Physiology & Behavior, Vol. 44, pp. 199–204. Copyright © Pergamon Press plc, 1988. Printed in the U.S.A. 0031-9384/88 $3.00 + .00

Spontaneous Bodily Rotations and Direction of Locomotion at Different Times After Radio Frequency Lesions at Sites in and Near the Substantia Nigra

ROBERT L. ISAACSON, ANNE M. DANKS

Department of Psychology, Center for Neurobehavioral Sciences
State University of New York at Binghamton, Binghamton, NY

A. BEATE OESTREICHER, JAN H. BRAKKEE AND WILLEM H. GISPEN

Institute for Molecular Biology, University of Utrecht, Utrecht, The Netherlands

Received 13 April 1988

ISAACSON, R. L., A. M. DANKS, A. B. OESTREICHER, J. H. BRAKKEE AND W. H. GISPEN. *Spontaneous bodily rotations and direction of locomotion at different times after radio frequency lesions at sites in and near the substantia nigra.* PHYSIOL BEHAV **44**(2) 199–204, 1988.—Rats were prepared with radio frequency lesions of the dorsolateral or ventromedial regions of the substantia nigra. Other rats were prepared as operated and unoperated controls for each type of lesion. Their behavior was evaluated in an open field at postoperative days 2, 7, 10, and 15. Three types of behavorial changes were observed over time: those noticeable for a brief period, i.e., a few days, after the lesion (rotational behavior), those lasting 7–10 days after the lesion (turning preferences) and those lasting through the end of the experiment that may be permanent (enhanced locomotion). The early effect of the medioventral lesions was pronounced contralateral rotation while the early effect of the dorsolateral lesion was ipsilateral rotation. This effect of the dorsal lateral lesions was reversed on test days 7 and 10. Lesion-induced turning changes associated with forward locomotion were observed on these two test days as well. By 15 days after surgery the only demonstrable effect of either lesion was enhanced locomotion. The results are discussed in terms of various theories of substantia nigra regulation of motor activities.

Substantia nigra Dopamine Rotations and turns

IN an attempt to better understand the dynamic changes that occur in the area surrounding lesions of the brain, in a recent study we made immunohistochemical evaluations of tissue changes occurring over time in brain stem regions in the area of the substantia nigra (SN) damaged by unilateral radio frequency (RF) lesions (18). We felt that understanding the cellular changes occurring near the lesion site and at more distant locations might assist in understanding the functional and behavioral consequences of the lesions. In this study, animals with lesions in these same areas, and their controls were prepared and behaviorally tested at the same postoperative times as the animals evaluated in the immunohistochemical experiment. The behavior of all animals was evaluated in a large, circular open field at the four postoperative periods without any pharmacologic interventions.

Our expectations were in accord with the generally accepted notion that rats will turn toward the side of the body whose neostriatal systems receive the least dopaminergic innervation [e.g., (25,26)]. However, it has been reported that small RF lesions confined to the pars compacta produce contralateral turning (12). A similar result has been reported when the lesion was confined to the pars reticulata (7). However, we also were aware that there is considerable literature about the effects of SN lesions and about the effects of interruptions of the nigrostriatal axis at different levels [e.g., (22)]. One important factor influencing postlesion behavior of the direction of spontaneous rotation and turning is location of lesion within the SN, although the issue is complex. One line of research stresses the importance of the medial-lateral location within the SN. Electrical stimulation of the medial portion of SN produces contralateral turning while similar stimulation of the lateral region produces ipsilateral

