries" (RA) from the ACA and penetrating branches from the TOL vessel. Part B demonstrates the vascular supply to the middle part of the CP and the initial portion of the GP. Penetrating vessels from the MCA and from the arterial circle at the origin of the MCA supply this region. Part C shows that the caudal CP and much of the GP is supplied by penetrating branches from the arterial circle at the origin of the MCA or from two major branches off of the arterial circle between the MCA and the posterior cerebral artery.
penetrating branches that arise from the arterial circle at the origin of the middle cerebral artery (MCA). These vessels appear to pass directly to the globus (fig. 2B). The remainder of the GP (A:6.8-4.8) and the CP (A:6.8-3.6) are supplied by 2 major branches from the arterial circle situated between the middle and posterior cerebral arteries (fig. 2C). In addition to the short branches from the first major branch off of the circle, the GP also receives penetrating vessels from the arterial circle and proximal portion of the middle cerebral. The 2 principal branch vessels from the arterial circle posterior to the MCA course along the lateral aspect of the internal capsule. These vessels provide numerous branches to the CP and are arranged in a lattice-like fashion. The first branch from the arterial circle reaches as far caudal as A:4.8. The second branch from the circle supplies the CP to the caudal limit of the nucleus (fig. 2C).

II. Some Variations in Vascular Patterns

The patterns of vascular supply show some variation. The most frequent site of variation involves the initial segment of the middle cerebral artery (MCA). The MCA may have a dual origin, that is, 2 branches from the circle fuse to form the more distal portion of the MCA. In this instance, both branches give rise to penetrating arteries that supply the CP. Occasionally, a short branch arises from the circle vessel just rostral to the MCA and this short vessel ends as 3-4 penetrating vessels supplying the CP. Generally, the penetrating vessels arising from the MCA emerge individually along the course of the MCA. On the other hand, these vessels may arise in a cluster from the middle cerebral as far lateral as the rhinal fissure. The regions supplied by the penetrating vessels from the MCA are essentially the same, in spite of the variation in origin.

The vessels supplying the rostral or caudal portions of the CP also demonstrate some variations. Those vessels supplying the callosal CP generally arise as 2 distinct branches from the arterial circle between the MCA and posterior cerebral artery. The 2 vessels may arise from a common stalk, then bifurcate to supply the CP. The callosal member of the generally paired vessels may arise in association with the posterior cerebral artery. The vascular supply to the rostro-lateral portion of the CP shows some variation, particularly related to the distribution pattern of branches from the TOL vessel. The TOL vessel occasionally provides a branch that courses rostrally in the rhinal fissure (fig. 2A, small arrow). Penetrating branches from this vessel supply the dorsolateral portion of the CP.

III. Morphology of Vessels Drawn from Endocasts

A striking feature of many of the vessels supplying the CP and GP is their serpentine nature (fig. 3). The vessels are long and their internal diameters are strikingly uniform along the course of each vessel. The internal diameters of the vessels supplying the CP and GP change abruptly at branch points. The sudden reduction in luminal diameter is clearly demonstrated by the "recurrent arteries" where they arise from the anterior cerebral artery (fig. 4A). The lumen of the recurrent arteries may be ≤15% of the internal diameter of the anterior cerebral (33 μm/231 μm). Similar reductions in luminal diameters of progressive branches are seen in figure 4B. The parent vessel is the circle of Willis (A) with an internal diameter of approximately 300 μm. The branch vessel (B) has a diameter of 95 μm, and this short vessel divides into 2 branches. Branch (C) has an internal diameter of approximately 84 μm and it gives rise to 3 smaller vessels (see vessel D). The diameter of D is 24 μm while that of vessel E is 10 μm. There appears to be a rapid transition to the capillary beds of the vessels supplying the CP and GP.

The angle of departure of the penetrating vessels from the circle and middle cerebral approximates 90° with respect to the long axis of the parent vessel (fig. 4B). The branch angles at more distal points along the course of the penetrating vessels appear more variable.

