lots. In addition, uncertainty may also affect measurements made in vision clinics. Many ophthalmologists recognize that the apparent size and shape of visual fields can be altered by the patient's uncertainty about the direction in which the luminous test target will move in from the periphery of the visual perimeter. But intuition aside, it would be useful to have accurate data on the extent to which stimulus-uncertainty actually does limit visibility in everyday situations.

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10. A key assumption would be that there was a linear relationship between RT and sensitivity of the mechanism under study. Although we doubt that linearity obtains strictly, the relatively small variation in RT with uncertainty gives us at least a small-signal approximation to linearity.
11. E. Levinson and R. Sekuler, paper presented at annual meeting of the Psychonomic Society, Boston, October 1974; K. Ball and R. Sekuler, paper presented at annual meeting of the Psychonomic Society, St. Louis, November 1976.
12. R. Sekuler and K. Ball, paper presented at annual meeting of the Association for Research in Vision and Ophthalmology, Sarasota, Fla., April 1977.
13. Our results also tend to discredit the adage "Out of sight, out of mind."
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Striatal Efferent Fibers Play a Role in Maintaining Rotational Behavior in the Rat

Abstract. *Rats in which ascending dopamine-containing neurons have been unilaterally destroyed by injections of 6-hydroxydopamine are known to rotate after being injected with apomorphine or* L*-dopa. The rotation is markedly reduced by either (i) ipsilateral electrocoagulations of the caudate-putamen or internal capsule or (ii) ipsilateral coronal knife cuts immediately rostral to the substantia nigra. Neostriatal efferent fibers, in particular the strionigral projection, appear to be required for the expression of this dopamine-dependent behavior.*

Recent advances in the localization of neurons in the brain that contain catecholamine (*1*) have been associated with expanding interest in their behavioral functions. Much behavioral research has focused on the ascending neurons that contain dopamine (DA), and that originate in the mesencephalic cell groups A8, A9, and A10. These neurons give rise to axons that course through the medial forebrain bundle and internal capsule to terminate in the neostriatum (caudate-putamen), the nucleus accumbens septi, olfactory tubercle, cortex, and other limbic forebrain regions. When these neurons are destroyed bilaterally, rats display a syndrome of behavioral deficits characterized by failure to eat or drink, inattention to sensory stimuli, akinesia, and catalepsy (*2*). Certain clinical disorders of movement (for example, Parkinson's disease) also appear to be attributable to abnormalities of these DA-containing neurons. A possible dysfunction of these neurons in psychotic and manic states is also being investigated (*3*).

Despite the apparent behavioral significance of the ascending dopaminergic systems, the course and distribution of efferent fiber systems responsible for the expression of central dopaminergic activity has not been determined. We now report experiments intended to localize the efferent neurons of the basal ganglia that maintain the rotational behavior of rats with unilateral 6-hydroxydopamine (6-OH-DA) lesions of the ascending dopaminergic neurons, a behavior that depends upon the activation of forebrain DA receptors (*4*, *5*). To study rotational behavior, rats were given an injection of the catecholamine neurotoxin 6-OH-DA to destroy most of the ascending dopaminergic neurons of one hemisphere. Several days later, when given systemic injections of compounds that result in direct DA-receptor stimulation (apomorphine or L-dopa), the rats turn vigorously away from the hemisphere of the DA neuron loss (*5*). This rotation appears to be due to the development of postsynaptic supersensitivity in the striatum ipsilateral to the 6-OH-DA injection such that the animal turns away from the hemisphere of the highest DA-receptor activity (*5*, *6*). We then made electrocoagulations or knife cuts in the same hemisphere as the earlier 6-OH-DA injection. By analyzing the brain sites destroyed by those lesions effective in blocking rotation, we have been able to suggest the course of fibers leaving the strio-pallidal complex that maintain this behavior.

