

Visual detection deficits following inactivation of the superior colliculus in the cat

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Abstract

Lesion or inactivation of the superior colliculus (SC) of the cat results in an animal that fails to orient toward peripheral visual stimuli which normally evoke a brisk, reflexive orienting response. A failure to orient toward a visual stimulus could be the result of a sensory impairment (a failure to detect the visual stimulus) or a motor impairment (an inability to generate the orienting response). Either mechanism could explain the deficit observed during SC inactivation since neurons in the SC can carry visual sensory signals as well as motor commands involved in the generation of head and eye movements. We investigated the effects of SC inactivation in the cat in two ways. First, we tested cats in a visual detection task that required the animals to press a central, stationary foot pedal to indicate detection of a peripheral visual stimulus. Such a motor response does not involve any components of the orienting response and is unlikely to depend on SC motor commands. A deficit in this task would indicate that the SC plays an important role in the detection of visual targets even in a task that does not require visual orienting. Second, to further investigate the visual orienting deficit observed during SC inactivation and to make direct comparisons between detection and orienting performance, we tested cats in a standard perimetry paradigm. Performance in both tasks was tested following focal inactivation of the SC with microinjections of muscimol at various depths and rostral/caudal locations throughout the SC. Our results reveal a dramatic deficit in both the visual detection task and the visual orienting task following inactivation of the SC with muscimol.

Keywords: Superior colliculus, Visual detection, Visual orienting, Muscimol

Introduction

Under normal conditions, a cat will rapidly turn its head, eyes, and ears toward a novel stimulus presented within the animal's visual field. This adaptive behavioral response, the visual orienting response, brings the image of the novel stimulus into the cat's central visual field where it can be more thoroughly assessed. Inactivation of the superior colliculus (SC) of the cat produces a deficit in the visual orienting response. In contrast to normal cats, a cat with unilateral inactivation of the SC will fail to orient to contralateral visual targets and will ignore contralateral visual stimuli presented under a variety of conditions. Such deficits were first documented in the cat following permanent ablation of the SC (Sprague & Meikle, 1965) and have been observed following reversible cryostatic inactivation of the SC (Payne et al., 1996). Sensory, motor, and attentional mechanisms have been proposed as possible explanations for this dramatic deficit.

The visual orienting deficit that occurs following SC inactivation or lesion has been studied using a classic perimetry paradigm.

Unfortunately, the nature of the perimetry task limits its usefulness in clarifying the mechanisms underlying the orienting deficit. In the perimetry task, a hungry cat must initially fixate a central food target, and must subsequently orient the head and eyes to a peripherally presented food target in order to acquire that food as a reward. This response depends on the ability of the cat first to detect the peripheral visual target and second to generate the appropriate motor command. Because the SC contains neurons that exhibit sensory responses to visual stimuli as well as neurons that are active preceding orienting movements of the eyes and head, the failure to orient during SC inactivation could be due to a visual detection deficit or a motor deficit or both.

The SC is critically involved in visual orienting and saccadic eye movements; and most studies of the SC emphasize its role in visuomotor function (for review, see Wurtz & Albano, 1980; Sparks & Hartwich-Young, 1989). For example, neurons in the deep SC demonstrate both visual and motor activity in tasks requiring animals to orient/saccade to peripheral visual targets (for examples, see Schiller & Koerner, 1971; Wurtz & Goldberg, 1972; Mays & Sparks, 1980; Peck et al., 1980; Munoz & Guitton, 1991*a,b*; Freedman & Sparks, 1997). And lesion or inactivation of the SC in the monkey affects the latency, velocity, accuracy, and direction of saccadic eye movements, in some cases rendering animals unable to saccade to peripheral targets (Kurtz & Butter,

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1980; Hikosaka & Wurtz, 1983, 1985a; Keating & Gooley, 1988; Lee et al., 1988).