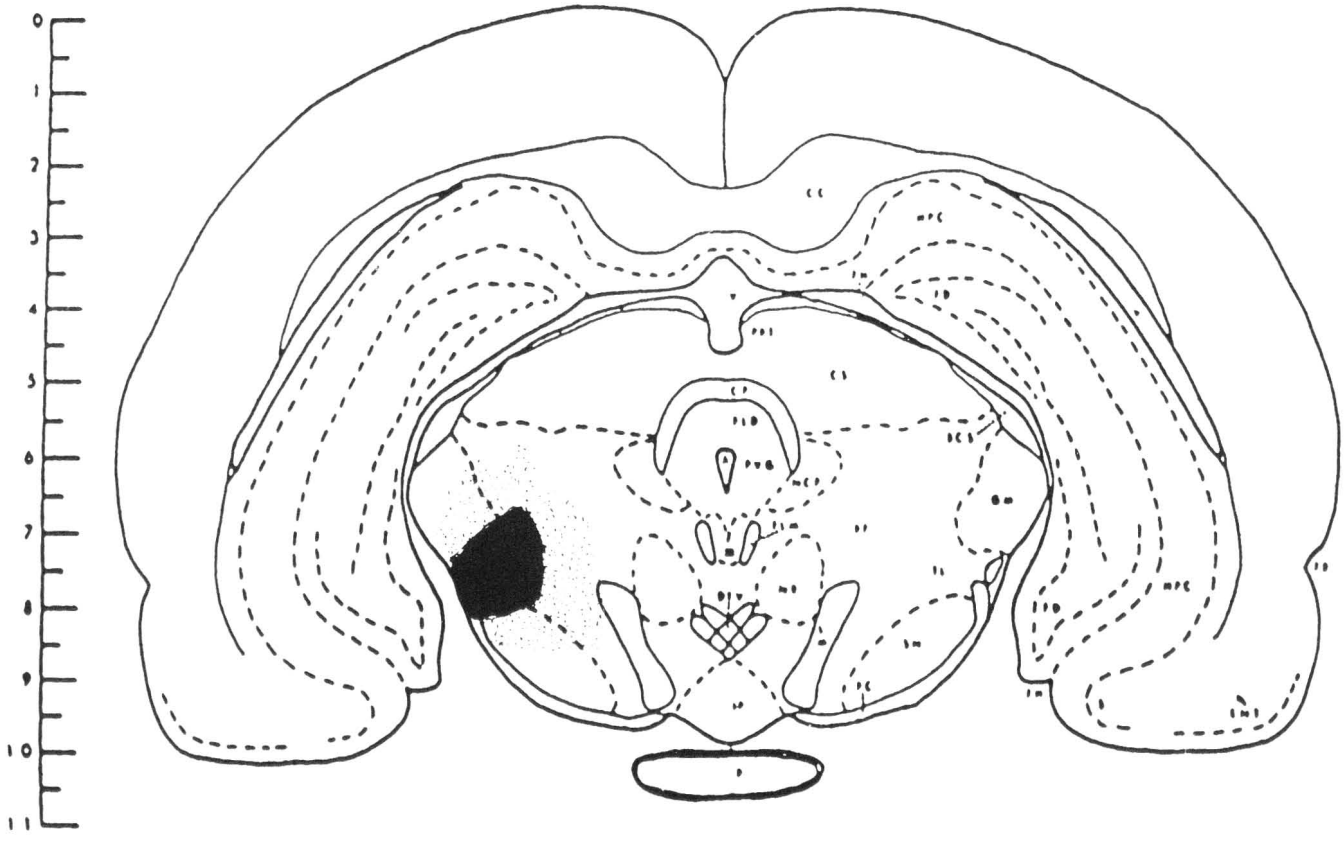

FIG. 1. Illustration of damage suffered by animals in the dorsolateral lesion group. Shaded areas: The extent of damage created in any animals of the group. No single animal had this amount of damage, rather the shaded area represents the range of damage that occurred within the group. The black area represents that region in which damage occurred in at least five animals of the group.

turning. Lesions in these areas produce the opposite effects (28). The rostral-caudal dimension must be considered as well. The application of a GABA uptake inhibitor into rostral portions produces ipsilateral circling and a reduction of striatal dopamine turnover. Opposite behavioral effects were obtained with caudal SN placements of the agents, even though no changes in striatal dopamine are observed. Further pharmacologic interventions indicated the effects to be GABA-mediated (14,19).

Because of the significance of location within the SN and because of the somewhat similar effects found after damage to nearby areas [e.g., (12)], RF lesions were made in two regions of the SN: a dorsolateral area and a ventromedial region.

METHOD

Subjects and Surgery

Male Wistar albino rats derived from the nonsystematically bred population maintained in the animal colony of the Institute for Molecular Biology (derived originally from stock maintained at TNO Zeist, The Netherlands), weighing betweeen 180 and 205 g, were the subjects of this report. The animals were housed in groups of 4 throughout the experiment. The vivarium was maintained at a temperature of 24°C on a 12:12 light-dark schedule.

