		Vasopressin		Angiotensin II		Phenylephrine		Isolevine		Common SD
	Control	16 mU	32 mU	0.10 μg	0.20 μg	9.2 μg	19.4 μg	0.11 μg	0.19 μg	
n	20	11	11	10	10	10	10	9	9	
Total body										
Body weight	198.5	202.3	205.4	192.0	195.5	218.0	203.5	185.0	207.8	34.8
Blood pressure	123.2	152.3[b]	160.1[b]	142.0[b]	152.5[b,c]	173.0[b]	172.5[b]	93.9[b]	77.8[b]	18.1
Cardiac index	20.6	17.8	18.7	16.3	13.6[b]	18.8	17.2[b]	23.1	27.4[b]	4.8
TPR	503.2	713.7[b]	730.2[b]	736.7[b]	961.0[b]	749.0[b]	805.5[b]	338.1[b]	227.0[b,d]	150.7
M. triceps surae										
Blood flow l	2.89	2.77	2.45	2.34[a]	1.85[b,c]	3.05	2.31	2.21	1.54[b]	0.85
Blood flow r	5.64	4.78	4.93	4.66	3.49[b]	5.00	3.61[b,c]	6.72	16.42[b,c]	3.42
left/right; percent	55.2	59.3	51.6	53.9	54.3	60.8	63.5	39.8[a]	11.0[b,d]	15.4
Resistance l	3722	5133[a]	5757[b]	5021[a]	7634[b]	5061[a]	6628[b]	3753	6127	2340
Resistance r	1930	2819[b]	2762[b]	2741[b]	3776[b,c]	2891[b]	4127[b,c]	1508	483[b,c]	904

Body weight: g; blood pressure: mm Hg; cardiac index: ml/min 100 g b.wt; TPR: 10^3 cm dyn sec^{-5}/100 g b.wt; blood flow: ml/min 100 g weight of m. triceps; resistance: 10^3 cm dyn sec^{-5}/100 g weight of m. triceps. l = left, r = right.
Differences. Control versus treated: [a]$p < 0.05$, [b]$p < 0.01$; treated versus treated: [c]$p < 0.05$, [d]$p < 0.01$.

and contralateral sides. Except for the larger dose of phenylephrine, these drugs did not change the blood flow and resistance on the 2 sides relative to each other.

Isolevine, especially the larger dose, significantly increased the cardiac index and decreased the TPR. The blood flow of the triceps muscle increased, while its resistance decreased compared to the control non-treated group. On the ligated side, these changes were opposite in direction. Thus, the ratio of blood flows on the 2 sides decreased and that for their resistances increased depending on the dose.

In our experiments the relationship between the ligated and control sides for nutritive blood flow and resistance did not change following administration of vasoconstrictor agents. Thus, the 'relative' sensitivity of nutritive collaterals in the muscle to vasoconstrictor agents can be regarded as similar to that of the contralateral, non-ligated side. On the contrary, isolevine caused dilatation of the muscle vessels on the control side while on the ligated side – probably due to a decrease in perfusion pressure – it resulted in a decrease in blood flow and an increase in resistance. In respect of total blood flow, there are published data reporting decreased sensitivity of muscle collateral vessels to vasodilating agents[4]. Similar observations were made for cardiac muscle[5]. On the basis of our experiments, it can be stated that the decreased reactivity is valid for the nutritive collaterals of the striated muscle of rats as well.

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Amphetamine induced turning behavior as an index of stroke in the mongolian gerbil

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Summary. The effects of i.p. injections of amphetamine and apomorphine were determined before and after unilateral ligation of the carotid artery in the gerbil. Significant increases in turning behavior were observed in the absence of neurohistological evidence of infarction.

Dopaminergic drugs induce turning behavior in animals that have been subjected to unilateral lesions of the nigrostriatal system[1]. Amphetamine which causes the release of (DA) gives rise to turning towards the lesioned side (ipsilateral) and apomorphine, a DA receptor stimulant, induces turning away from the lesion (contralateral). The apomorphine effect may be due to denervation supersensitivity of DA receptors on the lesioned side and only develops after a delay. The initial effects of apomorphine, like amphetamine, cause ipsilateral turning due to the more active dopaminergic system in the unlesioned side. These drugs in higher doses also produce turning behavior in some normal animals, implying an inherent imbalance in DA systems[2].

Uniquely, in the case of the Mongolian gerbil (Meriones unguiculatus) ligation of the carotid artery on one side will usually induce ischaemia in only that hemisphere[3]. This is due to the absence of significant connections between the basilar and carotid circulation in this species. Unilateral carotid ligation is fatal in a proportion of gerbils but at least 50% recover with no visible functional deficit and no histological signs of cerebral infarction[4]. In order to test the residual effects of this procedure in

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these apparently 'normal' surviving animals, we gave intraperitoneal injections of amphetamine and apomorphine and measured induced turning behavior.

