THE JOURNAL OF COMPARATIVE NEUROLOGY 377:596–610 (1997)

Ibotenic Acid Lesions of the Substantia Nigra Pars Reticulata Ipsilateral to a Visual Cortical Lesion Fail to Restore Visual Orienting Responses in the Cat

VIVIAN M. CIARAMITARO, STEVEN F. WALLACE, AND ALAN C. ROSENQUIST*
Department of Neuroscience, University of Pennsylvania, Philadelphia, Pennsylvania 19104

ABSTRACT

Unilateral removal of all known visual cortical areas in the cat renders the animal hemianopic in the contralateral visual field as measured by visual perimetry and other behavioral tests. We have shown that visual orientation behavior can be restored to the previously blind hemifield by destruction of a critical zone in the substantia nigra pars reticulata contralateral to a cortical lesion (Wallace et al., J. Comp. Neurol. *296:*222–252, 1990). The model proposed to explain this recovery postulates that damage to the crossed nigrotectal projection disinhibits the superior colliculus ipsilateral to the cortical lesion and this leads to recovery. If disinhibition can account for recovery, then destruction of the uncrossed nigrotectal projection, which is known to exert a tonic inhibition on the superior colliculus, should also result in recovery.

We made unilateral visual cortical ablations and ipsilateral ibotenic acid lesions of the substantia nigra pars reticulata. Visual orienting behavior was assessed in animals for a period of 4 to 31 weeks. Contrary to the prediction of the model, we failed to observe a recovery of visual orienting behavior in the blind hemifield in any of 23 animals. J Comp Neurol 377:596–610, 1997. © 1997 Wiley-Liss, Inc.

Indexing terms: basal ganglia; hemianopia; superior colliculus

When a salient visual stimulus is suddenly introduced into a cat's visual field, the animal detects it and orients its eyes, pinnae and head towards it. This behavioral response is known as the visual orienting response. The visual orienting response is mediated in part by the superior colliculus (SC) contralateral to the hemifield in which the stimulus is presented. If all known visual cortical areas are removed unilaterally, a cat is rendered hemianopic in the contralateral visual field, and the visual orienting response is lost in that hemifield. In 1966, Sprague first demonstrated the recovery of visual orienting behavior in the previously blind hemifield of a cat with a unilateral visual cortical lesion (Sprague, 1966a). Ablation of the SC contralateral to a cortical lesion or transection of the commissure of the superior colliculus (CSC) restores the visual orienting response.

It has been shown that recovery is not mediated by remaining cortical areas, neither the intact contralateral cortex nor spared frontal areas ipsilateral to the visual cortical lesion (Sherman, 1974, 1977; Sprague and Chambers, unpublished observations). In fact, bilateral recovery is observed in animals sustaining large bilateral removal of cortical areas following transection of the CSC (Sherman, 1977). Thus, visual cortex is not necessary for the visual orienting response. The subcortical area which appears to mediate recovery is the SC, because the visual orienting response is abolished in the recovered animal if the SC ipsilateral to the cortical lesion is ablated (Wallace et al., 1989).

Sprague (1966a) put forth an hypothesis to explain the recovery of visual orienting in the previously blind hemifield. He speculated that the SC ipsilateral to the cortical lesion was under tonic inhibition from the contralateral SC. Ablation of the contralateral SC or transection of the CSC would lead to recovery via disinhibition of the SC ipsilateral to the cortical lesion. More recent work has shown that the inhibitory pathways important for recovery do not arise from cells in the contralateral SC, but from

Steven F. Wallace's present address is Western Montana Clinic, 515 W. Front Street, Missoula, MT 59802.

*Correspondence to: Alan C. Rosenquist, Department of Neuroscience, University of Pennsylvania, Philadelphia, PA 19104.
E-mail: rosenqui@mail.med.upenn.edu

Received 28 February 1996; Revised 24 July 1996; Accepted 17 September 1996

© 1997 WILEY-LISS, INC.

other areas. Ibotenic acid lesions of the SC contralateral to the cortical lesion destroy all tectotectal projections but do not lead to recovery (Wallace et al., 1989). Furthermore, transection of the rostral CSC, which carries nearly all tectotectal fibers (Edwards, 1977; Magalhaes-Castro et al., 1978; Fish et al., 1982), does not result in recovery, whereas transection of the caudal CSC does result in recovery (Wallace et al., 1989).

The fibers which traverse the caudal CSC arise from a number of nuclei including the substantia nigra pars reticulata (SNpr; Wallace et al., 1990). Ibotenic acid lesions of a critical zone in the rostrolateral portion of the SNpr contralateral to a cortical lesion result in recovery of visual orienting into the previously hemianopic visual field (Wallace et al., 1990). Anatomical evidence for a crossed nigrotectal projection exists in several species (Hopkins and Niesen, 1976; Rinvik et al., 1976; Edwards et al., 1979; Beckstead et al., 1981; Beckstead and Frankfurter, 1983; Gerfen et al., 1982; May and Hall, 1986; Harting et al., 1988; Appell and Behan, 1990; Wallace et al., 1990). The crossed nigrotectal projection is likely to be inhibitory, given that unilateral SNpr deactivation enhances visually evoked activity in SC neurons bilaterally (Dunning et al., 1990). However, the pharmacology, physiology and functional importance of this projection in the control of the SC and orienting behavior has not been studied extensively.

By contrast, the uncrossed nigrotectal pathway has been well characterized in the cat and monkey. The ipsilateral nigrotectal projection is localized to the rostral half of the SNpr and is distributed throughout the mediolateral and dorsoventral extent of the SNpr (Beckstead et al., 1981). SNpr neurons exert a powerful, gamma-aminobutyric acid (GABA)ergic inhibitory tone directly onto ipsilateral SC neurons (Vincent et al., 1978; Chevalier et al., 1981; Di Chiara et al., 1982; Kilpatrick et al., 1982; Araki et al., 1984; Karabelas and Moschovakis, 1985; Behan et al., 1987; Ficalora and Mize, 1989).

SNpr cells have large visual receptive fields whose boundaries are poorly delineated (Hikosaka and Wurtz, 1983a; Joseph and Boussaoud, 1985). Cells respond to stimuli presented in the contralateral visual field and portions of the ipsilateral field (Hikosaka and Wurtz, 1983a; Joseph and Boussaoud, 1985). Neurons have a high discharge rate which decreases in the presence of visual stimuli. Thus, during fixation, cells in the SNpr tonically inhibit output neurons of the SC. Following the signal for an impending saccade, there is a decrease in SNpr activity, an increase in SC activity and a subsequent eye movement (Hikosaka and Wurtz, 1983b). The decrease in SNpr activity is maintained until the end of the movement (Hikosaka and Wurtz, 1983c; Boussaoud and Joseph, 1985). A subset of such cells fails to decrease firing prior to spontaneous saccades and shows a decrease in firing time-locked to the occurrence of the saccade in a delayed saccade task, where the visual target is no longer visible when the saccade is initiated (Hikosaka and Wurtz, 1983d; Joseph and Boussaoud, 1985). Cells in the SNpr showing visual and saccade-related activity project to the intermediate layers of the SC, which play a role in the initiation of eye movements (Hikosaka and Wurtz, 1983b). Thus, the SNpr ipsilateral to the SC is well suited to influence visuo-motor function.

Altering GABAergic transmission via pharmacological manipulation of the SC directly or indirectly via pharmacological manipulation of the SNpr disinhibits or inhibits eye movements (Hikosaka and Wurtz, 1985a,b; Boussaoud and Joseph, 1985). Thus, in the monkey, injection of a GABA agonist into the SNpr decreases SNpr activity leading to a disinhibition of the SC and an increase in spontaneous eye movements to the appropriate retinotopic locus. A decrease in the latency to initiate a saccade and an increase in the amplitude of saccades into the contralateral field is also seen (Hikosaka and Wurtz, 1985b). In the cat, injection of a GABA agonist in the SNpr yields contralateral head turning and a decreased frequency of spontaneous saccades into the ipsilateral field as well as the absence of visually guided saccades to stimuli in the ipsilateral field. Injection of a GABA antagonist has no effect on posture or oculomotor behavior (Boussaoud and Joseph, 1985).

In summary, the uncrossed nigrotectal pathway sends a robust, GABAergic, inhibitory projection onto the SC, and this pathway is known to be involved in the modulation of visual orienting behavior. Thus, if recovery of visual orienting in the cortically blind cat can be accounted for by disinhibition of the SC ipsilateral to a visual cortical lesion, then destruction of the ipsilateral SNpr should disinhibit the ipsilateral SC and result in recovery. The purpose of the present study is to test the hypothesis that destruction of the SNpr ipsilateral to a visual cortical lesion will result in recovery of visual orienting into the previously hemianopic field.

Preliminary results have been reported previously in abstract form (Ciaramitaro et al., 1993). In 23 animals sustaining visual cortical ablation and ipsilateral ibotenic acid lesions of the SNpr, we failed to observe a recovery. Despite this negative finding, direct pharmacological disinhibition of the SC ipsilateral to a visual cortical lesion does restore visual orienting into the previously hemianopic field (Ciaramitaro et al., 1994). Thus, the failure of ipsilateral SNpr lesions to restore visual orienting remains enigmatic.

MATERIALS AND METHODS

General

Twenty-three adult cats (3–5 kg) were used in the present study. All animal procedures conformed to federal regulations and guidelines for animal welfare. Animals were individually housed and maintained on a 12-hour light/dark schedule with food and water ad libitum except for periods prior to surgery or behavioral testing. Prior to surgery, all animals were tested for normal neurological function and for normal binocular and monocular visual fields (see below). Any animal with abnormal responses was excluded from the study.

Surgical procedures

General. Twelve to 24 hours prior to surgery, animals were food-deprived. All surgical procedures were performed by using standard aseptic technique under barbiturate anesthesia. Barbiturate anesthesia was induced with an intramuscular injection of ketamine HCl (15–20 mg/kg) and a subcutaneous injection of atropine sulfate (0.025 mg/kg). An initial dose of 20–50 mg pentobarbital was delivered through a cannula in the femoral or cephalic vein. The animal was then given procaine penicillin (200,000 units) i.m. and the trachea was intubated. Supplemental anesthesia was given as needed and consisted of a

1:1 mixture of pentobarbital and sterile saline. The animal's head was placed in a standard cat stereotaxic frame and the head was prepared for sterile surgery. All animals received a unilateral visual cortical lesion and an ipsilateral substantia nigra lesion. The order of the two lesions was varied and the length of time between lesions ranged from 4 to 52 weeks.

Visual cortical lesions. A midline incision was made and the scalp and temporalis muscles were bluntly dissected from their medial points of attachment and retracted. A unilateral craniotomy was made and extended to expose all cortical areas to be removed. After the dura was cut and reflected, the following cortical areas were removed by suction aspiration: 5, 7, 17, 18, 19, 20a, 20b, 21a, 21b, dorsal lateral suprasylvian area (DLS), ventral lateral suprasylvian area (VLS), posterior suprasylvian area (PS), posterior medial lateral suprasylvian area (PMLS), posterior lateral lateral suprasylvian area (PLLS), anteromedial lateral suprasylvian area (AMLS), anterolateral lateral suprasylvian area (ALLS), and splenial visual area (SVA; Rosenquist, 1985). In addition, the ectosylvian visual area (EVA) was partially damaged.

Ibotenic acid lesions of the substantia nigra. On the day of the surgery, ibotenic acid hydrate (Siris Labs, San Rafael, CA) was dissolved in deionized water or sterile 1.0 M phosphate-buffered saline (pH 7.4) to obtain a concentration of 10–20 µg/µl. To maximize the amount of solute going into solution, the mixture was vortexed and microwaved at 750 watts several times for periods of 0.5–1 minutes each and then sonicated in warm water throughout the period prior to injection.

The brain was exposed using procedures similar to those described above. Once the dura was cut and reflected, stereotaxically guided injections of ibotenic acid were made using a 10-µl Hamilton syringe with a 26-gauge needle. Multiple injections (2–16) were made, delivering a total volume of 0.6–6.4 µl over a 5-minute period into various regions of the substantia nigra, based on the atlas of Reinoso-Suarez (1961).

Transection of the commissure of the superior colliculus. Bilateral occipital craniotomies were made extending medially to the sagittal sinus and caudally to the tentorium. Then the bone overlying the rostral cerebellum was removed. To expose the SC, the overlying dura was cut and reflected. For better visualization of the CSC, the cortex (with dura intact) was usually gently retracted with protective neurosurgical cottonoid sponges and if necessary, a small portion of the overlying parasplenial cortex was also aspirated. The appropriate portion of the CSC was then cut with a knife. Once homeostasis was achieved, Gelfilm was placed over the exposed areas. The animal was then sutured and allowed to recover.