Fewer studies have examined the role the SC plays in visual detection and sensory processing, although deficits in visual detection, localization, and form discrimination have been documented in the cat, rat, monkey, and tree shrew following SC lesions and inactivation (for examples, see Casagrande et al., 1972; Latto, 1977; Tunkl & Berkley, 1977; Butter et al., 1978; Albano et al., 1982; Overton & Dean, 1988; Lomber et al., 2001). Unfortunately, the interpretation of these studies is limited because of one or more of the following considerations: (1) Most of these experiments used permanent ablation of the SC rather than reversible inactivation. SC ablation initially produces dramatic motor and behavioral deficits that must resolve before animals can be tested again. During this recovery period, compensatory changes can occur that likely mitigate or otherwise alter any resulting deficits. (2) In some cases, lesions were not restricted to the SC, so deficits may have been due to damage to adjacent nuclei or fiber tracts. (3) Eye position was not monitored in many of the experiments, making it unclear if the observed deficits were due to visual impairment or a motor impairment that decreased the animals' tendency to scan for targets or evaluate targets. (4) Some of the animals in these studies received bilateral SC lesions. Once bilateral lesions are made, animals cannot be simultaneously tested under control conditions in the same task. This makes it more difficult to test for changes in motivation or motor problems that may have made the task more difficult to perform after the lesion. These experimental design issues permit alternate explanations for the observed behavioral deficits. To firmly establish and further investigate the role of the SC in visual detection, new experimental strategies need to be employed.

The experiments in this paper were conducted with two aims. First, we set out to determine if a visual detection deficit occurs during SC inactivation. Toward this end, we designed a task that does not require visual orienting but instead requires the cat to press a pedal with its paw to indicate detection of a visual target. Eye position was monitored with a scleral eye-coil and fixation was required. The possibility of long-term compensatory changes was diminished by using reversible inactivation with microinjections of muscimol instead of ablation. Importantly, in our experiments, the SC was unilaterally rather than bilaterally inactivated. This provided a control in each experiment for nonspecific impairment due to motor, attentional, or motivational problems. Since each side of the SC represents the contralateral visual hemifield, only performance in the contralateral visual hemifield should be impaired by unilateral SC inactivation, and animals should perform normally for targets in the ipsilateral hemifield if the deficit is visual in nature. At the same time we were testing the animals' ability to detect visual targets, we sought to further examine the perimetry deficit that occurs during SC inactivation, and compare the perimetry deficit and detection deficit observed within the same experiments. The results of these experiments demonstrate that the SC plays a critical role in detection of visual stimuli in a nonorienting detection task, thus indicating that the SC is important for visual sensory as well as visuomotor behaviors.

Materials and methods

General

Data for this study were collected from three castrated male cats. Cats were individually housed and maintained on a 12-h light/

12-h dark schedule. Food intake was restricted as described below but cats had *ad libitum* access to water. Cats were allowed group play time several times a week in the lab and had toys and perches in their cages for psychological enrichment.

Surgery

All surgical procedures were performed using standard aseptic technique. The surgical protocol was approved by the Institutional Animal Care and Use Committee, and complied with federal regulations and guidelines for animal welfare. Anesthesia was induced with an intramuscular injection of ketamine (11 mg/kg), acepromazine (0.15 mg/kg), and butorphanol tartrate (0.25 mg/kg). Animals were intubated and maintained with isoflurane inhalant anesthesia delivered at 2–4%. Cats were surgically implanted with a scleral eye coil for monitoring gaze position during behavioral testing. The coil (Cooner Wire, Chatsworth, MA) was attached to the sclera with 6-0 vicryl suture material. The wires from the coil were tunneled subcutaneously to the top of the skull where they were soldered to a connector that was then mounted on the skull with bone cement. Chronic indwelling guide cannulae were placed in a subsequent surgical procedure. Guide cannulae were stereotaxically positioned over the SC, based on the atlas of Reinoso-Suarez (1961). They were lowered into the brain through small holes drilled in the skull, so that the tips were 2 mm above the SC. The cannulae were fixed in place with bone cement that was anchored to several small screws placed in the skull. At the end of the surgical procedure and as needed in the first 24–48 h postoperation, animals were given an intramuscular injection of butorphanol tartrate (0.5 mg/kg) for postoperative pain control. Cats were active and eating well within 1 day postoperation and were allowed to recover for 2 weeks before training resumed.