The apparent surface of the endocast shows several morphological features. The large vessels contain many indentations that may correspond to the location of the nuclei of endothelial cells lining the lumen of the vessel. These indentations are also present on some of the casts of smaller vessels. Ring-like structures are also present on many smaller vessels (diameters < 60 μm) (fig. 4A). These annular figures appear to be out-pocketings from the lumen of the vessels and are pushing into the wall of the vessel. They may appear as a single or as multiple rings. Another feature revealed by the casts involves a trench-like structure or moat associated with the origin of branch vessels (fig. 5A). These moats are irregular in size and project into the lumen of the parent or stem vessel. The moats probably correspond to bifurcation pads.15

Discussion

The vascular supply to the caudatoputamen and globus pallidus is extensive and complex. This complexity is demonstrated by the detailed vascular patterns of the endocasts. The faithfulness of the replicas was better than anticipated. The casts include much of the capillary bed as indicated by the presence of many processes with internal diameters of 4-8 μm; such diameters fall well within the range of capillaries of the central nervous system (4-14 μm).16 18 Shrinkage of the cast associated with polymerization of the methacrylate resin may bias or distort the true luminal diameters; however, even a 50% shrinkage would provide luminal diameters within the range for capillaries. The resin appears to shrink approximately 1% based upon measurements of casts from glass tubes of known internal diameters. The casts also revealed structures associated with the tunica intima, more specifically, the impressions of endothelial cell nuclei and ring-like bands on small vessels. The casts clearly demonstrate bifurcation pads that may act as arterial valves and regulate blood flow into the branch.
vessels. Unfortunately, the casts do not provide details of the internal structure of the vessel walls, as can be revealed with scanning and transmission microscopy of properly prepared tissue. The endocasts do demonstrate the serpentine course of the penetrating vessels to the CP and GP, and the abrupt reduction in internal diameters of these vessels at branch points. In addition, this technique provides a good replica of the vascular patterns in the caudatoputamen and globus pallidus.

The vascular patterns described from the endocasts may include part of the venous drainage. Venous drainage patterns may complicate the interpretation of the cast, since the resin could enter venous channels by passing through the capillary bed or arterial-venous shunts. The occasional appearance of casts corresponding to the superior sagittal, superior petrosal and transverse sinus and jugular vein suggests that the resin has passed through the capillary bed or was perhaps shunted around the capillary bed. Identification of the major arteries at the base of the brain reduces the possibility of confusing arterial and venous patterns. The absence of observable continuities between known arterial branches, the capillary bed and known venous structures suggests that the venous side is not normally filled with the methacrylate monomere. Therefore, the vessels in the cast, even the smallest (4–8 μm i.d.), are probably a part of the arterial network to the basal ganglia.

The basic distribution patterns suggest that these vessels are not clustered as in primates and, therefore, terms such as medial, lateral or posterior striatal arteries may be misleading when applied to rats. The microangiograms of Yamori et al. correspond very closely to the vascular patterns revealed by the endocasts. The correlation is particularly obvious concerning the presence and distribution of "recurrent arteries." The lattice-like pattern of vessels to the caudal CP revealed by the endocasts was not apparent in the microangiograms. The differences in patterns of vessels supplying the caudal CP (AP:6.8–3.6) compared to the rest of the CP (AP:6.8–10.5) may be related to the susceptibility of the regions to stroke. The high incidence of stroke, 24% of strokes in SHRSP rats, and involvement of the basal ganglia, with 88% of the strokes in the rostral CP, correlates well with specific morphological features of the vessels supplying these areas. The serpentine course, the sudden reduction in internal diameters at branch points and the angles of departure of the branch vessels may contribute to the high incidence of stroke in this part of the brain.
FIGURE 4. Two scanning photomicrographs that demonstrate the sudden reduction of internal diameters at branch points in the stroke prone vessels to the caudatoputamen and globus pallidus. Plate A shows a "recurrent artery" and its 3 branches viewed from the medial aspect. The large parent vessel is the anterior cerebral artery (ACA). Annular figures (arrows) are also present. Calibration line equals 100 μm. Plate B also demonstrates the marked reduction in the internal diameter of consecutive branch points (A-E) (A = 300 μm, B = 95 μm, C = 84 μm, D = 24 μm, E = 10 μm). The angle of departure for vessel B from vessel A approximates 90°. Calibration line equals 100 μm.
Abbreviations

ACA anterior cerebral artery. CA anterior commissure. CC corpus callosum. CP caudatoputamen. GP globus pallidus. IC internal capsule. ICA internal carotid artery. MCA middle cerebral artery. OC optic chiasma. PCA posterior cerebral artery. RA recurrent arteries. RF rhinal fissure. TOL lateral olfactory tract. TOl vessel, vessel along lateral olfactory tract. v ventricle.