Behavioral procedures

General. All animals were handled regularly and adapted to the mild restraint necessary during testing. They were then food-deprived and trained to run in a visual perimetry paradigm (see below). To assess preoperative and postoperative status, animals were food-deprived for the 18–48 hours prior to behavioral testing. Cats were usually tested on a weekly basis until they completed the paradigm (see below). Testing did not resume subsequent to surgical procedures until transient motor impairments resolved, usually within 1–2 weeks.

Visual perimetry testing. The visual perimetry paradigm of Wallace et al. (1989) was used to assess monocular and binocular visual fields. To assess monocular fields, one eye was anesthetized by application of tetracaine HCl (2%) to the cornea and an opaque contact lens occluder was positioned over the eye.

The animal was trained to fixate a central visual stimulus and to indicate detection of a novel visual stimulus by orienting towards it and obtaining the reward. Food-deprived animals were placed on a table marked into twelve 15-degree sectors, ranging from a visual angle of 90 degrees to the left and 90 degrees to the right of straight ahead. The animal was restrained by the experimenter and allowed to fixate upon a central visual stimulus (a food reward held by a forceps) held at 0 degrees, approximately 40 cm from the cat's nose. While the cat was fixating, a second stimulus was introduced from above at one of the 15-degree sector lines and the cat was given 1–2 seconds to orient to the novel stimulus. This constituted the test trial. Once the cat detected and oriented towards the stimulus, the animal was released. Such behavior on a test trial was counted as a positive trial. Any other behavior was counted as a negative trial or an aborted trial. A trial was aborted if the animal broke fixation prior to the presentation of the novel stimulus or if the cat did not initiate fixation.

Every fourth trial was a control trial. On a control trial, the visual stimulus was presented outside of the visual field of the animal; i.e., the stimuli were introduced at 120 degrees to the left or right of central fixation. Control trials determined the prevelance of spontaneous scanning. The direction of the scan was noted on control trials and the data were normalized to account for spontaneous scanning behavior. The method for normalizing the data has been described elsewhere (Sherman, 1974, 1977; Wallace et al., 1989). In brief, the percentage of scans on control trials to the left was deducted from the percentage of positive results on test trials to the left and similarly for control and test trials to the right.

The behavioral testing paradigm consisted of a total of 180 test trials and 60 control trials for binocular testing and a total of 90 test trials and 30 control trials for each eye for monocular testing.

Neurological examination. Neurological examinations were conducted by using the methods described in Wallace et al. (1989). In brief, it includes: (1) tests for visuomotor capacities: open field following, visual placing, blink-to-threat, localization of stationary stimuli, eye movements, pupillary symmetry and responsiveness, open field visually guided behavior and relative neglect of either hemifield to the presentation of two simultaneous stimuli; (2) tests for the presence and symmetry of palpebral, pinneal, buccal and vibrissal responses to light touch; (3) tests for auditory-motor and somatomotor capacities; and (4) tests of spontaneous motor activity for detection of possible asymmetries in posture and locomotion.

Histology and anatomical reconstruction

Tissue preparation. After all behavioral data had been gathered, animals were given an overdose of pentobarbital and perfused through the heart with physiological saline, followed by a 10% formaldehyde in physiological saline solution. After perfusion, the brain was blocked in the standard stereotaxic frontal plane, removed from the skull, postfixed and processed for embedding in celloidin. The tissue was cut into 48-micron sections and every tenth section was stained for Nissl substance with cresyl violet and adjacent sections stained for fibers using the Heidenhain-Mahon myelin method.

Tissue analysis

Cortical lesions. Cortical lesions were reconstructed from serial coronal sections stained for Nissl or myelin. The extent of the lesion was determined by charting the damaged area onto a drawing of the intact hemisphere. To ensure that the lesion to areas 17 and 18 was complete, the dorsal lateral geniculate nucleus was examined for the completeness of cell loss.

Substantia nigra lesions. Ibotenic acid lesions of the substantia nigra were reconstructed by visualization of both Nissl- and myelin-stained sections under high power magnification on a compound microscope. Sections were charted by using an X-Y plotter which was electrically coupled to the microscope stage and imported to a computer graphics system, MD Plot, Minnesota Datametrics. The lesion was defined as the area containing reactive gliosis and lacking neurons. Sections were reconstructed and then projected onto the drawing to depict nuclei, fiber tracts and other anatomical landmarks. All sections were subsequently replotted onto a standard atlas to allow for comparisons across animals.

Standard atlas of the substantia nigra. A standard atlas of the SN was generated to represent the extent of each lesion relative to the entire extent of the SN. The standard atlas depicted the medial/lateral extent of the SN at each anterior-posterior (AP) level, according to the cat brain atlas of Reinoso-Suarez (1961).

In transferring the location of the lesion from the reconstructed section to the standard atlas, we used the most representative section to depict the medial/lateral extent of the lesion for a given AP level on the standard atlas. The lesion as depicted in the standard atlas is underestimated in the dorsal/ventral plane and in the anterior/posterior plane. It is underestimated in the dorsal/ventral plane because an area was considered to be part of the lesion only if greater than half of the cells in the vertical extent of the nucleus were damaged. It is underestimated in the anterior/posterior plane because the anterior/posterior plane was in increments of 1.0 mm and failed to represent lesions in sections at intervening, i.e. 0.5 mm, intervals.

Transection of the commissure of the superior colliculus. The reconstruction of the CSC transection has been described in detail elsewhere (Wallace et al., 1989). Briefly, the extent and location of the tectal commissurotomies relative to the full extent of the CSC was determined from the charted sections. The following convention was used to define the full rostrocaudal extent of the CSC: the rostral end of the CSC was defined as the most caudal section containing the posterior commissure, and the caudal end of the CSC was defined as the most caudal section containing SC. The distance between these sections was defined as 100%. The location of sections containing a transection traversing at least 50% of the dorsal/ventral extent of the CSC was quantitatively placed within the rostrocaudal percentage of the full CSC.

RESULTS

A total of 23 animals sustained unilateral cortical and substantia nigra lesions (see Table 1). In 16 animals, the cortical lesion was placed first, followed by a substantia nigra lesion an average of 19.2 weeks later (range: 6.2–52.0 weeks). In 7 animals, the substantia nigra lesion was first, followed by a cortical lesion an average of 5 weeks later (range: 4.0–7.0 weeks).

TABLE 1. Surgical Histories and Results

	Cat	Procedure	Time (wks)[1]	Visual field status
Group I SNcz lesions	SE87	Right visual cortex lesion	15.5	Left HH
		Right substantia nigra lesion	8.0	Left HH
	SE90	Left visual cortex lesion	22.5	Right HH
		Left substantia nigra lesion	8.0	Right HH
	SE97	Left visual cortex lesion	15.0	Right HH
		Left substantia nigra lesion	22.0	Right HH
	SE98	Right visual cortex lesion	16.0	Left HH
		Right substantia nigra lesion	19.0	Left HH
	SE121	Right visual cortex lesion	15.0	Left HH
		Right substantia nigra lesion	9.7	Left HH
	SE126	Right visual cortex lesion	10.0	Left HH
		Right substantia nigra lesion	11.0	Left HH
		CSC transection	7.0	Left field recovery 33 days post-operative
	SE129	Right visual cortex lesion	15.0	Left HH
		Right substantia nigra lesion	4.0	Left HH
	SE138	Left substantia nigra lesion	7.0	No effect
		Left visual cortex lesion	9.3	Right HH
Group II small SN lesion	SE75	Right visual cortex lesion	15.5	Left HH
		Right substantia nigra lesion	9.2	Left HH
	SE80	Left visual cortical lesion	19.5	Right HH
		Left substantia nigra lesion	12.5	Right HH
	SE94	Right visual cortex lesion	12.5	Left HH
		Right substantia nigra lesion	10.0	Left HH
	SE123	Right visual cortex lesion	5.7	Left HH
		Right substantia nigra lesion	13.0	Left HH
		CSC transection	6.0	Left HH
	SE128	Right substantia nigra lesion	6.0	No effect
		Right visual cortex lesion	11.4	Left HH
	SE130	Right visual cortex lesion	16.0	Left HH
		Right substantia nigra lesion	9.0	Left HH
	SE149	Right visual cortex lesion	6.2	Left HH
		Right substantia nigra lesion	8.7	Left HH
	SE150	Right visual cortex lesion	6.2	Left HH
		Right substantia nigra lesion	8.7	Left HH
Group III large SN lesion	SE54	Right substantia nigra lesion	4.0	No effect
		Right visual cortex lesion	11.5	Left HH
		CSC transection	9.6	Left HH
	SE125	Right substantia nigra lesion	5.0	No effect
		Right visual cortex lesion	8.0	Left HH
		CSC transection	4.0	Left HH
	SE131	Right visual cortex lesion	16.4	Left HH
		Right substantia nigra lesion	5.7	Left HH
	SE135	Right substantia nigra lesion	7.0	No effect
		Right visual cortex lesion	5.0	Left HH
	SE137	Left substantia nigra lesion	4.0	No effect
		Left visual cortex lesion	8.7	Right HH
	SE141	Left substantia nigra lesion	5.0	No effect
		Left visual cortex lesion	7.4	Right HH
	SE202	Right visual cortex lesion	24.0	Left HH
		Right substantia nigra lesion	5.9	No effect

[1]The time, indicated in weeks, reflects the period elapsing between the surgical interventions listed or between the last surgical intervention listed and the day of sacrifice. (HH, homonymous hemianopia)

Histological analysis

The primary goal of anatomical work was to determine the extent of damage to the cortex and substantia nigra.

Visual cortical lesions. Reconstruction of cortical damage revealed that in no animal were any visual cortical areas spared, except possibly portions of EVA. The cortical lesion was complete, including destruction of the medial and lateral banks of the lateral gyrus, posterolateral gyrus, suprasylvian gyrus, and the anterior and posterior ectosylvian gyrus (data not shown). In addition, the lateral geniculate nucleus was atrophied, assuring complete destruction of areas 17 and 18 (Sprague, 1966b).

Ibotenic acid lesions of the substantia nigra. The ipsilateral nigrotectal projection is localized to the rostral half of the SNpr and is widely distributed throughout the mediolateral and dorsoventral extent of the SNpr (Beckstead et al., 1981). Given that there is no a priori reason to know which part of the uncrossed nigrotectal pathway would need to be eliminated to result in recovery, three strategies guided the placement of lesions: (1) to create a