One cat, Bart, was implanted with four guide cannulae positioned at AP +1 and AP +3, bilaterally. The second cat, Homer, was initially implanted with bilateral guide cannulae at AP 0. These were surgically removed when the series of experiments for those cannulae was completed and new cannulae were placed bilaterally at AP +2. In the third cat, Monty, bilateral guide cannulae were placed at AP +2. All guide cannulae were positioned 3 mm from the midline. Experimental data were collected using all ten guide cannulae.

Behavioral training and testing

During all training and experimental testing periods, cats were mildly food deprived so that they would be motivated to perform the behavioral tasks consistently. Cats were fed daily; most of what they ate was earned as a reward for performance in either the perimetry task or the detection task. All cats maintained a healthy weight throughout the duration of experiments based on a well-accepted veterinary body condition scoring system (LaFlamme, 1993).

Detection task

After surgical placement of a scleral eye coil, cats were trained to perform the detection task. In the detection task, cats were comfortably restrained in a sitting position by a mesh harness (Alice King Chatham Medical Arts, Hawthorne, CA) with a pedal located directly in front of the right front paw. Visual stimuli were presented on a computer monitor positioned 16 cm from the cat's nose. The background illumination of the monitor was 15.8 cd/m².

The animal sat at the center of a pair of orthogonal magnetic fields and gaze position was continuously monitored (Fuchs & Robinson, 1966). During the training period, cats initially learned to tolerate the minimal restraint while being fed in the apparatus and then learned to fixate a central spot of light on the computer monitor for increasing periods of time. Once the animals learned to fixate, they were trained to press the pedal in front of their right paw if a peripheral target was presented during fixation. When cats were performing the task consistently, formal testing sessions in the detection task began.

In a given testing session, two types of trials (target trials and blank trials) were randomly interleaved. The intertrial interval was 3–5 s. A target trial began with the onset of a central fixation target (1.5-deg diameter, 150% contrast) and the presentation of a brief tone to alert the animal to the start of a trial. The animal had 2 s to achieve fixation before the trial would abort and enter the intertrial interval. When the animal achieved fixation within a 10-deg diameter circular window, the fixation target would brighten to reinforce the behavior. After fixation was maintained within this window for a variable period of time (500–1200 ms), a peripheral target (2–3 deg in diameter, contrast 150%) was briefly presented (80 ms) at one of six locations along the horizontal meridian (12, 24, and 36 deg to the left and right of the fixation target). The fixation target remained illuminated throughout the trial and the cat had to maintain fixation within the 10-deg window until the peripheral target was extinguished. To indicate detection of the peripheral target, the cat had to press the pedal with his right paw within a limited time to receive a bolus of pureed cat food delivered *via* a feeding tube to a trough in front of the cat's mouth. Initially the cat was permitted up to 2 s to press the pedal. This time limit was gradually decreased as performance improved. For all data collection trials the response time limit was fixed at 800 ms.

When the peripheral target was extinguished, cats were free to move their gaze position in any direction. Cats would occasionally look toward the peripheral target location at this point but on the vast majority of trials would immediately direct their gaze downward toward the response pedal.

Blank trials were identical to target trials except that no peripheral target was presented. In order to earn the food reward, the animal had to maintain fixation for the maximal fixation time (1200 ms) plus the response time limit (800 ms). If the cat broke fixation before the minimal required fixation time (500 ms) the trial was aborted. If cats pressed the pedal during the response interval of a blank trial they received no reward, the trial was ended and a delay was imposed before the next trial began. This delay added 1–2 s to the intertrial interval. Blank trials were scored as correct if the cat fixated during the fixation interval and did not hit the pedal during the response time limit interval. Blank trials were scored as false hits if the cat fixated during the fixation interval and hit the pedal within the response time limit. During experimental blocks, 40% of the trials were blank trials. This large percentage of blank trials was necessary to discourage the cats from adopting "guessing" strategies or banging on the pedal as they became frustrated with the task.

Detection scores at each of the six target locations were calculated as the percentage of target presentations to which the cat responded correctly by hitting the pedal within the response time limit. The percentage of blank trials in which the cat incorrectly hit the pedal was also determined for each block of trials. Criteria for inclusion of a block of trials in analysis or discussion in this paper are as follows: (1) a minimum of four trials were run at each target

location, and (2) no more than 25% of blank trials were false hits. Only three blocks of trials of the 113 detection experiments were discarded due to cats exceeding 25% on blank trials.