The experimental animals received unilateral (left) RF lesions of the areas in and near the substantia nigra or control procedures. For surgery the animals were anesthetized with 0.08 ml per 100 g body wt. Hypnorm (Phillips Duphar, Amsterdam), and placed in a stereotaxic instrument with the top of the skull horizontal. Lesions were made by passing a 20 mA, 70 volt maximum RF current (Grass Instrument Co., LM4 lesion maker) through an insulated stainless steel electrode (100 μm diameter) for 60 sec.

For the dorsolateral lesion group, 11 rats were lesioned at coordinates 2420 μM anterior, 2.3 mm lateral to bregma and at a depth of 1.80 mm below ear bar level. The coordinates for the 10 rats in the medioventral lesion group were 2400 μM anterior, 2.3 mm lateral, and 2.0 mm depth using the coordinates of Konig and Klippel (15). Five additional rats for the DL and 6 for the MV group underwent sham operation procedures by placing an electrode into the brain at the same coordinates used for the experimental groups, except that the electrode depth was 1 mm less, and without any current being passed through it. Also, five animals served as unoperated controls for each group.

These two separate unoperated control groups were used because the dorsolateral and medioventral lesion groups were not studied at the same time. The two types of lesions were made several months apart, and such factors as seasonal changes could have affected the behaviors of both experimental and control animals.

In the dorsolateral lesion group one rat died within the first 24 hr after surgery and the data from one of the ten remaining lesioned animals was discarded because of pro-