Male Sprague-Dawley rats ($N = 65$) weighing 150 to 200 g were given an injection of 6-OH-DA along the course of the ascending dopaminergic neurons of the left hemisphere (*7*). After 1 to 2 weeks, the rats were placed in a rotometer bowl (*4*) and given an intraperitoneal injection of apomorphine (0.25 mg per kilogram of body weight) or L-dopa (50 mg/kg). The number of turns to the left and right were recorded separately during the subsequent 60 minutes or until the rats stopped rotating. Testing was repeated 2 or 3 times per week for 1 to 3 weeks until each rat had exhibited stable rotation. Electrocoagulations (*8*) or knife cuts (*9*) were then made in the left hemisphere in an attempt to interrupt striatal efferent fibers that maintain the rotation. All rats were retested for rotation stimulated by apomorphine or L-dopa 2 to 4 times during the next 2 weeks. At the conclusion of the experiment each rat was killed, and its brain was removed for microscopic analysis of the lesion site. The brain was stained either with thionin stain or according to the fluorescence histochemical technique of Falck and Hillarp (*10*). We reconstructed the electrocoagulations or knife cuts using reproductions from the König and Klippel atlas (*11*), taking account of lesion-induced shrinkage and distortion of brain tissue.

Extensive destruction of the head of the caudate-putamen, completely sparing the globus pallidus and internal capsule, reduced apomorphine-induced rotation by 62 to 74 percent (*12*) in both

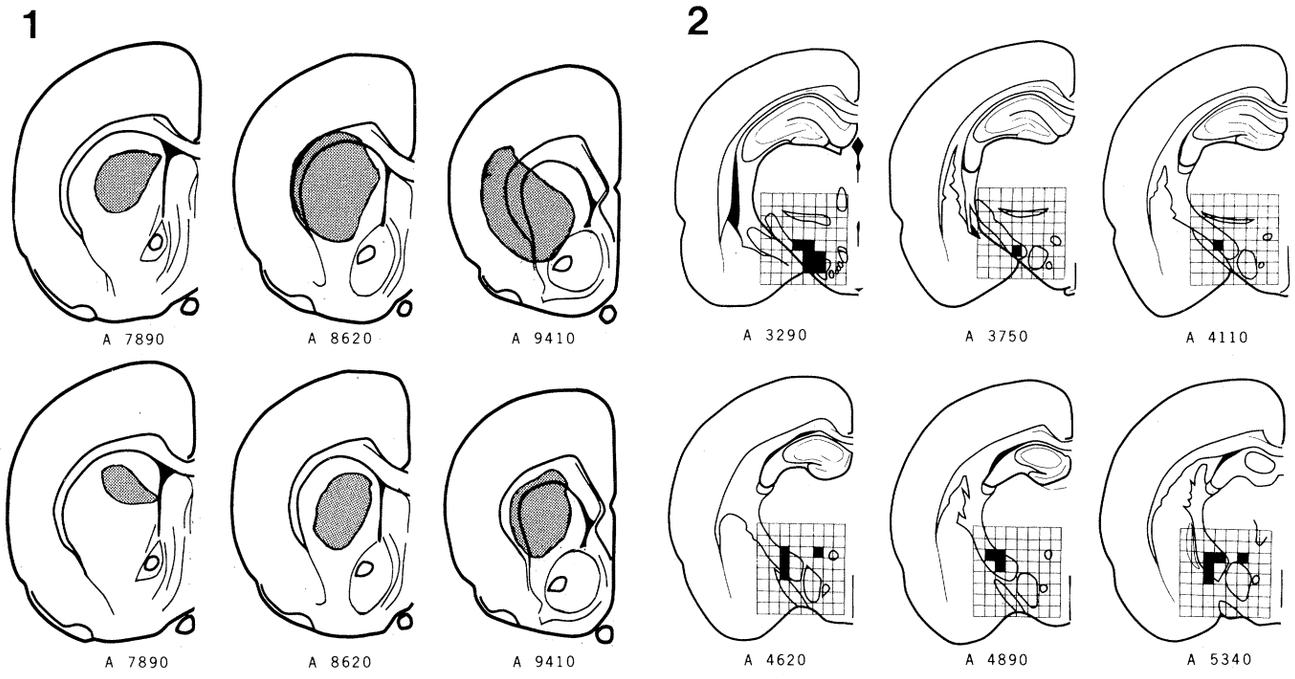

Fig. 1 (left). Reconstruction of neostriatal lesions produced in the same hemisphere previously injected with 6-OH-DA. (Top) Three frontal planes through a lesion effective in blocking apomorphine-induced rotation by 74 percent. (Bottom) Same frontal planes through a lesion ineffective in blocking rotation. Coordinates refer to the König and Klippel atlas (*11*). Fig. 2 (right). Drawings of selected frontal sections through the diencephalon, depicting the 8 by 8 grid of squares at each level which were analyzed for their contribution to blocking apomorphine-induced rotation. Blackened squares indicate regions associated with greater than 85 percent reduction in rotation.