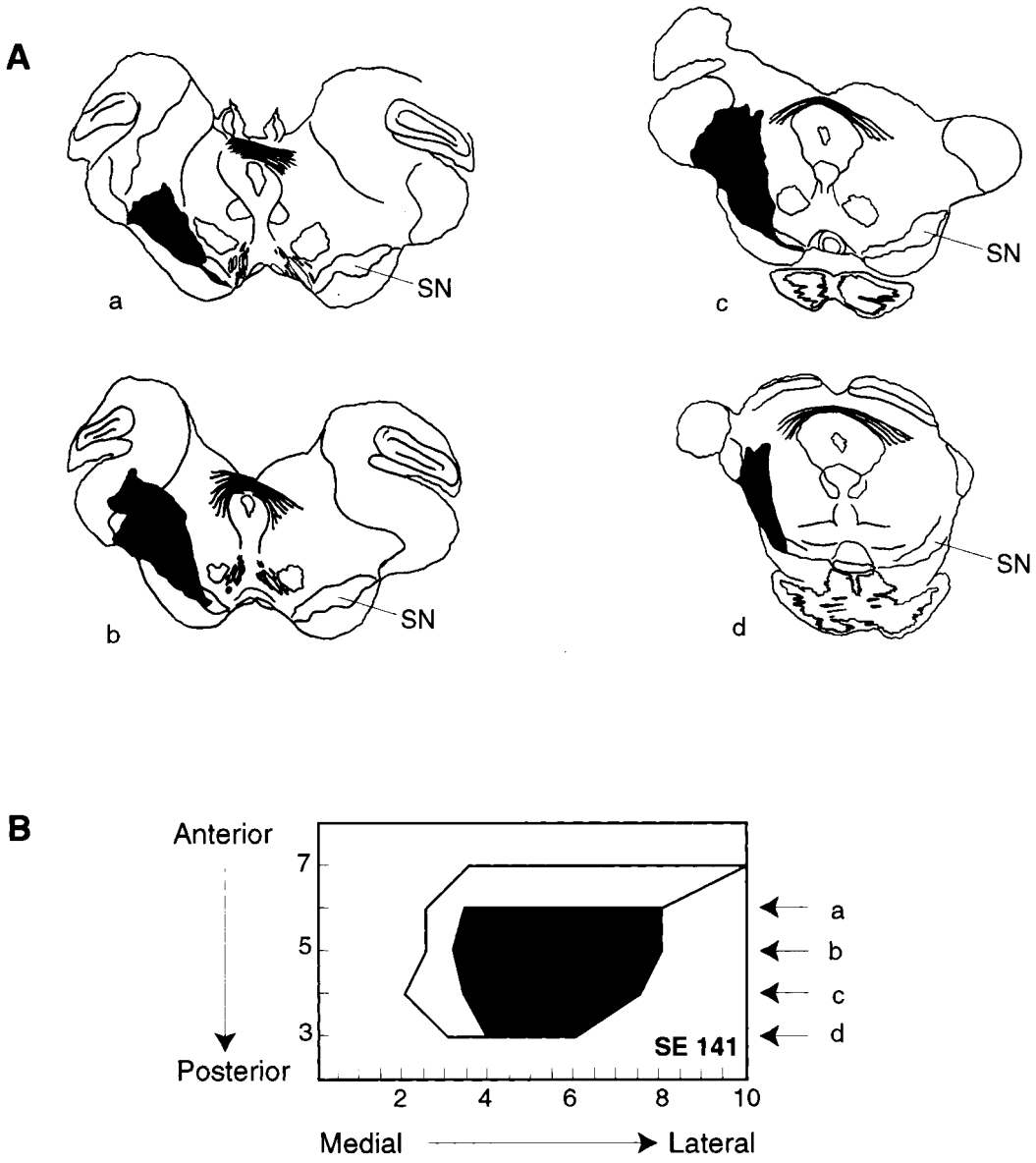

Fig. 1. **A:** Four drawings of coronal sections (a–d) through the midbrain of cat SE141 demonstrating the extent of complete neuronal loss due to ibotenic acid destruction (black) of the substantia nigra lesion. **B:** A transformation of the lesion depicted in A onto a 2-dimensional representation of the substantia nigra (SN), based on the atlas of Reinoso-Suarez (1961). The medial/lateral extent is depicted on one axis, ranging from +2.0 to +10.0 in 0.5-mm intervals. The anterior/posterior extent is depicted on the other axis, ranging from AP + 3.0 to AP + 7.0 in 1-mm intervals. Letters and arrows a–d place the sections seen in A onto the outline depicted in B.

lesion in the ipsilateral SNpr in the same area that led to recovery after damage to the contralateral SNpr, i.e., the "critical zone" in the rostrolateral portion of the contralateral SNpr; (2) to create a small lesion in differing regions of the SNpr to determine if some other area is important; and (3) to create a large lesion in the SNpr, which destroys the entire nigrotectal projection.

Ibotenic acid lesions of various sizes and in various anterior/posterior and medial/lateral regions were made in the SN as confirmed by anatomical reconstruction. Although ibotenic acid lesions were not confined to the SNpr and in some cases invaded the substantia nigra pars compacta and the zona incerta, it was not possible to determine to what extent ibotenic acid lesions extended into the thalamus given the extensive cell loss and gliosis in this structure resulting from the ipsilateral cortical lesion. Reconstructions for individual animals were transferred onto a standard atlas, a 2-dimensional representation of the SN, to allow for comparisons among animals. An example of a reconstructed lesion transferred to the standard atlas is shown in Figure 1 for case SE141.

A 2-dimensional representation of all ipsilateral SN lesions is depicted in Figures 2–4. Group I (Fig. 2) consists of animals with ipsilateral SNpr lesions placed similarly to those leading to recovery after contralateral SNpr critical zone lesions. Group II (Fig. 3) consists of cases with small

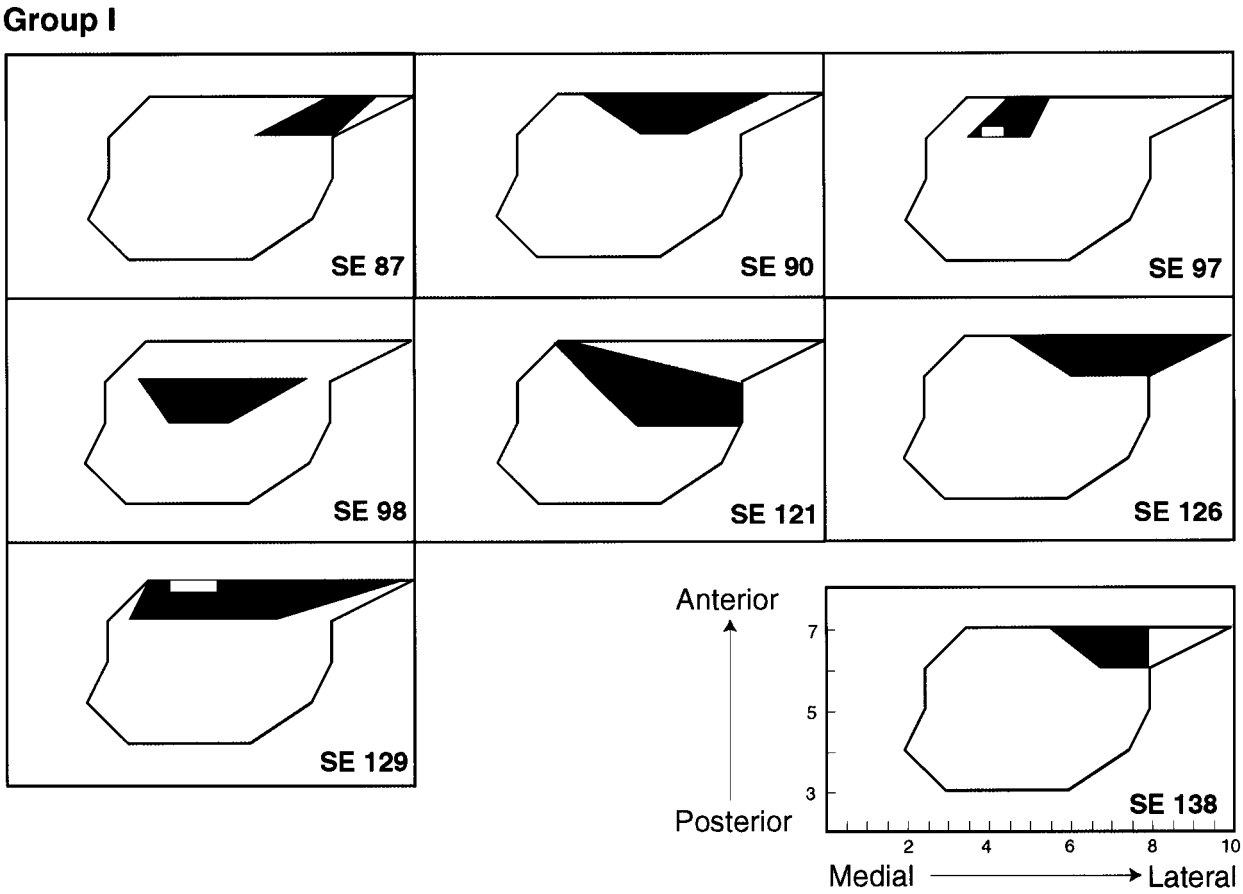

Fig. 2. The 2-dimensional representation of the location and extent of ipsilateral substantia nigra lesions for 8 animals, in which the lesions encompassed an area and location roughly comparable to the contralateral substantia nigra critical zone lesions that led to recovery (see Fig. 5 for comparison).

lesions to various other areas in the SNpr. Cases with large lesions destroying nearly the entire ipsilateral nigrotectal projection form Group III (Fig. 4). For comparison, a 2-dimensional representation of the contralateral SNpr critical zone lesions, which resulted in recovery (Wallace et al., 1990) is summarized in Figure 5.

Transection of the commissure of the superior colliculus. In 5 animals, SE54, 123, 125, 126, and 138, the commissure of the superior colliculus was transected. Anatomical reconstruction revealed that 3 of the 5 animals, SE125, SE126 and SE138, sustained transection of most of the CSC, including the more caudal aspect. In 2 of these 3 animals, SE125 and SE138, the SC ipsilateral to the cortical lesion was also damaged (data not shown).

Behavioral analysis

The primary aim of the behavioral work was to test the hypothesis that an SNpr lesion ipsilateral to a visual cortical lesion would restore visual orienting responses into the hemianopic visual field.

Prior to surgery, all animals exhibited normal binocular visual fields extending for at least 90 degrees to the left and right of midline. Monocular visual fields extended 90 degrees ipsilateral and 45 degrees contralateral to the open eye. All animals presented normal upon neurological examination.

Postoperative behavior

Postcortical lesion. Motor deficits: Following recovery from anesthesia, all animals sustaining unilateral occipito-parieto-temporal lesions displayed a marked turning and circling tendency *ipsilateral* to the side of the lesion. The loss of excitatory cortical afferents to the SC ipsilateral to the cortical lesion would result in the dominance of the contralateral SC and an ipsiversive turning bias. This motor bias usually resolved within 2–4 weeks, at which point behavioral testing began.

Orienting deficits: Animals were able to fixate normally and there were no changes in the ability of the animal to make spontaneous orientations into the contralateral visual field. Orienting to auditory targets in the contralesional hemifield was absent in 9 animals and sluggish or inconsistent in 8 of 22 animals for which data were available. Orienting to somatosensory targets in the contralesional hemifield was lost in 1 animal and sluggish or inconsistent in 12 of the 22 animals.

All animals presented with a complete and enduring homonymous hemianopia as assessed by visual perimetry testing and neurological examination. Thus, visual orienting was absent and cats could not detect stationary stimuli, follow moving stimuli, nor visually place or blink to threat in the contralateral visual field.

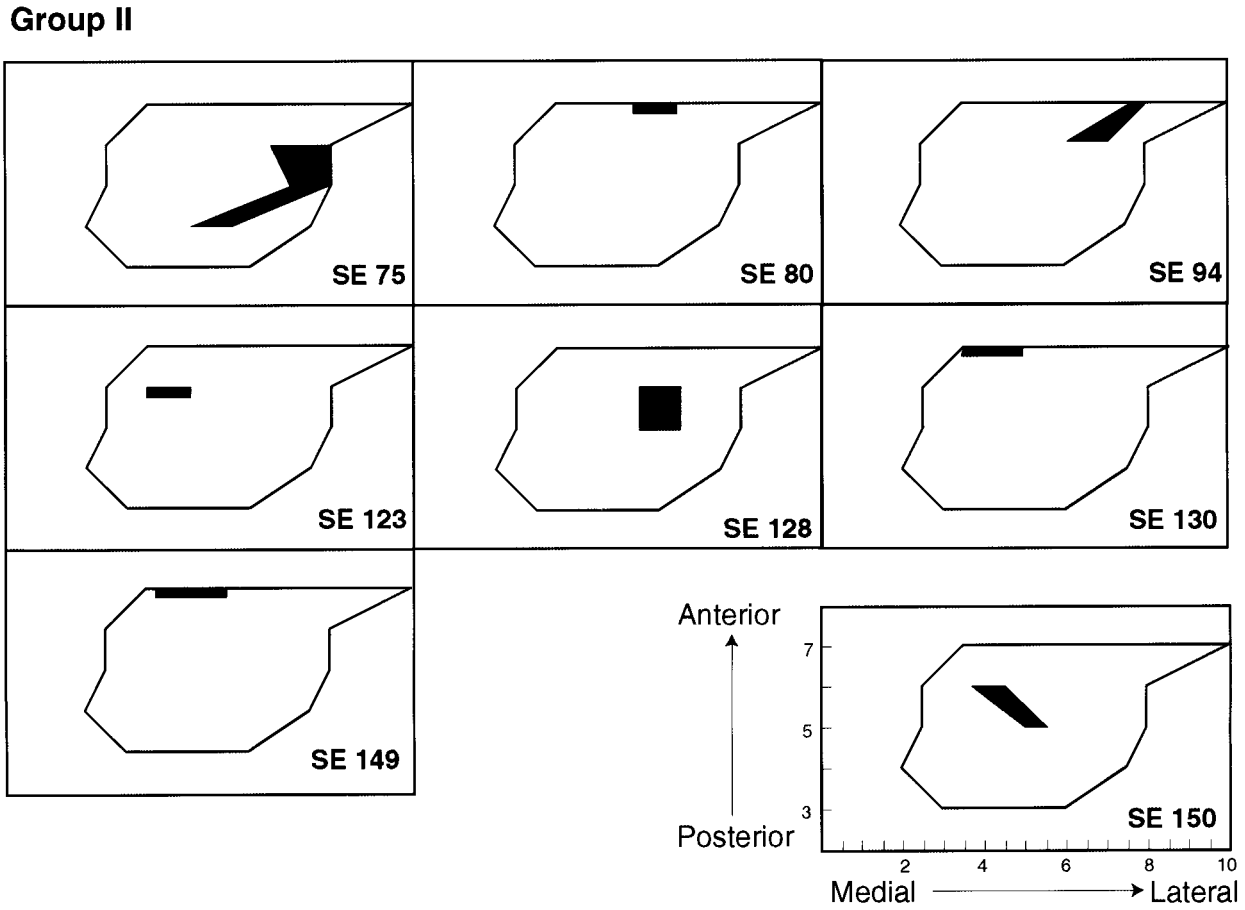

Fig. 3. The 2-dimensional representation of the location and extent of ipsilateral substantia nigra lesions for 8 animals, in which the lesions encompassed a smaller area of the substantia nigra.