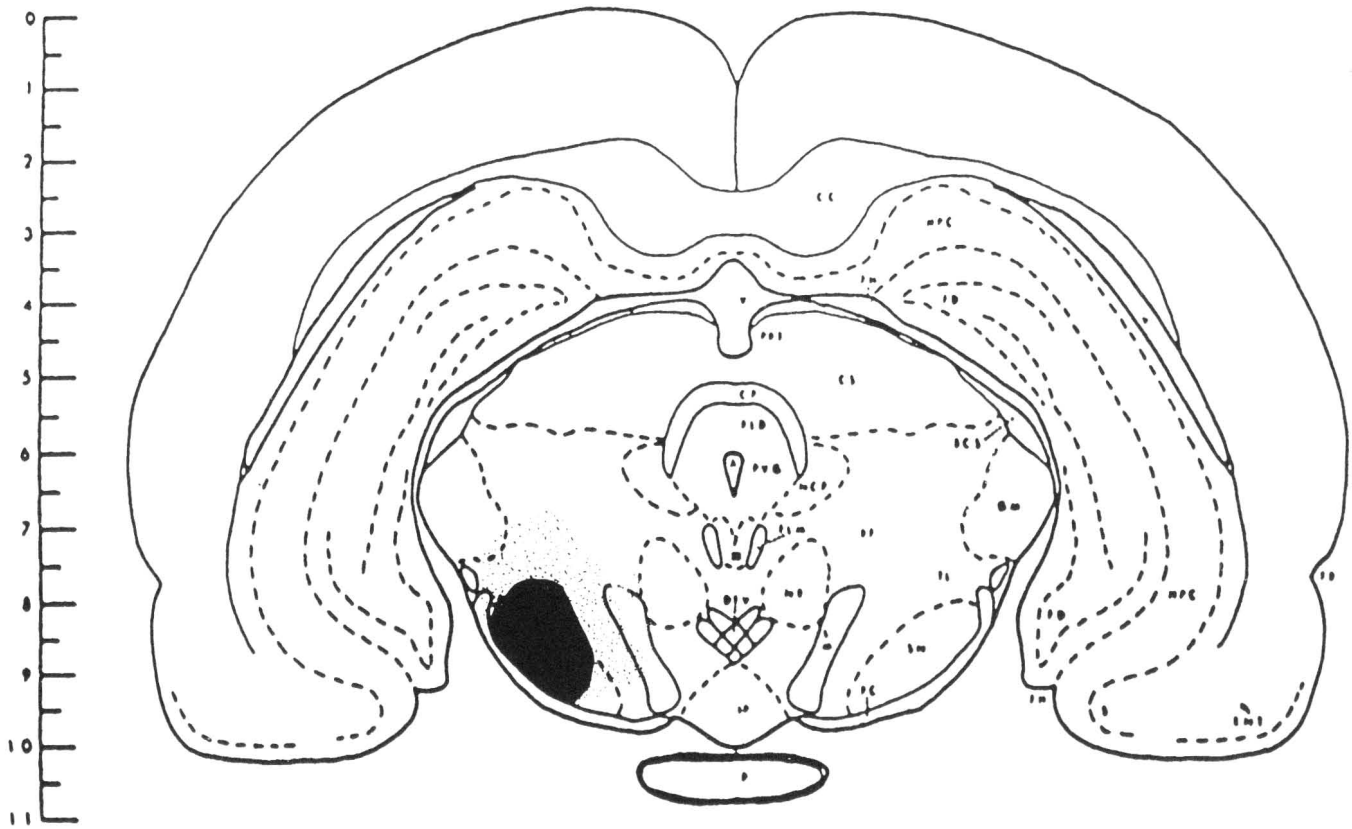

FIG. 2. Illustration of damage suffered by animals in the medioventral lesion group. Shaded and black areas as described in Fig. 1.

longed aberrant motor behavior. This reduced the number of animals with dorsolateral lesions to nine.

Histology

At the conclusion of behavioral testing the animals were sacrificed by an overdose of Narcovet and intracardially perfused with buffered saline followed by 4% paraformaldehyde. The brains were stored in the fixative until they were paraffin embedded, sectioned, stained with cresyl violet and slide mounted for microscopic examination of the lesion. The lesions were photographed and the extent of the lesion drawn on the outline drawings of the brain stem. Drawings of the extent of the lesions of the animals in the two lesion groups are provided in Figs. 1 and 2. These drawings were prepared by outlining the lesion of each animal on the same drawing. The outline of the combined areas destroyed in the lesioned animals in a group is indicated by the stippled area. This represents the composite outline of the lesions in *all* animals and thus, greatly overrepresents the most commonly occurring lesions. The black area indicates the outline of the lesioned area that was common to at least five rats in each group. Even though there is some overlap between the lesions of the two experimental groups, the lesions of the first experiment are generally more dorsal and involve relatively more of the pars compacta than the pars reticulata. The medioventral lesions tend to involve more of SN, absolutely, with extensive damage to major subregions of SN.

The lesions are generally elliptical in shape although every lesion had some irregularities. In an attempt to estimate the size of the lesions in the two groups of subjects, the maximal length and maximal width of each lesion was measured on the drawings of the histologic reconstructions. This was done separately for each group. The mean length of the DL group was 1.94 ($\pm$0.19) mm and the mean width of this group was 1.21 ($\pm$0.15) mm. The mean length of the MV lesions was 1.91 ($\pm$0.19) mm and the mean width was 1.12 ($\pm$0.08) mm. The differences between the two lesion groups was not significant. Therefore there is no reason to believe the behavioral effects observed are due to the amount of tissue destroyed, per se.

Behavioral Method

The rats were tested in a circular open field (diameter 100 cm) with both concentric circular and radial lines painted on the floor as described by Weijnen and Slangen (31). The open field was located in a dimly lit, sound-shielded room and behavior was observed from outside the room through a large glass window. Observations were made for 5 min at 2, 7, 10, and 15 days after surgery. Two forms of behavior were recorded: the direction and amount of movement through the open field, and the direction and number of rotations or "tight turns" (pivoting the body 180 or 360 degrees, roughly about the body's midpoint) that occurred without the animal actually making any forward progress.

The typical pattern of locomotion was for the animal to

TABLE 1

MEANS AND SEMs FOR THE FOUR BEHAVIORS USED IN THE DATA ANALYSES ON THE FOUR DAYS OF TESTING

	Ipsilateral Rotations					Contralateral Rotations					Ipsilateral Turns					Contralateral Turns				
	Controls			Lesions		Controls			Lesions		Controls			Lesions		Controls			Lesions	
Test Day	C	CD	CM	DL	MV	C	CD	CM	DL	MV	C	CD	CM	DL	MV	C	CD	CM	DL	MV
2		10.8	5.2	28.2	0.4	10.29			2.89	78.8	42.19			54.67	27.90	32.76			24.56	35.20
		0.35	0.83	5.4	0.21	1.13			0.78	7.85	3.63			10.53	3.83	2.04			3.79	5.24
7		3.2	6.8	10.0	7.9	4.8			12.7	8.2	32.0			53.2	35.5	32.8			23.4	67.5
		2.1	0.96	0.73	1.53	5.0			1.1	1.4	3.7			6.3	5.1	4.0			3.2	6.9
10		8.0	3.6	8.5	4.8	6.8			13.7	6.6	29.5			38.9	42.0	30.7			21.1	46.9
		0.43	0.65	1.4	0.57	1.2			0.94	1.6	3.7			5.1	6.33	3.6			3.8	4.8
15		10.7	5.6	10.5	4.7		11.6	5.36	10.0	9.4		38.0	24.2	51.4	30.8		34.5	21.0	41.0	31.0
		0.10	1.3	2.2	0.94		0.62	0.54	0.80	2.3		1.05	3.3	7.2	5.6		2.2	3.8	4.8	6.6