Perimetry Task

After acclimating cats to the laboratory and experimental surroundings, training for the perimetry task was initiated. Testing animals in this task required two investigators. One gently restrained the cat in the sternal position at the center of a circular table. The cat faced the edge of the table which was marked at 15-deg intervals so that stimuli could be presented at 13 locations ranging from 90 deg to the left to 90 deg to the right of fixation. A second investigator sat facing the cat at the edge of the table with shoulders below the surface and presented the visual stimulus which was a piece of kibble held in a forceps. This stimulus was presented at the central mark located 40 cm directly in front of the cat. When the cat fixated this central stimulus, a second identical stimulus was presented at one of the peripheral locations. The natural behavior of all cats studied was to orient the eyes, head, and pinnae toward the novel stimulus which the cat was then permitted to retrieve as a reward. This behavior was scored as a correct response. If the animal failed to orient to the peripheral stimulus within a 1–3 s period of stimulus presentation, the animal was released and permitted to retrieve the central fixation stimulus as a reward. This behavior was scored as a miss. A trial was aborted if the animal broke fixation early or did not initiate fixation. Blank trials were presented every fourth trial to encourage sustained fixation and to determine the prevalence of spontaneous scanning behavior. In these trials the investigator presented the stimulus outside of the cat's visual field after the cat achieved fixation. If the animal broke fixation and oriented to the left or right during the 1–3 s period in which the stimulus was presented, the behavior was counted as a scan.

Animals were easily trained to perform the perimetry task and rarely missed a stimulus trial under normal conditions. Behavior in this task stabilized after 2–3 weeks of training at which point an eye coil and injection cannulae were surgically implanted.

Reversible inactivation of the SC

Solutions of the GABA_A agonist muscimol (Sigma, St. Louis, MO) were prepared at concentrations ranging from 0.3 µg/ml to 4 µg/ml in physiological saline. Injection needles were constructed to protrude various lengths (from 1.5 mm to 8 mm) from the tip of the guide cannulae. Injections were made *via* 28- or 30-gauge needles depending on which of two types of assemblies had been implanted. The needles were connected *via* polyethylene tubing to a 1- or 5-µl Hamilton syringe. This injection assembly was filled with muscimol solution prior to injection. The dummy cannula was removed and the sterilized needle was inserted into the guide cannula while a second investigator gently restrained the cat. Once the needle was completely inserted, 20–30 s were allowed to pass to permit any compression of the tissue to reverse. An injection of 0.1–2 µl of muscimol solution was made over 30–60 s. The needle was kept in place for another 20–30 s to minimize backflow of the solution up the needle track. The needle was then removed and checked to make sure that solution flowed from the needle immediately postinjection when the plunger was advanced. Any delay in the flow of solution was recorded. Finally, the dummy cannula was replaced into the guide. Cats did not show any distress or behavioral changes while the injections were being made.

Experiment design

Once performance in the detection task was stabilized, experimental sessions began. For a given experiment, detection performance was tested in three control sessions within the week preceding an injection. Each session included 5–11 trials at each target location and 40% of all the trials were blank trials. The cat's average performance at each target location and on blank trials over these three sessions was calculated. On the day of an injection, post-injection sessions were run at various time points following the injection. In most experiments at least two blocks of trials were run, centered at approximately 25 and 55 min postinjection. In some experiments, earlier or later time points were tested to determine how early a detection deficit occurred and when the animal recovered. The number of trials at each target location for postinjection sessions ranged from 4 to 10. Fewer trials were run in each postinjection testing session to allow for testing at multiple time points because the cats would become satiated too quickly if they ran too many trials. In addition, some injections produced behavioral deficits that made it more difficult for the cat to perform the task and it would take longer under these conditions to run trials. Because an experiment required three sessions of preinjection data, injections were spaced apart by at least 3 days, and usually by a week or more.

Within a given experiment, testing in the perimetry task was interleaved with testing in the detection task. For each perimetry testing session, cats were tested once at each of the 12 target locations for their ability to orient to visual stimuli. Two to four perimetry sessions were run in the first hour following the injection, then testing became less frequent, occurring every 30 min to 2 h until recovery. Cats were tested in both the perimetry and detection tasks in most experiments so that any deficits in performance could be compared. In the case of Monty, only perimetry performance was evaluated due to his inability to learn the detection task.