Postsubstantia nigra lesion. Irrespective of the size or location of SNpr destruction, animals showed a number of responses.

Motor deficits: Six of the 7 animals with no previous cortical lesion showed a turning and/or circling tendency *contralateral* to the lesion site in the 48-hour period of recovery from anesthesia. Loss of the inhibitory ipsilateral nigral afferent would result in the dominance of the SC ipsilateral to the nigral lesion and thus a contralateral motor bias. The mechanism of action of ibotenic acid should initially overexcite cells and then silence them, possibly via the decarboxylation of ibotenic acid into the GABA agonist, muscimol (MacDonald and Nistri, 1977, 1978; Curtis et al., 1979; Shinozaki and Ishida, 1980). This biphasic mechanism of action has been suggested to result in biphasic turning. Thus, the animal should initially display an ipsilateral bias resulting from ibotenic acid overexciting SN neurons and thus increasing inhibition of the ipsilateral SC, which should resolve into a contralateral bias resulting from death of SN neurons and thus decreased inhibition of the ipsilateral SC.

Behavioral consequences of the biphasic mechanism of action of ibotenic acid have been observed in the rat. Thus, following ibotenic acid injection of the nigra, rats initially present with an ipsilateral turning bias which resolves into a contralateral bias within 5 minutes, with a maximal contralateral bias at 30–50 minutes postinjection (Arnt, 1981). In the present study, only one case exhibited an alteration from an ipsilateral to a contralateral bias over the 48-hour recovery period. However, the effects of ibotenic acid are influenced by anesthesia (Puil, 1979) and thus the biphasic turning bias could have been masked in the other cases.

Three of the 16 animals sustaining a cortical lesion prior to the nigral lesion showed a turning and/or circling tendency ipsilateral to the nigral lesion, whereas 9 showed a circling and/or turning bias contralateral to the lesion at the end of the 48-hour period of recovery from anesthesia. The differences in the motor bias of animals sustaining nigral lesions subsequent to cortical lesions versus animals sustaining nigral damage with no prior cortical lesion may reflect the dominance of the nigral versus cortical lesion in behavioral biases subsequent to various stages of recovery from anesthesia. A clear demonstration of a shift from dominance of the nigral lesion to dominance of the cortical lesion was seen in 3 of the 9 animals sustaining a nigral lesion after the cortical lesion where the initial contralateral bias (due to the nigral lesion) resolved into an ipsilateral bias (due to the cortical lesion) within the 48-hour period.

All motor biases resolved within several days and behavioral testing commenced within 1–2 weeks postopera-

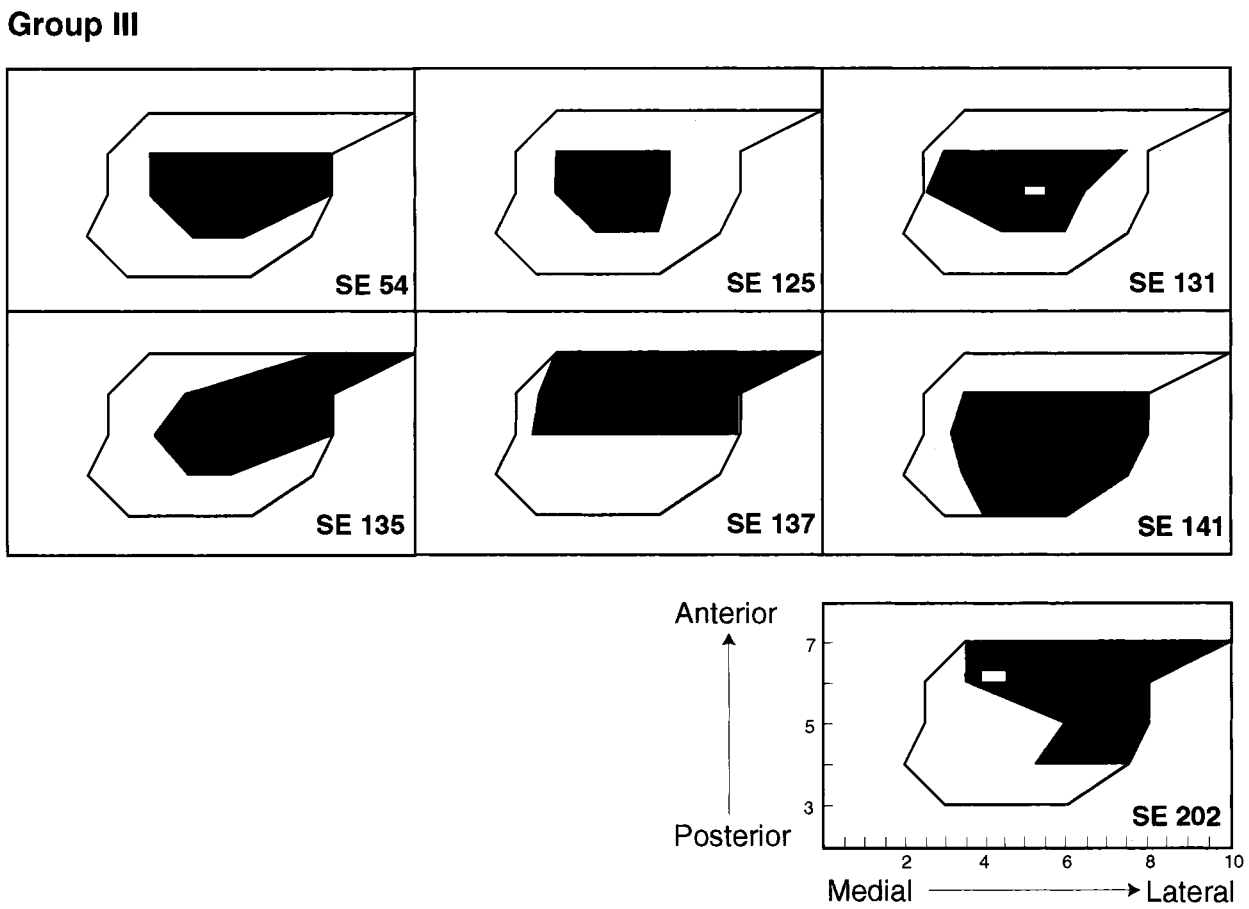

Fig. 4. The 2-dimensional representation of the location and extent of ipsilateral substantia nigra lesions for 7 animals, in which the lesions encompassed a larger area of the substantia nigra.

tively. No behavioral data were obtained for the remaining 4 animals.

Orienting deficits: Regardless of whether the nigra lesion preceeded or followed the cortical lesion, no problems were found in the animal's ability to fixate or to make spontaneous orientations into the visual field contralateral to the nigra lesion. Orienting to auditory targets in the contralesional hemifield was absent in 4 animals and sluggish or inconsistent in 9 of 21 animals for which data were available. Orienting to somatosensory targets in the contralesional hemifield was absent in 1 animal and sluggish or inconsistent in 7 of the 21 animals.

In animals sustaining a cortical lesion prior to the SN lesion, visual orienting continued to be absent in the hemifield contralateral to the nigral lesion. In animals sustaining an SN lesion prior to a cortical lesion, visual orienting was unimpaired in the hemifield contralateral to the nigra lesion.

Posttransection of the commissure of the superior colliculus. In 5 of the animals with both cortical and nigral lesions, the commissure of the superior colliculus was transected. Previous work has shown that transection of the caudal half of the CSC recovers visual orienting in the previously blind hemifield of the cortically blind cat (Wallace et al., 1989). Thus, despite the failure of the ipsilateral SN lesion, transection of the commissure should still produce a recovery of visual orienting. Behavioral results on visual perimetry testing confirmed anatomical reconstruction. Only 1 of the 5 animals, SE126, recovered visual orienting behavior into the previously hemianopic field (see Fig. 6). This was the only case where anatomical reconstruction confirmed destruction of the appropriate region of the CSC with no additional damage to the ipsilateral SC.

In summary, contrary to the predictions of the model, animals with unilateral visual cortical lesions and ibotenic acid destruction to various areas of the ipsilateral SNpr continue to show a complete and enduring homonymous hemianopia, as assessed by visual perimetry and neurological examination. However, the unilateral SN lesion did not preclude recovery. Visual orienting could be restored in the previously blind hemifield, even in an animal that failed to recover after an ipsilateral SN lesion, if the appropriate extent of the CSC was transected.

DISCUSSION

Visual function in the hemianopic field, as assessed by the visual orienting response, can be restored by several subcortical manipulations in the cortically blind cat (Sprague, 1966a; Wallace et al., 1989, 1990). A number of models have been postulated to explain this recovery. The underlying premise of all models is that a cortical lesion causes a depression of neuronal activity in the SC ipsilateral to the

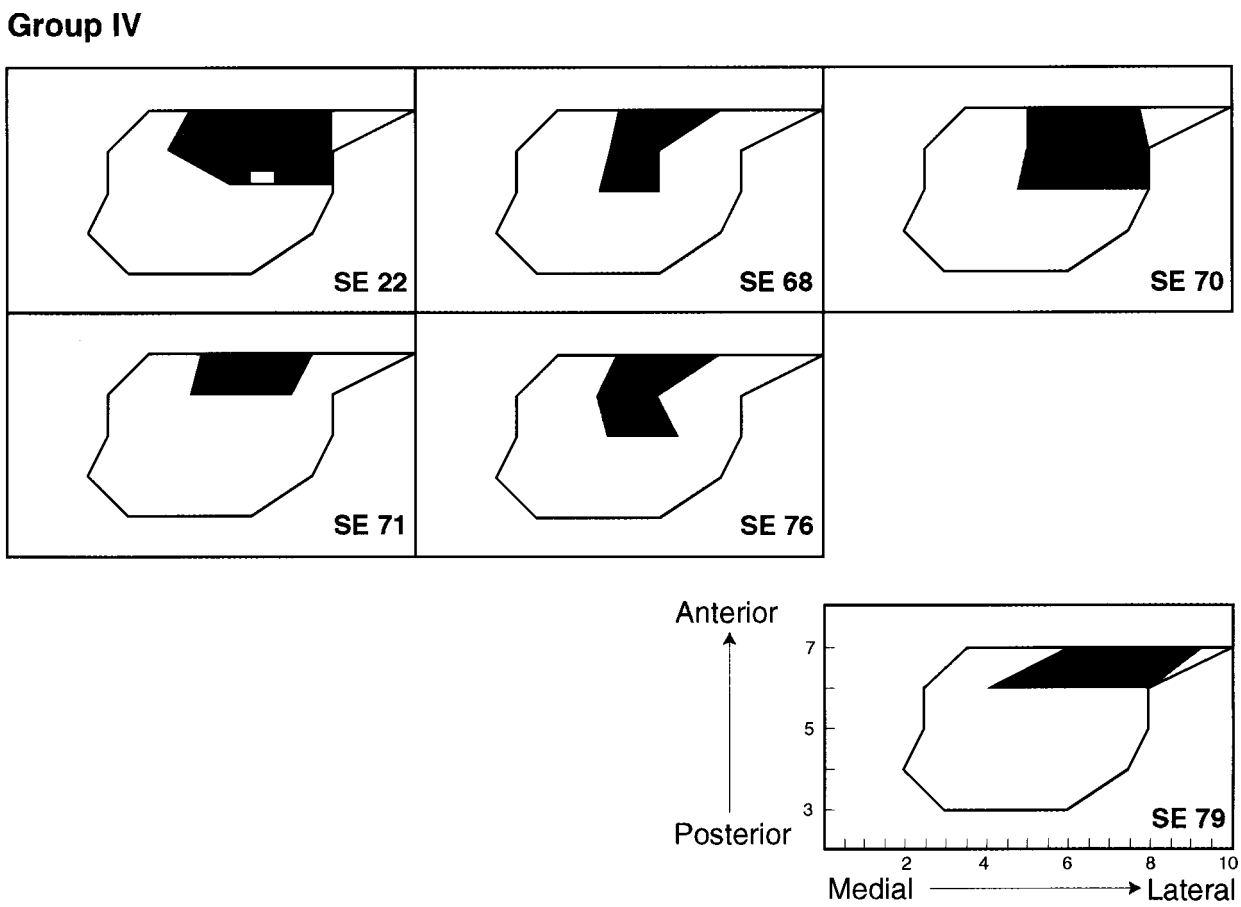

Fig. 5. The 2-dimensional representation of the location and extent of contralateral substantia nigra critical zone lesions for 6 animals, in which the lesions led to recovery (data taken from Wallace et al., 1990).

cortical lesion and reduction of this depressed activity, i.e., disinhibition, allows for recovery.