Abbreviations: C: combined controls; CD: controls for dorsolateral SN lesions; CM: controls for medioventral SN lesions; DL: dorsolateral SN lesions; MV: medioventral SN lesions; Test Days: days after surgery on which rats were tested.

progress in wide circles, usually following the wall of the enclosure. Locomotion could occur in a clockwise (contralateral) or counterclockwise (ipsilateral) direction. The amount of locomotion was determined by the number of radial or concentric circular lines crossed by the animals when moving in a particular direction. Therefore quantitative measures of four behaviors were obtained: ipsilateral rotations, contralateral rotations, ipsilateral movements, contralateral movements. The latter two measures could be combined to obtain estimates of the total locomotion of the animals.

RESULTS

As noted, the experiments with the SN lesions in the different locations were done several months apart. Therefore, we compared the performances of the control groups in the two experiments on each of the four behavioral measures on all four days of testing. For this purpose, the sham operated and the unoperated control animals were combined since there were no significant differences or apparent large discrepancies between the behaviors of these groups.

A comparison of the performances of the combined control groups in the two experiments made by median tests using exact χ^2 tables (10) indicated significant differences ($p<0.05$) in ipsilateral rotations on three of the four test days and on all four behaviors on the final test day. All of the other comparisons failed to yield significant differences. Therefore, for further analysis the performance of the lesioned animals was evaluated against the performance of all control animals on the measures of contralateral rotations and of turning in either direction on days 2, 7, and 10. The lesioned animals were only compared against the control animals for their particular lesion on ipsilateral rotations on all days, and for all four behaviors on postoperative day 15. The means and SEMs of all the groups are given in Table 1.

Although the data presented in Table 1 are presented in terms of conventional parametric measures, i.e., means and SEMs, it was considered most appropriate to make comparisons among groups on the basis of median tests [e.g., (23)] comparing the lesion group versus the appropriate control group, as described above. This seemed necessary because the size of the groups was often small, even with the combined control group, and it would be difficult to justify comparisons requiring homogeneity of variance among the groups.

The dorsolateral brain stem lesion group showed increased ipsilateral pivoting on the 2nd day afer surgery ($p<0.01$) relative to controls. Actually, this group also showed a small (but statistically significant) increase in ipsilateral rotations on day 7, as well, relative to the control group. This was due, however, to an overall tendency for the lesioned animals to exhibit a greater overall number of rotations than the controls and the fact that control animals exhibited an abnormally small number of ipsilateral rotations on that day. Therefore, its behavioral significance as a "lesion" effect is doubtful. The dorsolateral lesion produced no effect on rotations on postoperative days 10 and 15. The medioventral lesions group exhibited reduced ($p<0.01$) ipsilateral pivoting on day 2 and a greatly enhanced number of contralateral rotations ($p<0.001$). In regard to contralateral rotations, the two lesion groups were both significantly different both from the controls and from each other but in opposite directions. On day 7, as well as on subsequent test days, the medioventral group was not significantly different from controls in its rotations. The dorsolateral lesion group, however, changed remarkably in its rotational behavior between tests on postoperative days 2 and 7. On days 7 and 10 this group evidenced *more* contralateral rotations than did the control group ($p<0.01$; $p<0.05$, respectively). By day 15, neither lesion group differed from their control groups.

On postoperative day 2, neither lesion group differed from the control group in the number of turns made in either direction. However, on postoperative day 7, the dorsolateral lesion group exhibited more ipsilateral turns than did the controls. On postoperative days 7 and 10, the medioventral group exhibited more contralateral turns than did the control animals ($p<0.01$). By postoperative day 15 no significant differences were observed between either lesion group and their control groups in regard to turning in one direction or the other. A summary of these differences is presented in Table 2.