References


Figure 5. A scanning photomicrograph that demonstrates the moats or bifurcation pads associated with the points of origin for many branch vessels (arrow). The rough surface of the endocast is apparent and may represent the protrusion of endothelial nuclei into the lumen of the vessel. Calibration line equals 100 μm.
**Alpha-Adrenoreceptor Antagonists and Pial Vessel Diameter During Hypercapnia and Hemorrhagic Hypotension in the Cat**

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**SUMMARY** It has been proposed that sympathetic activation may prevent maximum dilatation of extraparenchymal cerebral vessels during hemorrhagic hypotension and hypercapnia. In the present study, the effect of alpha-adrenoreceptor antagonists (phenoxybenzamine 1.5 mg kg\(^{-1}\) or phentolamine 8 mg kg\(^{-1}\)) on pial vessel diameter was studied in the cat during hypotension and hypercapnia alone or in combination. Two levels of hypercapnia were used (mean Paco\(_2\) 74 and 122 mm Hg respectively). Pial arterial vessels (resting diameter 40–184 µm) were observed by means of a closed cranial window technique using a Leitz intravital microscope, an image splitting eyepiece, and a videoangiometer, the latter giving continuous data on changes of the inspected vessel diameters. Alpha-adrenoreceptor antagonists did not further increase the arterial diameter in any of the situations studied.

**REGULATION OF CBF by carbon dioxide** is generally believed to be mediated via extracellular H\(^+\) concentration, but other possibilities have been discussed such as regulation via carotid chemoreceptors and interaction between H\(^+\) and other vasoactive components. Discrete lesions in the mesencephalic reticular formation have been reported to reduce or abolish the response to carbon dioxide, and to reduce the response obtained after pretreatment with indomethacin. Stimulation of the cervical sympathetic chain during hypercapnia has been reported to result in a decrease of cerebral blood flow (CBF), an effect possibly caused by constriction of the extracerebral, including pial, vessels. Hypercapnia may cause sympathoadrenal activation, although cervical sympathetic stimulation did not inhibit pial arteriolar dilatation during subsequent hypercapnia, although the hypercapnic CBF-increase was abolished.

Cerebral vessels have been reported to autoregulate at a lower level when the pressure is reduced by drugs than by bleeding in previously normotensive baboons but not in renal hypertensive baboons. As alpha-adrenoreceptor blockade improved the maintenance of CBF in hemorrhagic hypotension, it was suggested that the increased sympathetic activity during hemorrhagic hypotension leads to a vasoconstriction of the main inflow vessels to the brain.

The present experiments were performed to evaluate a possible influence of the presumed increased sympathetic activity during hypercapnia and hemorrhage on pial vessels, i.e., to provide the answers to the following 3 questions:

1. Does alpha-adrenoreceptor blockade further dilate pial vessels during hypercapnia per se?
2. Do pial arterial vessels increase their diameter after alpha-blockade in hemorrhagic hypotension?
3. Does a sympathetic stimulation induced by bleeding reduce pial vessel dilatation during hypercapnia?

**Materials and Methods**

Seventeen cats were anesthetized with 40 mg kg\(^{-1}\) pentobarbital, immobilized with 60 µg kg\(^{-1}\) pancuroniumbromide, intubated endotracheally and respirated with a 3:1 mixture of N\(_2\)O:O\(_2\), using a Loosco respirator (Hoek-Loos, Amsterdam, Holland). Both femoral arteries and one femoral vein were cannulated with Portex catheters for continuous monitoring of blood pressure (Hellige-unit, Hellige, Freiburg, GFR), withdrawal of arterial blood for frequent blood gas controls (AVL gas check type 937C, List, Graz, Austria) and intravenous administration of drugs, respectively.

Pial vessels were observed by means of a closed cranial window technique using a Leitz intravital microscope (Leitz, Wetzlar, GFR), an image splitting eyepiece and a videoangiometer, the latter giving continuous data on changes of the investigated vessel diameters. Alpha-adrenoreceptor antagonists did not further increase the arterial diameter in any of the situations studied.

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