Metabolic studies in the adult cat reveal that following a cerebral hemispherectomy, there is a depression in SC activity as measured by 2-deoxy-glucose autoradiography and cytochrome oxidase histochemistry (Hovda et al., 1987; Hovda and Villablanca, 1990). In several species, acute physiological experiments in the anesthetized animal demonstrate a depression in SC neuronal activity subsequent to a visual cortical lesion (Anderson, 1970; Goodale, 1973; Sariava et al., 1978; Nagata et al., 1980). A unilateral visual cortical lesion decreases the amplitude of the evoked potential in the superficial layers of the ipsilateral SC to photic stimulation in the rat (Goodale, 1973) and decreases evoked potentials in the ipsilateral SC to optic tract stimulation in the cat (Anderson, 1970). Furthermore, transient deactivation of only a small area of cat visual cortex, area LS, produces a marked depression of SC neuronal activity in the deep laminae (McHaffie et al., 1993).

Most importantly, in several species, the depression of SC activity seen following cortical ablation is reversed subsequent to manipulations which would restore visual orienting in the hemianopic field, such as ablation of the contralateral SC (Anderson, 1970; Goodale, 1973; Sariava et al., 1978; Nagata et al., 1980). Although these results were obtained in the anesthetized animal, they provide evidence for the importance of disinhibition as a mechanism of recovery.

A visual cortical lesion could decrease the excitability of SC cells both directly and indirectly. There could be a direct decrease in excitability presumably due to the loss of excitatory corticotectal connections. There could also be an increase in inhibition on the SC presumably via the cortico-striato-nigro-tectal pathway.

The focus of the nigrotectal disinhibition model (see Fig. 7) is the cortico-striato-nigro-tectal circuit. Both the striatum and nigra have been shown to have a role in visual orienting behavior (see Hikosaka and Wurtz, 1989, for a review).

More specifically, the cortex sends a massive, excitatory, glutamatergic, projection onto the ipsilateral striatum (Graybiel and Ragsdale, 1979, 1983), which in turn sends an inhibitory, GABAergic projection onto the ipsilateral SNpr (Rhoades et al., 1982; Graybiel and Ragsdale, 1983; Araki et al., 1985; Chevalier et al., 1985; Gerfen, 1985). The SNpr projects ipsilaterally onto the intermediate and deep layers of the SC (Graybiel and Sciacia, 1975; Jayaraman et al., 1977; Faull and Mehler, 1978; Graybiel, 1978a; Grofova et al., 1978; Illing and Graybiel, 1985; Hashikawa et al., 1986; Tokuno and Nakamura, 1987; Harting et al., 1988) and projects contralaterally onto the SC (Hopkins

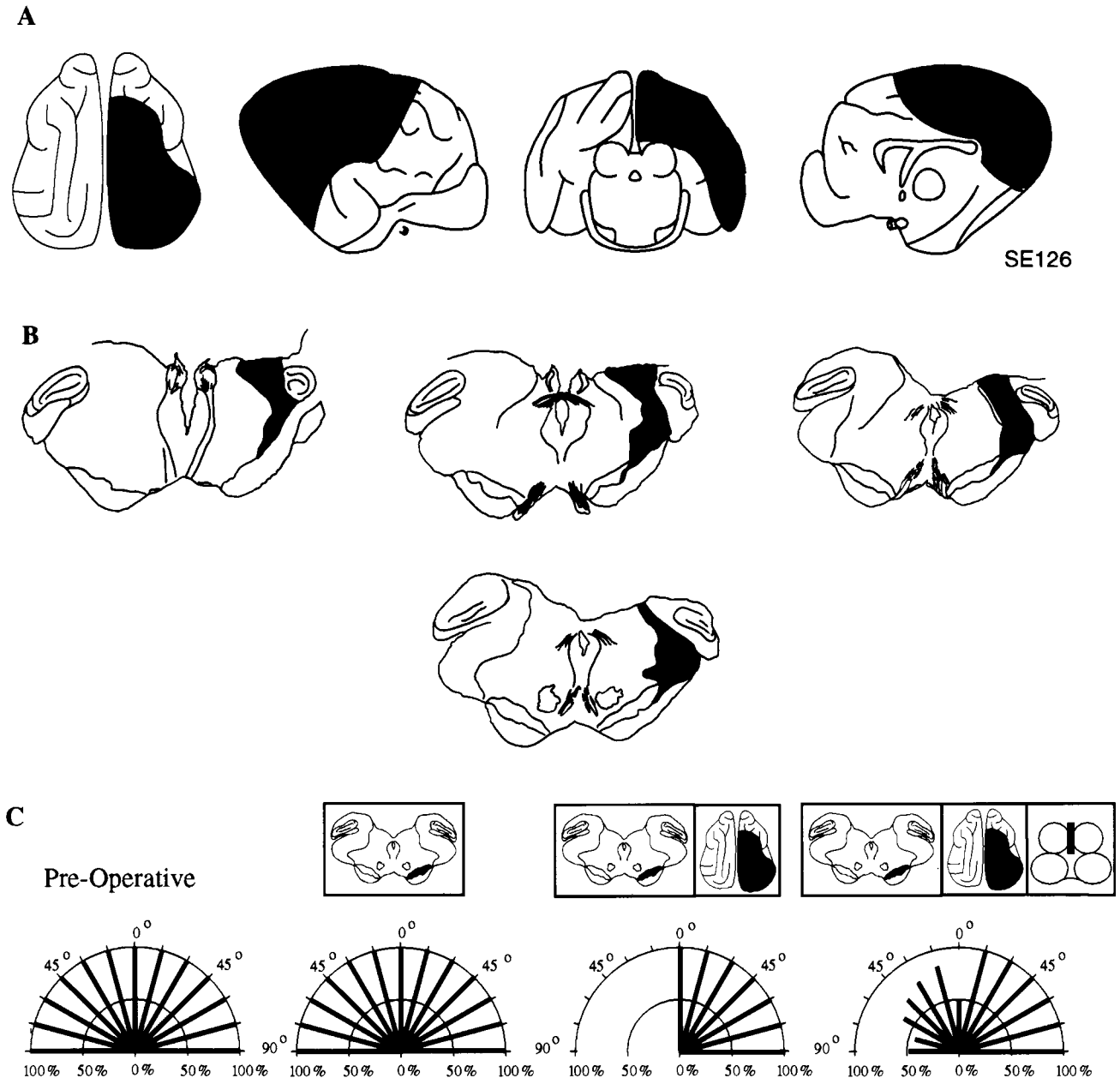

Fig. 6. Case SE126. **A:** The reconstruction of the right cortical lesion. **B:** Four drawings of coronal sections through the midbrain demonstrating the extent of the damage (black) to the right substantia nigra. **C:** A summary of the binocular visual field status of SE 126 at each stage of the experiment: preoperative performance, followed by postsubstantia nigra lesion performance, followed by postcortical lesion performance and finally, performance after transection of the commissure of the superior colliculus. (Note: monocular visual field data is not shown.)

and Niesen, 1976; Rinvik et al., 1976; Deniau et al., 1977; Jayaraman et al., 1977; Edwards et al., 1979; Beckstead et al., 1981; Beckstead and Frankfurter, 1983; Gerfen et al., 1982; May and Hall, 1986; Harting et al., 1988; Appell and Behan, 1990; Wallace et al., 1990; Redgrave et al., 1992). In the rat, double labelling studies have demonstrated a discrete ipsilateral projection, a discrete contralateral projection and a subpopulation of SNpr neurons projecting to and innervating both colliculi (Campbell and Takada, 1989). These bilaterally projecting neurons are found in the ventrolateral portion of the SNpr at its rostral extent.

The SNpr projects primarily to the deeper layers of the SC which project to brainstem nuclei involved in the control of head and eye movements (see Wurtz and Albano, 1980; Huerta and Harting, 1984 for a review). Mohler and Wurtz (1976) identified a subset of neurons in the intermediate and deep layers of the SC ideally suited for visual orienting. "Visually triggered eye movement cells" discharge prior to a visual stimulus, initiating an eye movement which brings the visual axis onto the locus of points in space defining the visual receptive field of the cell. Most importantly, such cells fail to discharge prior to purely

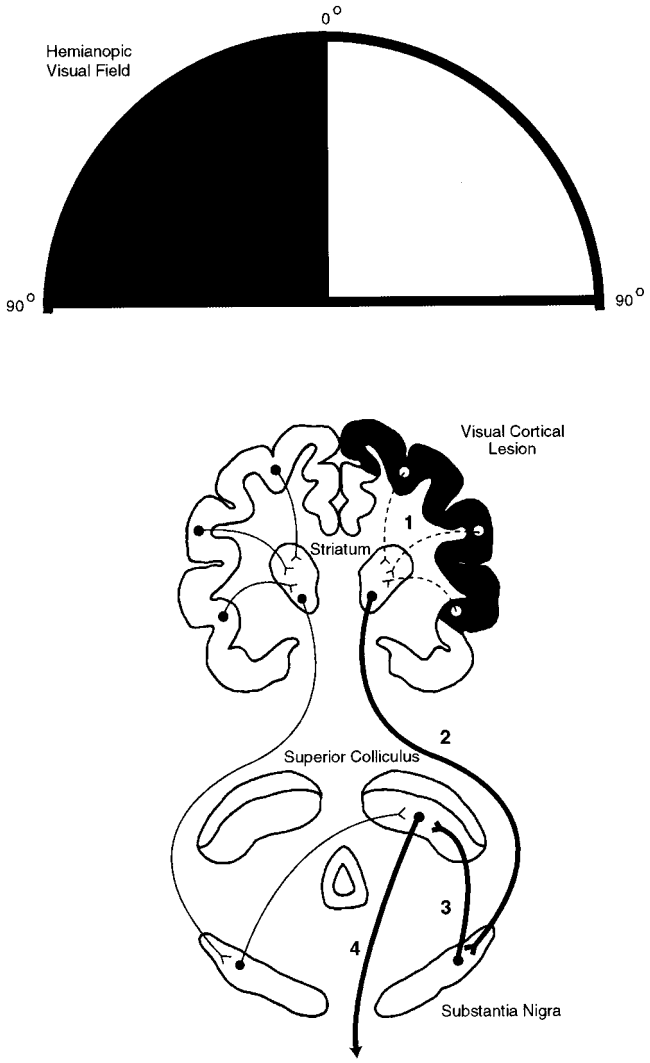

Fig. 7. A schematic drawing, modified from Wallace et al. (1990), showing the cortico-striato-nigro-tectal projection in the cat. The central hypothesis guiding this study is that a visual cortical lesion results in a depression of neuronal activity in the deeper laminae of the ipsilateral superior colliculus. The right visual cortical lesion (shown in black) produces a left visual field hemianopia and results in the loss of excitatory input onto the striatum (1) with the subsequent reduction of inhibitory striatal input to the substantia nigra. (2) Reduced striatal inhibition releases nigral cells to inhibit the deep laminae of the superior colliculus (3) which have descending outputs, tectospinal and tectopreoculomotor pathways (4), controlling orientation behavior. This inhibition would impair visual orienting in the hemianopic visual field.

spontaneous or reflex saccades (Mohler and Wurtz, 1976). Thus, the SNpr is in a prime anatomical position to influence the SC and visual orienting behavior.