The total locomotion of the animals was determined by adding together the turns in both directions. On postoperative days 2 and 7 there were no differences between the control groups in the two experiments and no differences

TABLE 2

SUMMARY OF SIGNIFICANT CHANGES

Directions:	Rotations				Turns			
	Ipsilateral		Contralateral		Ipsilateral		Contralateral	
	DL	MV	DL	MV	DL	MV	DL	MV
Test Day 2	↑	↓	↓	↑	—	—	—	—
Test Day 7	↑ (?)	—	↑	—	↑	—	—	↑
Test Day 10	—	—	↑	—	—	—	—	↑
Test Day 15	—	—	—	—	—	—	—	—

Directions of arrows indicate significant changes in behavior, upward pointing arrows indicating increases, downward pointing arrows indicating decreases. The (?) reflects uncertainty about this result as indicated in the text.

between either lesion group and the controls. On postoperative days 10 and 15, however, the control groups of the two experiments did differ from each other, the animals for the first experiment exhibiting the greater number of turns. Therefore, the lesioned groups were compared against their individual control groups for the last two test days. On both postoperative days 10 and 15 the groups that sustained either form of brain damage exhibited higher total turning scores than did their control groups (Median tests, $p<0.05$).

DISCUSSION

The most obvious behavioral effects produced by the lesions are those that were found two days after the damage. Animals receiving medioventral lesions exhibited high levels of contralateral rotations without forward movement. The opposite effect, although of smaller magnitude, was found after the dorsolateral lesions. These changes were associated with apparent contralateral or ipsilateral motor weaknesses in the medioventral and dorsolateral lesion groups. However, these apparent unilateral weaknesses had disappeared by postoperative day 7. The direction of rotation of the dorsolateral lesion group was reversed on test days 7 and 10, although once again the amount was not of great magnitude.

However, contralateral turning *with* forward progress through the maze was noted for as long as 10 days after the medioventral lesion (Tables 1 and 2). This indicates that while the most apparent initial lesion effect, an apparent unilateral somatic muscle weakness, dissipated quickly, a more general sensorimotor effect lasted much longer and influenced the direction in which the animals moved in the test environment. Moreover, other lesion effects were observable as long as 15 days after the lesion. At this time no directional effects of the damage could be observed but both lesion groups exhibited greater overall amounts of locomotion than did the controls.

Overall, our results are similar to those found after electrolytic lesion of SN in the general area of our medioventral lesions, i.e., spontaneous, "compulsive" rotation toward the side opposite the lesion (20). A similar result has been obtained by others (6, 7, 12, 30).

While both types of lesions damaged the pars compacta, an area of densely packed dopamine-containing cells [e.g., (17)], the medioventral lesions damaged some different areas of pars compacta and far more pars reticulata than did the dorsolateral lesion. There is little doubt that the cells of the SN are heterogeneous in function [e.g., (2, 4, 8)].

Spontaneous rotations and/or turning subsequent to SN lesion should be distinguished from the drug-induced behaviors found subsequent to lesions of the nigrostriatal system. Apomorphine-induced circling begins to develop about two days after a lesion of the dopaminergic afferents and is most pronounced a month or more after the lesion (5). Pharmacological supersensitivity induced by chronic haloperidol treatment can be observed beginning about two days after termination of the drug treatment. This supersensitivity is due, in part, to a proliferation of receptors linked to a dopamine-sensitive adenylate cyclase (11), although there is evidence for an involvement of both D1 and D2 dopamine receptors acting in interconnected fashion to induce circling (3). The complexities of striatal dopaminergic relationships to turning have been clearly indicated by the work of Glick and his collaborators [e.g., (21,22)].