Tissue fixation and processing

At the conclusion of all behavioral testing, animals were given an overdose of pentobarbital and were perfused through the heart with saline followed by 10% formalin. The brain was then blocked in the standard stereotaxic frontal plane, removed from the skull, and embedded in celloidin. The tissue was cut into 48- μ m-thick sections. Every tenth section was stained for cell bodies with cresyl violet and adjacent sections were stained for fibers using the Heidenhain-mahon myelin technique. To aid in the precise localization of the injection sites, additional sections in the region of needle damage were also stained and analyzed when necessary.

Stained sections were analyzed under a microscope and reconstructed by hand by projecting them onto paper and drawing the lesions and major anatomical structures in the section. The anterior–posterior (A–P) extent of damage from injection needle penetrations was determined by comparing the anatomical landmarks in the reconstructed sections to standard atlases (Reinoso-Suarez, 1961; Berman, 1968), and the central locus of damage, determined to be the section with the largest area of damage, was replotted onto a standard dorsal view of the SC. A map of the sensory representation of the visual field in the cat SC (Berman & Cynader, 1972) was then superimposed on this map so that the functional locus of inactivation could be estimated.

Results

Anatomic reconstruction

Two of the cats (Homer and Bart) were surgically implanted with four cannulae stereotaxically positioned so that in each cat, two cannulae would be over the rostral SC and two over the caudal SC. The third cat (Monty) had bilateral cannulae positioned over the central SC. Reconstruction of the brains confirmed that all ten cannula locations resulted in injections within the SC. Fig. 1A shows representative sections from the rostral and caudal SC in Homer and Bart. Shaded regions correspond to gliosis and tissue damage caused by the injection needles. Arrows depict the location and trajectory of the indwelling cannulae based on tracts left in the overlying cortex (not shown). Fig. 1B depicts the location of all ten injection sites from the three cats plotted on a standard dorsal view of the SC. Homer and Bart had bilateral injection loci in the rostral SC at AP +3 to AP +4 mm. Based on the sensory map of Berman and Cynader (1972), these locations include the most central representation of the visual field, within 10 deg of fixation. In addition, Homer and Bart had bilateral injection loci in the caudal SC at AP 0.5 to AP 1.5 mm. These injection sites correspond to more peripheral locations in the visual field. Monty's cannulae were centered at AP +2.5 mm in both colliculi, corresponding to roughly 10 deg from fixation.

Detection task

Detection deficit

Detection data were collected from two cats, Bart and Homer. (Monty failed to learn the detection task.) Both Bart and Homer had four indwelling cannulae which permitted injections to be made at a total of eight SC locations at depths ranging from the surface of the SC to the midbrain tegmentum underlying the SC. Inactivation of the SC at all eight cannula locations produced dramatic detection deficits. In Fig. 2, data from four experiments are shown in columns. The average performance and standard deviation at each of the six target locations for three preinjection testing sessions is presented in the top graph for each experiment. The error bars from these graphs are redisplayed on each of the three graphs below it for direct comparison with the postinjection performance. The lower graphs depict postinjection detection performance at the time point indicated at the top of each graph.

Following inactivation of the SC in these four experiments, cats missed many of the contralateral targets presented at time points ranging from 15 min to 80 min postinjection. The detection deficits observed in these experiments were typical for injections of similar size and location. The severity of the deficits varied considerably with size and depth of the muscimol injection. Detection deficits were observed as early as 10 min postinjection. The deficit usually became more severe during the first 60–90 min postinjection, and in some experiments, deficits were recorded as late as 5 or 6 h postinjection. However, in most cases the cats were beginning to recover or had fully recovered by 4 to 6 h postinjection.