In the nigrotectal model, the source of inhibition onto the SC which must be removed to allow for recovery arises from the SNpr. According to the model, both the contralateral and ipsilateral nigrotectal projections are important. Ibotenic acid destruction of the SNpr contralateral to a cortical lesion has been shown to result in recovery (Wallace et al., 1990). The purpose of the present experiment was to test a prediction of the model, namely, that ibotenic acid destruction of the SNpr ipsilateral to a cortical lesion would also lead to recovery, presumably through disinhibition of the SC ipsilateral to the cortical lesion.

To test the prediction of the model, we made lesions to the SNpr ipsilateral to a cortical lesion. There is no a priori reason to implicate a particular area of the SNpr as being involved in recovery given the widespread distribution of the uncrossed nigrotectal pathway. Thus, ibotenic acid lesions were made to destroy an area comparable to the critical zone destroyed in the contralateral SNpr, to destroy some other area of the ipsilateral SNpr, or to destroy a large region of the SNpr.

Contrary to the predictions of the model, we failed to observe recovery in any of the 23 animals sustaining damage to various areas of the SNpr ipsilateral to the cortical lesion. We present four hypotheses to explain why destruction of the SNpr ipsilateral to a cortical lesion does not result in recovery.

The sparing hypothesis

Given the negative findings of the present study, it is arguable that some region of the SNpr ipsilateral to the cortical lesion was spared and that the spared SNpr cells could function to preclude recovery. Thus, although all the animals in group III of the present study sustained damage encompassing fairly large areas of the SNpr, no case showed destruction of the entire SNpr. However, it would seem unlikely that removal of the entire ipsilateral nigrotectal pathway is necessary for recovery. Wallace et al. (1990) have noted that SNpr lesions contralateral to a cortical lesion result in recovery only if the lesion is not extensive. Animals with lesions which include but extend beyond the contralateral SNpr critical zone fail to recover.

There is no evidence to suggest that the ipsilateral and contralateral nigrotectal pathways are similar and that similar lesions will be effective in recovery. Thus, the contralateral and ipsilateral nigrotectal projections could terminate on very different populations of SC neurons, differing in location in the SC as well as the type and distribution of postsynaptic receptors. However, given the paucity of evidence, studies of the contralateral SNpr are the most pertinent to understanding the role of the ipsilateral SNpr in recovery.

Ancillary damage hypothesis

Ipsilateral SNpr lesions may have failed to result in recovery due to: (1) damage extending beyond the substantia nigra pars reticulata, particularly damage to the substantia nigra pars compacta (SNpc); and (2) damage to areas adjacent to the substantia nigra.

Damage to the substantia nigra pars compacta may have prevented recovery. In the present experiment, all animals sustained damage to the nigra extending into the SNpc (based on the atlas presented in Jimenez-Castellanos and Graybiel, 1987). The SNpc is the dopaminergic component of the substantia nigra and lies medial and dorsal to the SNpr.

Schultz (1982) provides an extensive review of the role of the SNpc in sensorimotor processing. Unilateral 6-OHDA lesions of the nigra destroy the SNpc and result in neglect of olfactory, auditory, somatosensory, and visual stimuli on

the contralateral side of the body. The deficit is not simply a motor problem because animals recover responsiveness to auditory, visual or olfactory stimuli while retaining the inability to respond to somatosensory stimuli.

In the present study, extensive damage to the substantia nigra, extending into the SNpc, could result in a contralateral neglect. An SNpr lesion would be unlikely to recover visual orienting into the contralateral, hemianopic, field, if the lesion itself results in ancillary damage to the SNpc, producing a neglect and a loss of visual orienting into the contralateral field.

However, we failed to observe neglect following ancillary damage of the substantia nigra pars compacta in the normal cat. If the neglect was transient we could have failed to observe it because our animals were not tested during the 7 to 14-day postoperative recovery period. This is possible given that in the rat recovery commences within 6 days of surgery (Schultz, 1982). Alternatively, partial lesions of the SNpc in the rat show no clear or consistent neglect (Schultz, 1982). In the present study, damage to the dopaminergic component of the SNpc was incomplete and could have resulted in no clear or consistent neglect. Thus, it is unclear if SNpc damage in the cat can result in deficits in sensorimotor processing, i.e., neglect.

Alternatively, the zona incerta is one area adjacent to the substantia nigra which sustained damage in several cases. This area projects to the SC and evidence suggests that the cells of origin of the incertotectal pathway are GABAergic (Araki et al., 1984; Ficalora and Mize, 1989; Kim et al., 1992). In a study of the substantia nigra, Hikosaka and Wurtz (1983c) recorded from cells that were later localized to the zona incerta and found eye movement related responses. However, Wallace et al. (1990) demonstrated that lesions restricted to the zona incerta contralateral to a cortical lesion, which fail to damage the underlying SN, do not result in recovery. Thus, this structure does not appear to be involved in recovery. It is unknown if destruction of this area, in and of itself, could lead to sensorimotor impairments, such as neglect.

Ultimately, ancillary damage regardless of whether or not it can produce a neglect, does not preclude recovery. Visual orienting can be restored in the previously blind hemifield, in an animal that fails to recover after an ipsilateral SN lesion which extends into other areas, if the appropriate extent of the CSC is transected.

The other circuit hypothesis

The nigrotectal projection is only one of several inhibitory projections onto the SC. Behan et al. (1987) showed that the majority of nigrotectal terminals contact medium or small dendrites, which fails to account for most of the inhibitory terminals onto the cell bodies and proximal dendrites of collicular neurons. Furthermore, there are noninhibitory projections onto the SC. Several lines of evidence point to the likelihood that projections other than the nigrotectal projection are important in recovery from hemianopia. Thus, recovery is still possible in the case of an animal with a nigral lesion ipsilateral to a cortical lesion if the CSC is transected. In addition, preliminary results indicate that lesions of the pedunculopontine nucleus (PPN) contralateral to a cortical lesion can result in recovery (Durmer et al., 1994).

The PPN is a heterogeneous cluster of neurons lying lateral to the brachium conjunctivum at its rostral extent and dorsal and ventral to the brachium conjunctivum at its caudal extent. This diffuse area of the brain sends a bilateral (Edwards et al., 1979; Moon-Edley and Graybiel, 1983; Hall et al., 1989; Appell and Behan, 1990), primarily acetylcholinergic (i.e., Jones and Beaudet, 1987; Jones and Webster, 1988; Fitpatrick et al., 1989; Hall et al., 1989; Jeon et al., 1993), yet also GABAergic (Appell and Behan, 1990), projection onto the intermediate and deep layers of the SC. Furthermore, there are reciprocal projections between the PPN and SN. The PPN projects to both the SNpc (Jackson and Crossman, 1983; Gould et al., 1989; Lavoie and Parent, 1994) and the SNpr (Gould et al., 1989). In the rat, the PPN excites SNpc neurons via nicotinic acetylcholine inputs (Clarke et al., 1987) and via excitatory amino acid inputs (Scarnati et al., 1986; Di Loreto et al., 1992). The SNpr sends a projection to the PPN (i.e., Beckstead, 1979; Gerfen et al., 1982; Moon-Edley and Graybiel, 1983) which is GABAergic (Childs and Gale, 1983) and inhibitory (Kang and Kitai, 1990; Datta et al., 1991; Noda and Oka, 1984, 1986; Granata and Kitai, 1991).

Within the intermediate layers of the SC, PPN afferents set up a patch-like matrix of acetylcholinesterase-positive immunoreactivity (Graybiel, 1978b). Acetylcholinesterase-rich patches are formed by presynaptic afferents and not intrinsic neurons or efferents from the SC (Berson et al., 1991; Berson and Graybiel, 1991) and lesions of the PPN result in a significant loss of cholinergic afferents, as measured by acetylcholinesterase (Shute and Lewis, 1967; Hoover and Jacobwitz, 1979; Jones and Webster, 1988) as well as choline acetyltransferase immunoreactivity, in the intermediate and deep layers of the SC (Woolf et al., 1990). GABAergic efferents from the SNpr and glutamatergic efferents from frontal cortex converge onto the acetylcholinesterase-rich patches of the SC, whereas efferents from lateral suprasylvian and anterior ectosylvian visual areas converge onto acetylcholinesterase-poor domains of the SC (Illing and Graybiel, 1985, 1986; Harting and Lieshout, 1991). Thus, PPN and SN afferents are in close spatial proximity within the SC and comodulatory interactions could occur.

The functional significance of the acetylcholinergic subdivisions within the SC is not understood and the potential role of acetylcholine in modulating eye movements and attention has not been investigated extensively. It has been postulated that the increase in acetylcholinesterase staining seen as one progresses caudally in the SC may correlate with the generation of more peripheral eye movements (Illing and Graybiel, 1986; Hall et al., 1989). Stimulation of the PPN can elicit startle responses and orienting responses in the intact cat (Mori et al., 1989). In the hemianopic cat, lesions to the PPN contralateral to a visual cortical lesion can result in recovery of visual orienting (Durmer et al., 1994).

The mechanisms by which a PPN lesion could result in recovery is unknown. Either the direct projections from the PPN onto the SC or the indirect projection from the PPN via the SN (either directly onto the SNpr or indirectly via the SNpc onto the SNpr) onto the SC could be important in modulating visual orienting. Furthermore, acetylcholine, as well as GABA, could play a role in orienting behavior. Thus, the recovery mechanism could involve pathways other than the nigrotectal projection and could involve non-GABAergic and possibly noninhibitory mechanisms.

The compensatory mechanisms hypothesis

Given that the SNpr sends a robust, GABAergic, inhibitory projection onto the ipsilateral SC and that destruction of this pathway does not lead to recovery of visual orienting in the hemianopic animal, one could argue that SC disinhibition may not be the mechanism mediating recovery. However, we have shown that SC disinhibition is a mechanism of recovery. Thus, injection of the $GABA_A$ antagonist, bicuculline methiodide, into the intermediate layers of the SC ipsilateral to a visual cortical lesion transiently restores visual orienting into the contralateral, previously hemianopic field (Ciaramitaro et al., 1994).

To explain the negative results of ipsilateral SNpr lesions and maintain disinhibition as a mechanism of recovery, we raise the possibility that in a cat with a cortical lesion, an ipsilateral SNpr lesion fails to disinhibit the SC due to compensatory mechanisms in the basal ganglia and SC caused by the cortical lesion. If nigrotectal function is altered subsequent to a cortical lesion, ablation of the SNpr should not necessarily be expected to disinhibit the SC. Thus, the failure of ipsilateral SNpr lesions would not disprove the hypothesis that disinhibition of the SC is a mechanism of recovery.

All the anatomical, physiological and behavioral work suggesting that the nigrotectal projection is inhibitory and influences visuomotor behavior was done in animals with intact cortices, using acute methods of reversible activation and inactivation of the SNpr, not the chronic methods of permanent destruction used in the present study. Chronic manipulations such as cortical lesions have transsynaptic effects over time, altering the structural properties of neurons (Nitsch et al., 1984), altering gene expression and immunoreactivity (Uhl et al., 1988; Sommers and Beckstead, 1990; Salin and Chesselet, 1992, 1993) and altering the dynamics of neuronal activity (Garcia-Rill et al., 1979; Aldridge et al., 1990) throughout the basal ganglia. Changes are seen in the substantia nigra as well as in various afferents to the substantia nigra such as the striatum and the external segment of the globus pallidus.

The effects of chronic deafferentation persist over time and could be due to postlesion plasticity, i.e., axonal sprouting (Adelson et al., 1995; Napieralski et al., 1996) and synaptic plasticity (Chen and Hillman, 1990). Such compensatory effects are not confined to circuitry ipsilateral to the lesioned area and affect contralateral projections as well. Thus, in the adult cat, hemispherectomy results in the reorganization of the corticotectal pathway, with the subsequent sprouting of a contralateral corticotectal pathway not found in the intact neonatal or adult animal (Adelson et al., 1995). In the adult rat, a cortical lesion can result in the sprouting of a contralateral corticostriatal pathway (Napieralski et al., 1996).

In summary, changes are seen throughout the basal ganglia subsequent to a cortical lesion. Compensatory mechanisms could result in two main changes: (1) a chronic alteration in the normal functioning of the ipsilateral SNpr, or (2) a chronic alteration in the function of contralateral pathways to the SC, such that these pathways supercede the influence of the ipsilateral SNpr. If the ipsilateral pathway is shut down or inhibited, ablation of the ipsilateral SNpr would not disinhibit the SC. Likewise, if sprouting of a contralateral pathway overrides any influence of the ipsilateral pathway, ablation of the ipsilateral SNpr would not disinhibit the SC. It remains to be determined what compensatory mechanisms explain the current negative findings.