The rotations, turning, and locomotion seen after SN lesions may be due to projection systems that reach the dorsal diencephalon, tectum, and/or into lower brain stem or spinal cord. All of these projections arise principally from cells in pars reticulata (1,13). It is possible that the most direct "cause" of turning behavior arises from the cells in the *caudal* pars reticulata with descending processes (whose activity does not affect DA activity in the striatum, [e.g., (14, 16, 24)]. The activity of these cells could be inhibitory to ipsilateral motor activities with the amount of inhibition usually being modified and regulated by monoaminergic, peptidergic, and GABA-ergic influences arising from the pars compacta, forebrain basal ganglia sites, and from other brain stem systems. Thus, our medioventral lesions could have released lower motor mechanisms from a chronic inhibitory influence, producing ipsilateral activities and contralateral turning. The cells of the medial pars compacta may act to inhibit downward projecting cells in reticulata. Since these cells of the pars compacta are both dopamine-containing and dopamine-sensitive, a dopaminergic antagonist introduced into the medial pars compacta should induce contralateral

turning by reducing inhibitory influences reaching the reticulata cells. Continuous electrical activation of these medial compacta cells produced the same result by inhibiting the descending inhibitory cells of reticulata. Similar pharmacological or electrical intervention with the lateral pars compacta produces ipsilateral turning, presumably because of an inhibitory effect of the lateral pars compacta cells on the medial compacta cells (27, 29, 30). This would allow the descending inhibitory effects originating the reticulata to be increased. Perhaps the most direct test of these speculations would be to study the effects of direct electrical or pharmacologic interventions of pars compacta at various post intervention intervals in animals in which the posterior reticulata area had been lesioned by a relatively nonspecific cell toxin, such as ibotenic acid.

The changes that occur between 2 and 7 days after surgery may well be due to changes in descending influences from the forebrain on remaining pars reticulata cells or other cells in nearby areas of the brain stem that also contribute to lower motor mechanisms (9,12). The onset of receptor supersensitivity in the striatum corresponds with a change in the direction of rotation of animals with dorsolateral SN lesions. This could reflect an overcompensation for the loss of direct and indirect inhibitory influences of pars compacta cells on pars reticulata cells due to enhanced descending activity from forebrain sites. By 15 days, a balance of activities of the descending motor regulatory systems has been restored but at the expense of an alteration in the control of overall activity.