Adult gerbils (60–80 g) were subjected to pentobarbital anesthesia and the left common carotid was dissected away from the vagus nerve and adjoining blood vessels. The artery was then either permanently ligated or temporarily clamped for 30 min using a suture.

In a pilot study 20 animals received permanent unilateral ligation and after one week the 15 survivors were tested for turning behavior to amphetamine. As compared to the effects of amphetamine prior to surgery there was a significant increase in turning behavior towards the side of the ligation. Subsequently, the effects of saline, amphetamine, and apomorphine were compared before and 1 or 8 weeks after a 30 min unilateral carotid clamp. Turns in both directions were measured separately. With regard to the side of the surgery ipsilateral turns were designated positive and contralateral turns were designated negative. Net turns refer to the arithmetic sum of these 2 values. Where total turns are analyzed both these numbers are signed positive and added. Large increases in turning behavior after amphetamine injection were again observed in these animals (table). The use of net turns in the data analysis implies that animals should turn consistently towards the stroked side in the case of amphetamine and away from the stroked side in the case of apomorphine. Although the overall effects are significant it should be pointed out that some animals do not increase turning behavior to amphetamine after the carotid clamp and some animals are induced to turn in the contralateral direction, thus subtracting from the significance of ipsilateral or net turning for the group. In this study 55% of all animals showed increased ipsilateral turning to amphetamine after carotid clamp. However an additional 4% of clamped animals responded to amphetamine by turning consistently in the contralateral direction. Therefore total turns summed irrespective of direction were also subjected to analysis as, a priori, the drug induced direction of turning may not be predicted without a knowledge of the site of any ischaemic damage. Apomorphine produced no significant effect at 1 week but was significant at 8 weeks when total turns are considered. In the case of apomorphine injections 26% demonstrated increased contralateral turns after 8 weeks but the group effect was significant only where computed as total turns irrespective of direction. The brains of 17 gerbils from the combined survivors were prepared for histological examination at the end of the experimental regimen. These gerbils were selected from the animals who were most sensitive to the effects of amphetamine as judged by turning behavior. Nissl stains of coronal sections were examined for evidence of swelling and infarction. As has been previously reported[4] no ischaemic lesions were evident in any of the survivors as revealed by the light microscope.

	Mean difference scores for postoperative minus preoperative turns per min			
	Saline	Amphetamine	Apomorphine	N
1 week postoperative net turns	−0.03	+1.16*	+0.4	16
1 week postoperative total turns	0.24	1.13*	0.78	16
8 weeks postoperative net turns	+0.09	+1.64*	−0.21	12
8 weeks postoperative total turns	0.24	1.25*	1.9*	12

Effect of (+)-amphetamine (5.0 mg/kg) and apomorphine (2 mg/kg) before and after a 30 min unilateral carotid clamp. Turning was measured for 1 min periods at 40 and 50 min after injection and averaged. Drugs were administered in 0.1 ml saline/20 g b.wt. Ipsilateral turns were designated as positive (+) and contralateral turns were designated as negative (−).

*Significant at $p < 0.05$ using a paired t-test. $N \geq 12$ for all groups.

It would appear then that gerbils that recover from this procedure are not normal but are markedly affected by amphetamine, causing turning behavior. Therefore, it may be assumed that amphetamine now has a differential action on both sides of the brain which was not observed prior to the carotid clamp. It is possible that some neurochemical or enzymatic disturbance is induced by the clamp on the ipsilateral side thus interfering with the ability of amphetamine to act on this half of the brain. Since the initiation of our own studies a report has appeared suggesting that in the Mongolian gerbil DA levels but not norepinephrine levels are markedly reduced in the ipsilateral hemisphere after carotid ligation[5]. As one of the major effects of amphetamine in brain is to increase available dopamine in the synaptic region then it is possible that the turning behavior which we have observed is due to the unavailability of dopamine for release on the lesioned side. These studies suggest that although a certain proportion of gerbils recover from unilateral ligation with no visible deficit, either behavioral or histological, an underlying pathology may be revealed by the administration of amphetamine which induces turning behavior. This test which apparently amplifies an inherent imbalance in brain function will provide a sensitive method by which to correlate the functional aspects of ischaemia with the underlying neurochemical alteration.

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Preferential neurotoxicity of pentobarbital on nerve and glial cells in culture[1]

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Summary. The effect of pentobarbital was studied in a mixed population of nerve and glial cells dissociated from brains of 7-day chick embryos and maintained in culture. Pentobarbital-Na was added in various concentrations ranging from 5×10^{-5} M to 1×10^{-3} M. The neuronal density was monitored by counting of neurons, neuronal identity was established by staining for Nissl Bodies and acetylcholinesterase. Over a culture period of 3 weeks, it was found that the barbiturate exerts a preferential dose-dependent cytotoxic effect on neurons.

Chronic administration of a barbiturate to newborn rats has been found to retard brain growth[2]. It is not clear whether this phenomen is caused by an effect on neurons, on glial cells or a combination of both cell types. In view

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