rats that incurred such damage (Fig. 1, top). The attenuation of rotation did not seem to result from damage to the nucleus accumbens septi, since this structure was spared completely in one instance and damaged only along its lateral border in the other. Neostriatal lesions of a more moderate size that also spared palladial and capsular elements were completely ineffective in six of seven cases (Fig. 1, bottom). The persistence of rotation in spite of as much as 65 percent damage to the cross-sectional area of the neostriatum suggests that near-total destruction of this structure is necessary for major behavioral impairments (*13*).

Interruption of the internal capsule immediately caudal to the caudate-putamen also resulted in a marked reduction of rotational behavior. In a group of ten rats that suffered extensive damage to the internal capsule within the telencephalon, apomorphine- or L-dopa-induced rotation was reduced by a mean of 68 percent. However, all of these animals incurred additional slight or moderate damage to the globus pallidus. Therefore, in six animals we created extensive lesions of the pallidum but largely spared the capsule. This group showed a mean reduction of rotation of only 1 percent.

In the next experiment, we examined whether diencephalic lesions were similarly effective in blocking rotational behavior. Twenty-one rats were given unilateral 6-OH-DA injections and tested for apomorphine-induced rotation as in the previous experiment. After stable rotation had been achieved, ipsilateral electrocoagulations were made within the ventrolateral diencephalon. Because of the number and variety of lesion sites, the results were pooled in the analysis. After reconstructing the lesions, each frontal plane (*11*) through the lesion was partitioned into a grid of 0.4- by 0.4-mm squares. We then determined which squares in each frontal plane were damaged by each of the lesions. We calculated a score for each square, which represented how well its damage predicted a reduction in rotation (*14*). The diencephalic areas most closely associated with the blockade of apomorphine-induced rotation were clustered along the length of the internal capsule (Fig. 2).

The findings suggest that the efferent fibers of the basal ganglia that maintain rotational behavior pass through the internal capsule at telencephalic and diencephalic levels. To determine whether descending fibers terminating in the nigra, such as the strionigral system, might be involved in the expression of this behavior, we attempted to transect them with a wire knife. In seven rats, a knife cut in the frontal plane was made at the rostral border of the substantia nigra. In an additional 12 rats, a parallel cut was made in the frontal plane just behind the nigra (*15*). The effects of these two transections on L-dopa–induced rotational behavior differed. The cut made anterior to the substantia nigra blocked rotation by a mean of 54.3 ± 9.3 percent. In contrast, the knife cuts behind the substantia nigra blocked rotation by only 24.5 ± 6.3 percent.

Our research has taken advantage of the rotational behavior induced by apomorphine or L-dopa in rats with unilateral destruction of the ascending dopaminergic neurons induced by 6-OH-DA in order to determine the course of neural systems critical for maintaining rotational behavior. This model provides a unique opportunity to separate the anatomical distribution of the ascending dopaminergic neurons from that of striatal efferents. Any further destruction of the DA-containing neurons caused by the electrocoagulation or knife cuts would be expected to increase the denervation supersensitivity of striatal DA receptors and thus result in a potentiation of rotation to apomorphine or L-dopa. Instead, we found that lesions (of the striatum and internal capsule) and knife cuts (particularly in front of the nigra) can substantially block rotational behavior, which suggests that these lesions damage neostriatal efferent fibers that maintain the behavior.

It appears that, as these fibers leave the neostriatum, they are associated with the internal capsule within the telencephalon. The relevant fibers remain within the capsule through its diencephalic

course. The results with knife cuts suggest that many, though perhaps not all, of the relevant fibers may terminate within the ventrolateral mesencephalon, probably within the substantia nigra. Collectively, our findings are consistent with the course and distribution of the strionigral pathway which terminates predominantly within the zona reticulata of the substantia nigra (*16*). They challenge the hypothesis that the strionigral projection functions solely as a feedback pathway onto DA-containing cells. Instead, our data support the hypothesis that this fiber system plays a role as an output pathway from the neostriatum.