REFERENCES

1. Anderson, M.; Yoshida, M. Electrophysiological evidence for branching nigral projections to the thalamus and the superior colliculus. Brain Res. 137:349–354; 1977.
2. Arnt, J. Turning behavior and catalepsy after injection of excitatory amino acids into rat substantia nigra. Neurosci. Lett. 23:337–342; 1981.
3. Arnt, J.; Hyttel, J. Differential inhibition by dopamine D1 and D2 antagonists of circling behavior induced by dopamine agonists in rats with unilateral 6-hydroxydopamine lesions. Eur. J. Pharmacol. 102:349–354; 1984.
4. Carter, D. A.; Fibiger, H. C. Ascending projections of presumed dopamine-containing neurons in the ventral tegmentum of the rat as demonstrated by horseradish peroxidase. Neuroscience 2:569–576; 1977.
5. Consolo, S.; Ladinshy, H.; Saminin, R.; Bianchi, S.; Ghezzi, D. Supersensitivity of the cholinergic response to apomorphine in the striatum following denervation or disuse supersensitivity of dopaminergic receptors in the rat. Brain Res. 155:45–54; 1978.
6. Donaldson, I. McG.; Dolphin, A.; Jenner, P.; Marsden, C. D.; Pycock, C. The roles of noradrenaline and dopamine in contraversive circling behavior seen after unilateral electrolytic lesions of the locus coeruleus. Eur. J. Pharmacol. 39:179–191; 1976.
7. Dray, A.; Fowler, L. J.; Oakley, N. R.; Simmonds, M. A.; Tanner, T. V. Regulation of nigro-striatal dopaminergic neurotransmission in the rat. Neuropharmacology 16:511–518; 1977.
8. Fallon, J. H.; Riley, J. N.; Moore, R. Y. Substantia nigra dopamine neurons: separate populations project to neostriatum and allocortex. Neurosci. Lett. 7:157–162; 1978.
9. Faull, R. L. M.; Laverty, R. Changes in dopamine levels in the corpus striatum following lesions in the substantia nigra. Exp. Neurol. 23:332–340; 1969.
10. Finney, D. J.; Lastsha, R.; Bennett, B. M.; Hsu, P. Tables for testing significance in a 2×2 contingency table. Cambridge: Cambridge University Press; 1963.
11. Goldstein, M.; Lew, J. Y.; Asano, T.; Ueta, K. Alterations in dopamine receptors: effect of lesion and haloperidol treatment. Commun. Psychopharmacol. 4:21–25; 1980.
12. Hodge, G. K.; Butcher, L. L. Role of pars compacta of the substantia nigra in circling behavior. Pharmacol. Biochem. Behav. 10(5):695–709; 1979.
13. Hopkins, D. A.; Niessen, L. Substantia nigra projections to the reticular formation, superior colliculus and central gray in the rat, cat and monkey. Neurosci. Lett. 2:253–259; 1976.
14. James, T. A.; Starr, M. S. The role of GABA in the substantia nigra. Nature 275:229–230; 1978.
15. Konig, J. F. R.; Klippel, R. A. The rat brain: A stereotaxic atlas of the forebrain and lower parts of the brain stem. Baltimore: Williams and Wilkins; 1967.
16. Oberlander, C.; Dumont, C.; Boisser, J. R. Rotational behavior after unilateral intranigral injection of muscimol in rats. Eur. J. Pharmacol. 43:389–390; 1977.
17. Oertel, W. H.; Tappaz, M. L.; Berod, A.; Mugnaini, E. Two-color immunohistochemistry for dopamine and GABA neurons in rat substantia nigra and zona incerta. Brain Res. Bull. 9(1–6):463–474; 1982.
18. Oestreicher, A. B.; DeVay, P.; Isaacson, R. L.; Gispen, W. H. Changes in the distribution of neuron-specific B-50, neurofilament protein, and glial fibrillary acidic proteins following an unilateral mesencephalic lesion in the rat. Brain Res. Bull. submitted, 1988.
19. Scheel-Kruger, J.; Arnt, J.; Magelund, G. Behavioral stimulation induced by muscimol and other GABA agonists injected into substantia nigra. Neurosci. Lett. 4:351–356; 1977.
20. Schwartz, W. J.; Gunn, R. H.; Sharp, F. R.; Evarts, E. V. Unilateral electrolytic lesions of the substantia nigra cause contralateral circling in rats. Brain Res. Bull. 105:358–361; 1976.
21. Shapiro, R. M.; Glick, S. D.; Camarota, N. A. A two-population model of rat rotational behavior: effects of unilateral nigrostriatal 6-hydroxydopamine on striatal neurochemistry and amphetamine-induced rotation. Brain Res. 426:323–331; 1987.
22. Shapiro, R. M.; Glick, S. D.; Hough, L. B. Striatal dopamine uptake asymmetries and rotational behavior in unlesioned rats: revising the model. Psychopharmacology (Berlin) 89:25–30; 1986.
23. Steel, R. G. D.; Torri, J. H. Principles and procedures of statistics. New York: McGraw-Hill; 1960.
24. Straughan, D. W.; James, T. A. Microphysiological and pharmacological studies on transmitters in the substantia nigra. In: Simon, P., ed. Advances in pharmacology and therapeutics. vol. 2. Oxford: Pergamon Press; 1978:87–96.
25. Ungerstedt, U. 6-Hydroxydopamine induced degeneration of central monoamine neurons. Eur. J. Pharmacol. 5:107–110; 1968.
26. Ungerstedt, U.; Arbuthnott, G. W. Quantitative recording of rotational behavior in rats after 6-hydroxy-dopamine lesions of the nigrostriatal dopamine system. Brain Res. 24:485–493; 1970.
27. Vaccarino, F.; Franklin, K. B. J. Self-stimulation and circling reveal functional differences between medial and lateral substantia nigra. Behav. Brain Res. 5:281–295; 1982.
28. Vaccarino, F.; Franklin, K. B. J. Dopamine mediated ipsi- and contraversive circling elicited from the substantia nigra. Pharmacol. Biochem. Behav. 17:431–434; 1982.
29. Vaccarino, F.; Franklin, K. B. J. Opposite locomotor asymmetries elicited from medial and lateral SN by modulation of DA receptors. Pharmacol. Biochem. Behav. 21:73–77; 1984.
30. Vaccarino, F.; Franklin, K. B. J.; Propas, D. The role of midbrain reticular formation in the expression of two opposing nigral denervation syndromes. Physiol. Behav. 35:749–752; 1985.
31. Weijnen, J. A. W. M.; Slangen, J. L. Effects of ACTH-analogues on extinction of conditioned behavior. In: de Wied, D.; Weijnen, J. A. W. M., eds. Progress in brain research. vol. 32. Adrenal and the brain. Amsterdam: Elsevier; 1970:221–233.