ACKNOWLEDGMENTS

This work was supported by grants 2 R01 EY 02654, 2 P01 EY01583 and 2 T32 EY07035. We thank Wendy Algeo Todd for valuable technical assistance and Drs. Larry Palmer, Marie-Françoise Chesselet, and Andrew Christie as well as Marnie FitzMaurice, Geoffrey Aguirre and Jeffrey Durmer for comments and feedback on several versions of this manuscript.

LITERATURE CITED

Adelson, P.D., D.A. Hovda, J.R. Villablanca, and K. Tatsukawa (1995) Development of a crossed corticotectal pathway following cerebral hemispherectomy in cats: A quantitative study of the projecting neurons. Dev. Brain Res. *86:*81–93.

Aldridge, J.W., S. Gilman, and G. Dauth (1990) Spontaneous neuronal activity in the primate basal ganglia and the effects of precentral cerebral cortical ablations. Brain Res. *516:*45–56.

Anderson, K.U. (1970) Cortico-tectal and tecto-tectal interactions in the cat. Bull. Georgia Acad. Sci. *28:*41–42.

Appell, P.R., and M. Behan (1990) Sources of subcortical GABAergic projections to the superior colliculus in the cat. J. Comp. Neurol. *302:*143–158.

Araki, M., P.L. McGeer, and E.G. McGeer (1984) Presumptive γ-aminobutyric acid pathways from the midbrain to the superior colliculus studied by a combined horseradish peroxidase-gamma-aminobutyric acid transaminase pharmaco-histochemical method. Neuroscience *13:*433–439.

Araki, M., P.L. McGeer, and E.G. McGeer (1985) Striatonigral and pallidonigral pathways studied by a combination of retrograde horseradish peroxidase tracing and a pharmacohistochemical method for γ-aminobutyric acid transaminase. Brain Res. *331:*17–24.

Arnt, J. (1981) Turning behavior and catalepsy after injection of excitatory amino acids into rat substantia nigra. Neurosci. Lett. *23:*337–342.

Beckstead, R.M. (1979) Efferent connections of the substantia nigra and ventral tegmental area in the rat. Brain Res. *175:*191–217.

Beckstead, R.M., and A. Frankfurter (1983) A direct projection from the retina to the intermediate gray layer of the superior colliculus demonstrated by anterograde transport of horseradish peroxidase in monkey, cat and rat. Brain Res. *52:*261–268.

Beckstead, R.M., S.B. Edwards, and A. Frankfurter (1981) A comparison of the intranigral distribution of nigrotectal neurons labeled with horseradish peroxidase in the monkey, cat and rat. J. Neurosci. *1:*121–125.

Behan, M., C.S. Lin, and W.C. Hall (1987) The nigrotectal projection in the cat: An electron microscope autoradiographic study. Neuroscience *21:*529–39.

Berson, D.M., and A.M. Graybiel (1991) Tectorecipient zone of cat lateral posterior nucleus: Evidence that collicular afferents contain acetylcholinesterase. Exp. Brain Res. *84:*478–486.

Berson, D.M., A.M. Graybiel, W.D. Bowen, and L.A. Thompson (1991) Evidence for intrinsic expression of enkephalin-like immunoreactivity and opioid binding sites in cat superior colliculus. Neuroscience *43:*513–529.

Boussaoud, D., and J.P. Joseph (1985) Role of the cat substantia nigra pars reticulata in eye and head movements. II. Effects of local pharmacological injections. Exp. Brain Res. *57:*297–304.

Campbell, K.J., and M. Takada (1989) Bilateral tectal projection of single nigrostriatal dopamine cells in the rat. Neuroscience *33:*311–321.

Chen, S., and D.E. Hillman (1990) Robust synaptic plasticity of striatal cells following partial deafferentation. Brain Res. *520:*103–114.

Chevalier, G., A.M. Thierry, T., Shibazaki, and J. Feger (1981) Evidence for a GABAergic inhibitory nigrotectal pathway in the rat. Neurosci. Lett. *21:*67–70.

Chevalier, G., S. Vacher, J.M. Denian, and M. Desban (1985) Disinhibition as a basic process in the expression of striatal functions. I. The striato-nigral influence on tecto-spinal/tecto-diencephalic neurons. Brain Res. *334:*215–226.

Childs, J.A., and K. Gale (1983) Neurochemical evidence for a nigrotegmental GABAergic projection. Brain Res. *258:*109–114.

Ciaramitaro, V., A.C. Rosenquist, and S.F. Wallace (1993) Lesions to the substantia nigra ipsilateral to a visual cortical lesion fail to restore visual orientation behavior in the cat. Soc. Neurosci. Abst. *19:*766.

Ciaramitaro, V., J.S. Durmer, W.E. Todd, and A.C. Rosenquist (1994) $GABA_A$ mediated disinhibition of the superior colliculus restores visual orienting responses in the previously hemianopic visual field of the cortically blind cat. Soc. Neurosci. Abst. *20:*1186.

Clarke, P.B.S., D.W. Homer, A. Pert, and L.R. Skirboll (1987) Innervation of substantia nigra neurons by cholinergic afferents from the pedunculopontine nucleus in the rat: Neuroanatomical and electrophysiological evidence. Neuroscience *23:*1011–1019.

Curtis, D.R., D. Lodge, and H. McLennan (1979) The excitation and depression of spinal neurons by ibotenic acid. J. Physiol. *291:*19–28.

Datta, S., R. Curro Dossi, D. Pare, G. Oakson, and M. Steriade (1991) Substantia nigra reticulata neurons during sleep-waking states: Relation with ponto-geniculo-occipital waves. Brain Res. *566:*344–347.

Deniau, J.M., C. Hammond-LeGuyader, J., Feger, and J.S. McKenzie (1977) Bilateral projection of nigro-collicular neurons: An electrophysiological analysis in the rat. Neurosci. Lett. *5:*45–50.

DiChiara, G., M. Morelli, A. Imperato, and M.L. Porceddu (1982) A reevaluation of the role of superior colliculus in turning behavior. Brain Res. *237:*61–77.

Di Loreto, S., T. Florio, and E. Scarnati (1992) Evidence that non-NMDA receptors are involved in the excitatory pathway from the pedunculopontine region to nigrostriatal dopaminergic neurons. Exp. Brain Res. *89:*79–86.

Dunning, D.D., B.E. Stein, and J.G. McHaffie (1990) Effects of cortical and nigral deactivation on visual neurons in cat superior colliculus. Soc. Neurosci. Abst. *16:*110.

Durmer, J.S., V. Ciaramitaro, W.E. Todd, and A.C. Rosenquist (1994) Ibotenic acid lesions of the pedunculopontine nucleus restore visual orienting responses in the previously hemianopic visual field of the cortically blind cat. Soc. Neurosci. Abst. *20:*1187.

Edwards, S.B. (1977) The commissural projection of the superior colliculus in the cat. J. Comp. Neurol. *173:*23–40.

Edwards, S.B., C.L. Ginsburg, C.K. Henkel, and B.E. Stein (1979) Sources of subcortical projections to the superior colliculus in the cat. J. Comp. Neurol. *184:*309–330.

Faull, R.L.M., and W.R. Mehler (1978) The cells of origin of nigrotectal, nigrothalamic and nigrostriatal projections in the rat. Neuroscience *3:*989.

Ficalora, A.S., and R.R. Mize (1989) The neurons of the substantia nigra and zona incerta which project to the cat superior colliculus are GABA immunoreactive: A double-label study using GABA immunocytochemistry and lectin retrograde transport. Neuroscience *29:*567–581.

Fish, S.E., D.K. Goodman, D.C. Kuo, J.D. Pulcer, and R.W. Rhoades (1982) The intercollicular pathway in the golden hamster: An anatomical study. J. Comp. Neurol. *204:*6–20.

Fitzpatrick, D., I.T. Diamond, D. Raczkowski (1989) Cholinergic and monoaminergic innervation of the cat's thalamus: Comparison of the lateral geniculate nucleus with other principal sensory nuclei. J. Comp. Neurol. *288:*647–675.

Garcia-Rill, E., C.D. Hull, M.S. Levine, and N.A. Buchwald (1979) The spontaneous firing patterns of forebrain neurons. IV. Effects of bilateral and unilateral frontal cortical ablations on firing of caudate, globus pallidus and thalamic neurons. Brain Res. *165:*23–36.

Gerfen, C.R. (1985) The neostriatal mosaic. I. Compartmental organization of projections from the striatum to the substantia nigra in the rat. J. Comp. Neurol. *236:*454–476.

Gerfen, C.R., W.A. Staines, G.W. Arbuthnott, and H.C. Fibiger (1982) Crossed connections of the substantia nigra in the rat. J. Comp. Neurol. *207:*283–303.

Goodale, M. (1973) Corticotectal and intertectal modulation of visual responses in the rat's superior colliculus. Exp. Brain Res. *17:*75–86.

Gould, E., N.J. Woolf, and L.L. Butcher (1989) Cholinergic projections to the substantia nigra from the pedunculopontine and laterodorsal tegmental nuclei. Neuroscience *28:*611–623.

Granata, A.R., and S.T. Kitai (1991) Inhibitory substantia nigra inputs to the pedunculopontine neurons. Exp. Brain Res. *86:*459–466.

Graybiel, A.M. (1978a) A satellite system of the superior colliculus: The parabigeminal nucleus and its projections to the superficial collicular layers. Brain Res. *145:*365–374.

Graybiel, A.M. (1978b) Organization of the nigrotectal connection: An experimental tracer study in the cat. Brain Res. *143:*339–348.

Graybiel, A.M., and C.W. Ragsdale (1979) Fiber connections of the basal ganglia. In M. Cuenod, G.W. Kreutzberg, and F.W. Bloom (eds): Developmental and Chemical Specificity of Neurons. Progress in Brain Research, Vol. 57. Amsterdam: Elsevier, pp. 239–283.

Graybiel, A.M., and C.W. Ragsdale (1983) Biochemical anatomy of the striatum. In C.M. Emson (ed): Chemical Neuroanatomy. New York: Raven Press, pp. 427–505.

Graybiel, A.M., and T.R. Sciascia (1975) Origin and distribution of nigrotectal fibers in the cat. Soc. Neurosci. Abst. *1:*271.

Grofova, I., O.P. Ottersen, and E. Rinvik (1978) Mesenchephalic and diencephalic afferents to the superior colliculus and periaqueductal gray substance demonstrated by retrograde axonal transport of horseradish peroxidase in the cat. Brain Res. *146:*205–220.

Hall, W.C., D. Fitzpatrick, L.L. Klatt, and D. Raczkowski (1989) Cholinergic innervation of the superior colliculus in the cat. J. Comp. Neurol. *287:*495–514.

Harting, J.K., and D.P. Lieshout (1991) Spatial relationships of axons arising from the substantia nigra, spinal trigeminal nucleus, and pedunculopontine tegmental nucleus within the intermediate gray of the cat superior colliculus. J. Comp. Neurol. *305:*543–558.

Harting, J.K., M.F. Huerta, T. Hashikawa, J.T. Weber, and L.D.P. Van (1988) Neuroanatomical studies of the nigrotectal projection in the cat. J. Comp. Neurol. *278:*615–631.

Hashikawa, T., J.T. Weber, R. Hartwich-Young, D.P.V. Lieshout, and J.K. Harting (1986) Nigrotectal projections in the cat: Anterograde and retrograde transport studies. Soc. Neurosci. Abst. *12:*1031.

Hikosaka, O., and R.H. Wurtz (1983a) Visual and oculomotor functions of monkey substantia nigra pars reticulata. II. Visual responses related to fixation of gaze. J. Neurophysiol. *49:*1254–1267.

Hikosaka, O., and R.H. Wurtz (1983b) Visual and oculomotor functions of monkey substantia nigra pars reticulata. IV. Relation of substantia nigra to superior colliculus. J. Neurophysiol. *49:*1285–1301.

Hikosaka, O., and R.H. Wurtz (1983c) Visual and oculomotor functions of monkey substantia nigra pars reticulata. I. Relation of visual and auditory responses to saccades. J. Neurophysiol. *49:*1230–1253.

Hikosaka, O., and R.H. Wurtz (1983d) Visual and oculomotor functions of monkey substantia nigra pars reticulata. III. Memory-contingent visual and saccade responses. J. Neurophysiol. *49:*1268–1284.

Hikosaka, O., and R.H. Wurtz (1985a) Modification of saccadic eye movements by GABA-related substances. I. Effects of muscimol and bicuculline in monkey superior colliculus. J. Neurophysiol. *53:*266–291.

Hikosaka, O., and R.H. Wurtz (1985b) Modification of saccadic eye movements by GABA-related substances. II. Effects of muscimol in monkey substantia nigra pars reticulata. J. Neurophysiol. *53:*292–308.