Our results may also help to elucidate the contribution of basal ganglia circuitry to other behaviors. Ventrolateral diencephalic electrocoagulations similar to those effective in blocking rotation have also been shown to prevent the restoration of feeding and drinking by L-dopa or apomorphine in rats with bilateral damage to the ascending DA-containing neurons (*17*). It now seems likely that many aspects of the syndrome of behavioral impairments seen in rats with lesions centered in the lateral hypothalamus can be attributed to a spread of the damaged region to include both ascending dopaminergic axons and neostriatal efferent fibers.

Finally, we anticipate that the approach outlined in this paper should be useful in determining the basal ganglia circuitry involved in the expression of clinical movement disorders, for example, the tardive dyskinesias or Huntington's chorea. With modifications, the approach might also prove useful in determining neural systems underlying DA-related psychotic states.

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8. Electrocoagulations were made by current from a radio-frequency (Siemens Radiotom) or direct-current (Grass) lesion maker through the tip of a stainless steel insect pin, insulated except for a 0.5-mm tip.
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14. This score for each square was calculated as the mean reduction in rotation for each animal in which the lesion encroached upon that square. Those rats in which the lesions did not damage a particular square were not used in determining its contribution. For example, if a particular square was damaged by the lesions of four rats in which rotation was blocked by 0, 10, 10, and 20 percent, it would receive a score of 10 percent. Only those squares damaged by three or more lesions contributed to the analysis.
15. The rostral cuts were made by positioning the tip of the knife holder 4.0 mm in front of the earbar (level skull), 3.3 mm lateral, and 4.3 mm above the earbar. The knife was extended 2.0 mm medially and lowered stereotaxically to 1.8 mm above the earbar. The caudal cuts were made in a similar manner, with the knife holder positioned anterior 1.5, lateral 2.5, and 3.6 mm above the earbar, and lowered to 1.0 mm above the earbar. The rostral cuts were situated at the anterior border of the zona reticulata, averaging 1.5 mm in their mediolateral and dorsoventral extent. The caudal cuts were of a similar size, situated at the posterior tip of the zona reticulata. With each type of transection, the damage to the underlying crus cerebri was variable.
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Clockwise Growth of Neurites from Retinal Explants

Abstract. *When retinal explants from goldfish are grown on a polycation substratum, a marked tendency for directionality of neurite outgrowth is observed. While the direct relevance to nerve growth in vivo is not known, the phenomenon is interpreted as reflecting an inherent helicity of the neurites.*

Whereas cells in culture frequently migrate, neurons characteristically do not but rather send out processes which seem, by a number of criteria, to represent their natural axonal and dendritic extensions. There has been considerable speculation regarding the possible factors that influence the nature of this outgrowth and their relation to mechanisms in vivo whereby growing nerve fibers selectively reach their predetermined targets. Possible intrinsic mechanisms mediated by the nature of the neuron itself, and possible extrinsic factors such as chemical and electrical gradients, as well as the interaction of the growing neurite with its substratum or with neighboring neurites, have been proposed as playing a part in determining observed growth patterns in culture (*1, 2*). We report here that both collagen film– and polycation-coated glass or plastic surfaces support neurite extension in goldfish retina explants, but that on the polycation substrata, a marked directionality in fiber outgrowth is invariably observed.

Ten to 20 days after the optic nerve was crushed intraorbitally, goldfish retinas were removed under sterile conditions and cut into 600-μm squares as described (*3*). Prior crushing of the optic nerve was necessary in order to obtain vigorous neuritic outgrowth (*3, 4*). The retinal explants were placed in culture dishes coated with a collagen film (*5*) or with poly-L-lysine (*6*). Polycation-coated surfaces have been shown to promote cell adhesion (*7*) and, more recently, neurite extension (*6, 8*). Cultures were examined with a Leitz Diavert inverted microscope. The observed image is that which would be seen by looking at the culture dish from above. After several days of growth in vitro on the poly-L-ly-