A total of 113 experiments were conducted in two cats at eight cannula locations. Injection depths ranged from above the SC to 5.5 mm below the SC surface. In most experiments the deficits were dramatic, as seen in Fig. 2. A small number of experiments had very mild deficits in the contralateral or ipsilateral hemifield. We therefore established the following criterion. For a deficit to be considered significant, the postinjection detection score at a minimum of one target location had to be more than two standard

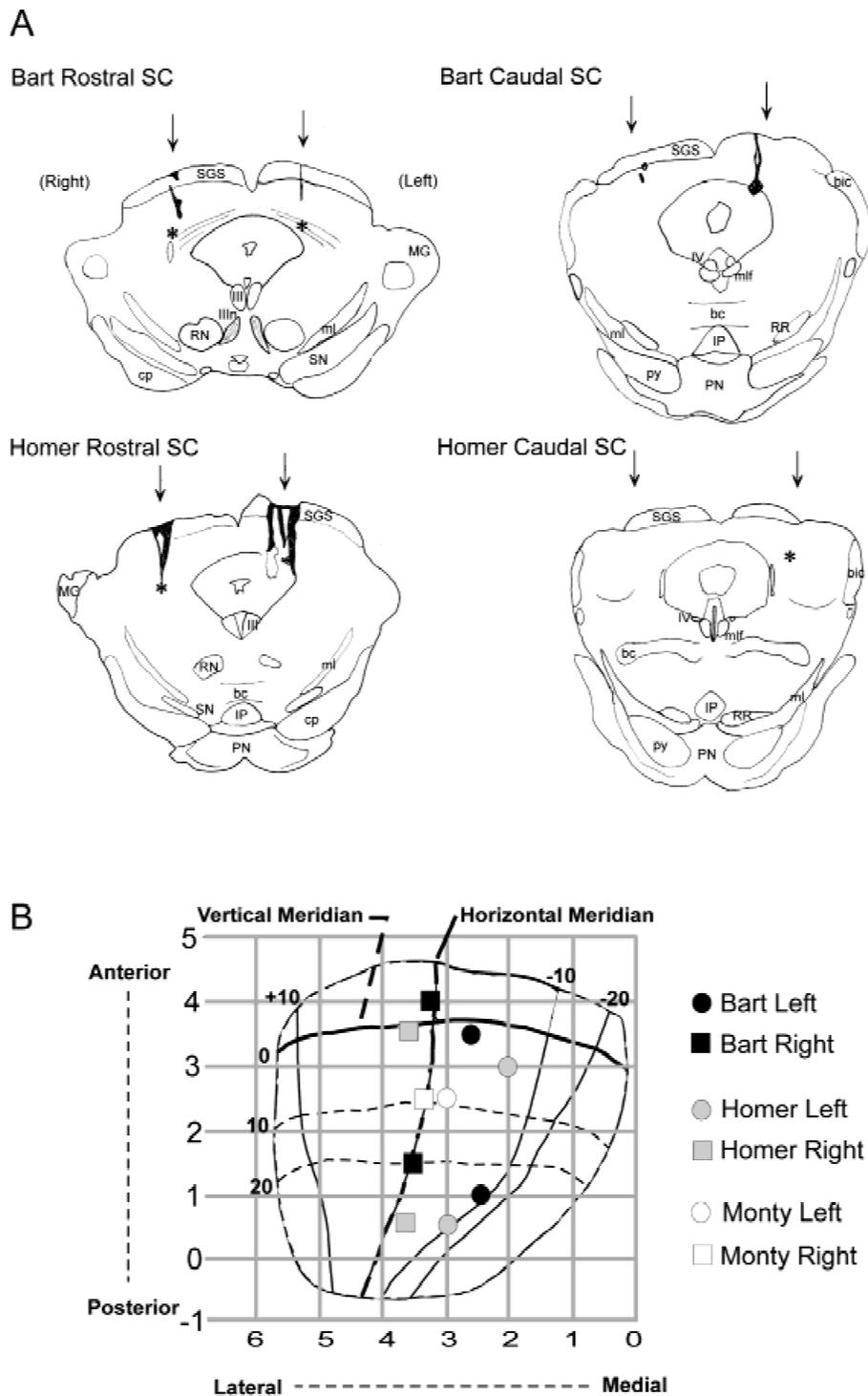


Fig. 1. Anatomic reconstruction of injection sites. (A) The four drawings of coronal brain sections show a representative section from the rostral and caudal SC in Bart and Homer. The sections were chosen to demonstrate gliosis bilaterally rather than to show the locus of maximum damage on either side. Gliosis is represented in black. Arrows above the SC show the location and angle of the cannula tracts observed in the overlying cortex. Asterisks show the location of electrolytic lesions, generated by inserting a microelectrode through the injection cannula and passing a 10- μ A current for 10 s. In Homer's caudal SC, the location of the injections were inferred from the location of the overlying guide cannulae. These cannulae were removed more than a year before the animal was perfused and any gliosis in the SC had resolved by the time of tissue processing. (B) The central locus of damage of each of the ten injection sites is plotted on a two-dimensional dorsal view of the SC which is then superimposed on a map of the sensory representation of the SC (Berman & Cynader, 1972). Dashed lines depict the vertical meridian and various eccentricities of azimuth as labeled. Solid lines depict the horizontal meridian and various eccentricities of elevation as labeled. Filled circles and squares show the location of left and right injection sites respectively in Bart (black), Homer (grey), and Monty (white). (SGS: stratum griseum superficiale; MG: medial geniculate nucleus; SN: substantia nigra; RN: red nucleus; IP: interpeduncular nucleus; PN: pontine nuclei; RR: retrorubral nucleus; cp: cerebral peduncle; ml: medial lemniscus; bc: brachium conjunctivum; py: pyramidal tract; bic: brachium of the inferior colliculus; mlf: medial longitudinal fasciculus; III: oculomotor nucleus; IIIIn: third cranial nerve; and IV: trochlear nucleus).