Hikosaka, O., and R.H. Wurtz (1989) The basal ganglia. In R.H. Wurtz and M.E. Goldberg (eds): The Neurobiology of Saccadic Eye Movements. Review of Oculomotor Research. Vol. 3. New York: Elsevier Science Publishers BV (Biomedical Division), pp. 257–281.

Hoover, D.B., and D.M. Jacobwitz (1979) Neurochemical and histochemical studies of the effect of a lesion of the nucleus cuneiformis on the cholinergic innervation of discrete areas of the rat brain. Brain Res. *170:*113–122.

Hopkins, D.A., and L.W. Niessen (1976) Substantia nigra projections to the reticular formation, superior colliculus and central gray in the rat, cat and monkey. Neurosci. Lett. *2:*253–259.

Hovda, D.A., and J.R. Villablanca (1990) Sparing of visual field perception in neonatal but not adult cerebral hemispherectomized cats. Relationship with oxidative metabolism of the superior colliculus. Behav. Brain Res. *37:*119–132.

Hovda, D.A., R.L. Sutton, and D.M. Feeney (1987) Recovery of tactile placing after visual cortex ablation in cat: A behavioral and metabolic study of diaschisis. Exp. Neurol. *97:*391–402.

Huerta, M.F., and J.K. Harting (1984) The mammalian superior colliculus: Studies of its morphology and connections. In H. Vanegas (ed): The Comparative Neurology of the Optic Tectum. New York: Plenum Press, pp. 687–773.

Illing, R.B., and A.M. Graybiel (1985) Convergence of afferents from frontal cortex and substantia nigra onto acetylcholinesterase-rich patches of the cat's superior colliculus. Neuroscience *14:*455–482.

Illing, R.B., and A.M. Graybiel (1986) Complementary and non-matching afferent compartments in the cat's superior colliculus: Innervation of the acetylcholinesterase-poor domain of the intermediate gray layer. Neuroscience *18:*373–394.

Jackson, A., and A.R. Crossman (1983) Nucleus tegmenti pedunculopontinus: Efferent connections with special reference to the basal ganglia, studied in the rat by anterograde and retrograde transport of horseradish peroxidase. Neuroscience *10:*725–765.

Jayaraman, A., R.R. Batton III, and M.B. Carpenter (1977) Nigrotectal projections in the monkey: An autoradiographic study. Brain Res. *135:*147–152.

Jeon, C.J., R.F. Spencer, and R.R. Mize (1993) Organization and synaptic connections of cholinergic fibers in the cat superior colliculus. J. Comp. Neurol. *333:*360–374.

Jimenez-Castellanos, J., and A.M. Graybiel (1987) Subdivisions of the dopamine-containing A8-A9-A10 complex identified by their differential mesostriatal innervation of striosomes and extrastriosomal matrix. Neuroscience *23:*223–242.

Jones, B.E., and A. Beaudet (1987) Distribution of acetylcholine and catecholamine neurons in the cat brainstem: A choline acetyltransferase and tyrosine hydroxylase immunohistochemical study. J. Comp. Neurol. *261:*15–32.

Jones, B.E., and H.H. Webster (1988) Neurotoxic lesions of the dorsolateral pontomesencephalic tegmentum-cholinergic cell area in the cat. I. Effects upon the choline innervation of the brain. Brain Res. *451:*13–32.

Joseph, J.P., and D. Boussaoud (1985) Role of the cat substantia nigra pars reticulata in eye and head movements. I. Neural activity. Exp. Brain Res. *57:*286–296.

Kang, Y., and S.T. Kitai (1990) Electrophysiological properties of pedunculopontine neurons and their postsynaptic responses following stimulation of substantia nigra reticulata. Brain Res. *535:*79–95.

Karabelas, A.B., and A.K. Moschovakis (1985) Nigral inhibitory termination on efferent neurons of the superior colliculus: An intracellular horseradish peroxidase study in the cat. J. Comp. Neurol. *239:*309–329.

Kilpatrick, I.C., G.L. Collingridge, and M.S. Starr (1982) Evidence for the participation of nigrotectal γ-aminobutyrate-containing neurones in striatal and nigral-derived circling in the rat. Neuroscience *7:*207–222.

Kim, U., E. Gregory, and W.C. Hall (1992) Pathway from the zona incerta to the superior colliculus in the rat. J. Comp. Neurol. *321:*555–575.

Lavoie, B., and A. Parent (1994) Pedunculopontine nucleus in the squirrel monkey: Projections to the basal ganglia as revealed by anterograde tract-tracing methods. J. Comp. Neurol. *344:*210–231.

MacDonald, J.F., and A. Nistri (1977) Actions of microiontophoretically applied ibotenate on cat spinal interneurones. Canad. J. Physiol. Pharmacol. *55:*965–967.

MacDonald, J.F., and A. Nistri (1978) A comparison of the action of glutamate, ibotenate and other related amino acids on feline spinal interneurons. J. Physiol. *275:*449–465.

Magalhaes-Castro, H.H., A.D. deLima, P.S. Saraiva, and B. Magalhaes-Castro (1978) Horseradish peroxidase labeling of cat tectotectal cells. Brain Res. *148:*1–13.

May, P.J., and W.C. Hall (1986) The sources of the nigrotectal pathway. Neuroscience *19:*159–180.

McHaffie, J.G., M. Norita, D.D. Dunning, and B.E. Stein (1993) Corticotectal relationships: Direct and "indirect" corticotectal pathways. In R.R. Mize, R.E. Marc, and A.M. Sillito (eds): The Visually Responsive Neuron: From Basic Neurophysiology to Behavior. Progress in Brain Research. Vol. 95. New York: Elsevier Science Publishers BV (Biomedical Division), pp. 139–150.

Mohler, C.W., and R.H. Wurtz (1976) Organization of monkey superior colliculus: Intermediate layer cells discharging before eye movements. J. Neurophysiol. *39:*722–744.

Moon Edley, S., and A.M. Graybiel (1983) The afferent and efferent connections of the feline nucleus tegmenti pedunculopontinus, pars compacta. J. Comp. Neurol. *217:*187–215.

Mori, S., T. Sakamoto, Y. Ohta, and K. Takakusaki (1989) Site-specific postural and locomotor changes evoked in awake, freely moving intact cats by stimulating the brainstem. Brain Res. *505:*65–74.

Nagata, T., H. Magalhaes-Castro, P. Saraiva, and B. Magalhaes-Castro (1980) Absence of tectotectal pathway in the rabbit: An anatomical and electrophysiological study. Neurosci. Lett. *17:*125–130.

Napieralski, J.A., Butler, A.K., and M-F. Chesselet (1996) Anatomical and functional evidence for lesion specific sprouting of corticostriatal input in the adult rat. J. Comp. Neurol. *373:*484–497.

Nitsch, C., K. Mews, A. Wagner, and R. Hassler (1984) Effects of frontal motor cortex ablation on the ultrastructure of cat substantia nigra. Acta Anatomica. *119:*193–202.

Noda, T., and H. Oka (1984) Nigral inputs to the pedunculopontine region: Intracellular analysis. Brain Res. *322:*332–336.

Noda, T., and H. Oka (1986) Distribution and morphology of tegmental neurons receiving nigral inhibitory inputs in the cat: An intracellular HRP study. J. Comp. Neurol. *244:*254–266.

Puil, E. (1979) The excitatory portion of the biphasic response of central neurons to ibotenic acid. Soc. Neurosci. Abst. *5:*569.

Redgrave, P., L. Marrow, and P. Dean (1992) Topographical organization of the nigrotectal projection in rat: Evidence for segregated channels. Neuroscience *50:*571–595.

Reinoso-Suarez, F. (1961) Topographisher Hirnatlas der Katze fur Experimental-Physiologische Untersuchungen. Darmstadt: E Merck.

Rhoades, R.W., D.C. Kuo, J.D. Pulsar, S.E. Fish, and T.J. Voneida (1982) Indirect visual cortical input to the deep layers of the hamster's superior colliculus via the basal ganglia. J. Comp. Neurol. *208:*239–254.

Rinvik, E., I. Grofova, and O.P. Otterson (1976) Demonstration of nigrotectal and nigroreticular projections in the cat by axonal transport proteins. Brain Res. *112:*338–394.

Rosenquist, A.C. (1985) Connections of visual cortical areas in the cat. In A. Peters and E.G. Jones (eds): Cerebral Cortex. Vol. 3. New York: Plenum, pp. 81–117.

Salin, P., and M.-F. Chesselet (1992) Paradoxical increase in striatal neuropeptide gene expression following ischemic lesions of the cerebral cortex. Proc. Natl. Acad. Sci. *89:*9954–9958.

Salin, P., and M.-F. Chesselet (1993) Expression of GAD (Mr 67,000) and it's messenger RNA in basal ganglia and cerebral cortex after ischemic cortical lesion in rats. Exp. Neurol. *119:*291–301.

Saraiva, P., B. Magalhaes-Castro, H. Magalhaes-Castro, and S.R. Torres (1978) Electrophysiological aspects of the superior colliculus of the opossum. Cortico-tectal and tectotectal influences. In C.E. Rocha Miranda and R. Lent (eds): Opossum Neurobiology. Rio de Janeiro: Academia Biasileiva deCiencias. pp. 151–165.

Scarnati, E., A. Proia, E. Campana, and C. Pacitti (1986) A microiontophoretic study on the nature of the putative synaptic neurotransmitter involved in the pedunculopontine-substantia nigra pars compacta excitatory pathway of the rat. Exp. Brain Res. *62:*470–478.

Schultz, W. (1982) Depletion of dopamine in the striatum as an experimental model of Parkinsonism: Direct effects and adaptive mechanisms. Prog. Neurobiol. *18:*121–166.

Sherman, S.M. (1974) Visual fields of cats with cortical and tectal lesions. Science *185:*355–357.

Sherman, S.M. (1977) The effect of superior colliculus lesions upon the visual fields of cats with cortical ablations. J. Comp. Neurol. *172:*211–229.

Shinosaki, H., and M. Ishida (1980) Inhibitory action of ibotenic acid on the crayfish neuromuscular junction. Brain Res. *198:*157–165.

Shute, C.C.D., and P.R. Lewis (1967) The ascending cholinergic reticular system: Neocortical, olfactory and subcortical projections. Brain *90:*497–520.

Sommers, D.L., and R.M. Beckstead (1990) Striatal preprotachykinin and preproenkephalin mRNA levels and the levels of nigral substance P and pallidal Met^5-enkephalin depends on corticostriatal axons that use the excitatory amino acid neurotransmitters aspartate and glutamate: Quantitative radioimmunocytochemical and in situ hybridization evidence. Mol. Brain Res. *8:*143–158.

Sprague, J.M. (1966a) Interaction of cortex and superior colliculus in mediation of visually guided behavior in the cat. Science *153:*1544–1547.

Sprague, J.M. (1966b) Visual, acoustic and somesthetic deficits in the cat after cortical and midbrain lesions. In D.P. Purpura and M. Yahr (eds): The Thalamus. New York: Columbia University Press, pp. 391–417.

Tokuno, H., and Y. Nakamura (1987) Organization of the nigrotectospinal pathway in the cat: A light and electron microscopic study. Brain Res. *436:*76–84.

Uhl, G.R., B. Navia, and J. Douglas (1988) Differential expression of preproenkephalin and preprodynorphin mRNAs in striatal neurons: High levels of preproenkephalin expression depend on cerebral cortical afferents. J. Neurosci. *8:*4755–4764.

Vincent, S.R., T. Hattori, and E.G. McGeer (1978) The nigrotectal projection: A biochemical and ultrastructural characterization. Brain Res. *151:*159–164.

Wallace, S.F., A.C. Rosenquist, and J.M. Sprague (1989) Recovery from cortical blindness mediated by destruction of nontectotectal fibers in the commissure of the superior colliculus in the cat. J. Comp. Neurol. *284:*429–450.

Wallace, S.F., A.C. Rosenquist, and J.M. Sprague (1990) Ibotenic acid lesions of the lateral substantia nigra restore visual orientation behavior in the hemianopic cat. J. Comp. Neurol. *296:*222–252.

Woolf, N.J., J.B. Harrison, and J.S. Buchwald (1990) Cholinergic neurons of the feline pontomesencephalon. II. Ascending anatomical projections. Brain Res. *520:*55–72.

Wurtz, R.H., and J.E. Albano (1980) Visual-motor function of the primate superior colliculus. Annu. Rev. Neurosci. *3:*189–226.