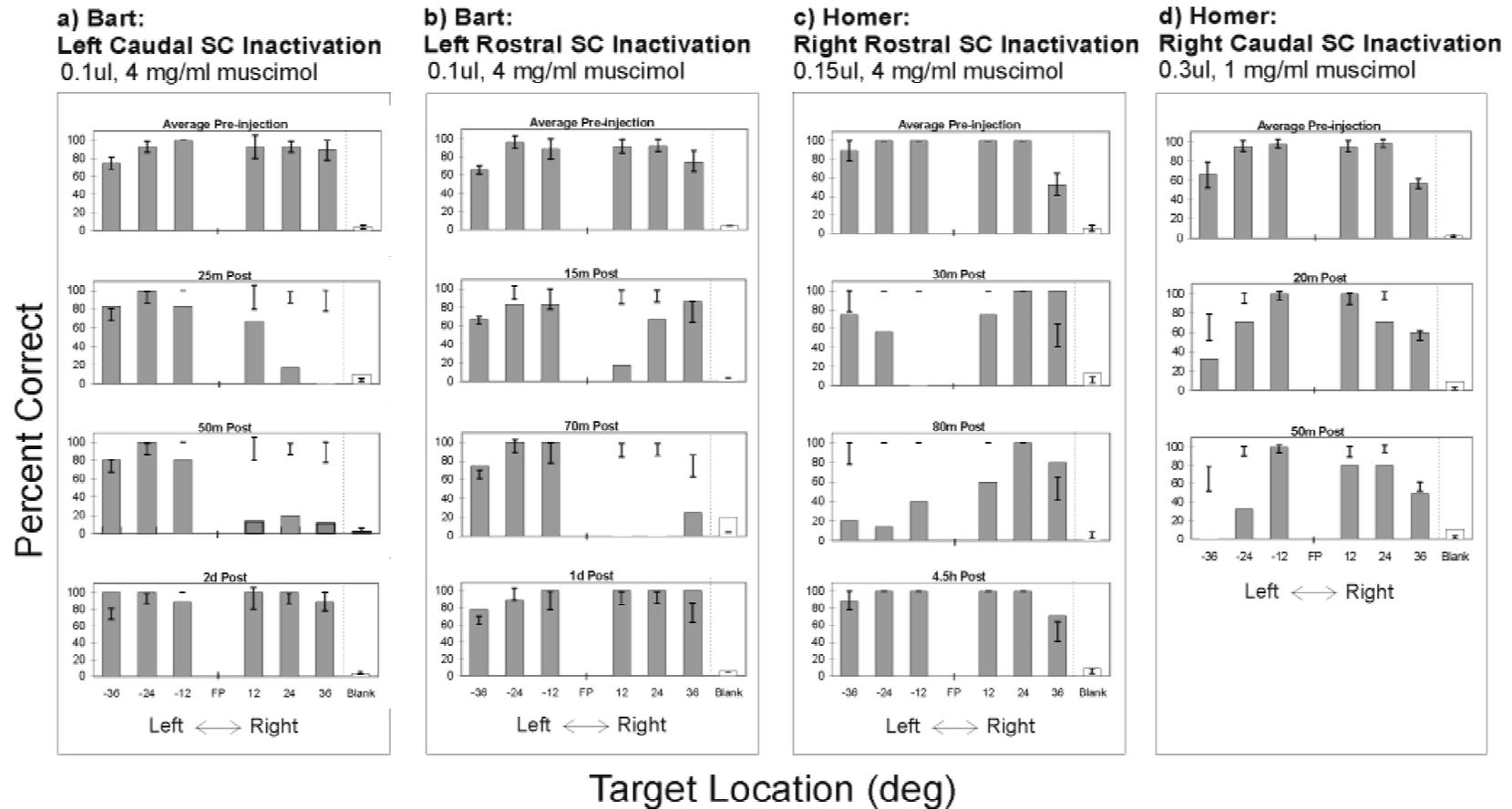


Fig. 2. Inactivation of the SC results in a detection deficit for contralateral visual targets. Data from four experiments are shown in columns. Each graph shows the percentage of trials at each target location that were correctly detected. The top graph in each column shows the average performance and standard deviation for three preinjection testing sessions. The lower graphs depict performance at specified postinjection timepoints. The error bar from the top graph is redisplayed on the lower graphs for comparison. The pattern of targets missed following SC inactivation is consistent with the retinotopic organization of the SC.

deviations below the preinjection score even if one of the post-injection missed trials was discarded. By discarding one of the missed trials, we avoided interpreting the spurious missing of one trial as a deficit. Based on this criterion, a significant detection deficit at one or more target locations in the contralateral visual hemifield was observed following inactivation of the SC in 76 of the 113 experiments (67%).

In 32 experiments (28%), no deficit was observed in the detection task (or the perimetry task). This occurred most commonly for small injections at superficial sites. In these situations, where no deficit was observed in either task, it was impossible to be certain that the injection had worked, and so the injection site (i.e. cannula location and depth) was usually tested multiple times. Often a repeated injection produced a deficit, suggesting that a mechanical failure may have occurred the first time. At some locations, small (0.1 μl) injections repeatedly failed to produce a detection deficit while larger injections were effective, suggesting that the muscimol needed to spread to more distant tissue to produce a detection deficit. However, in seven of the failed experiments, at superficial injection depths we were unable to produce a deficit in either task with repeated large-volume injections. We suspect that these injections were made above the SC surface based on the length of the injection needle and the stereotaxic placement of the injection cannula, and used this assumption to estimate the injection depth of other injections made *via* the same cannula.

In five experiments of the total 113 (4%), a deficit in the perimetry task was observed, confirming that the injection had worked, but no detection deficit was observed. In three of these experiments, the injections were centered deep to the SC in the underlying tegmentum.

In the majority of experiments (91%), performance at ipsilateral target locations was the same before and after SC inactivation. However, in ten experiments (9%), a deficit at one ipsilateral target location was also observed. These ipsilateral deficits were much less dramatic than the contralateral deficits often just reaching significance by the criterion we established. Unlike the contralateral deficits, which grew more severe at subsequent time points, ipsilateral deficits were sporadic and likely due to chance fluctuations in performance.

Cats were strongly discouraged from arbitrarily pressing the response pedal. A large proportion of trials were blank trials (40%), and cats were penalized with "time outs" if they hit the response pedal prematurely in a target trial or during the fixation period in a blank trial. As a result, both cats had low percentages of false hits, averaging fewer than 10% overall, on blank trials preinjection and postinjection. This can be seen in Figs. 3 and 4 in the "Blanks" data presented in each graph. The rate of false hits was compared for experiments conducted at each cannula location for preinjection and postinjection blocks to determine if there was a consistent difference. All experiments in which a significant detection deficit was observed were included in these calculations and all blocks of trials within the first hour postinjection were averaged. For most cannula locations, performance on blank trials preinjection and postinjection was statistically the same. However, cats had a small but significant increase in false hits following injections at three of the eight cannula locations. These increases may reflect a change in strategy during postinjection blocks where a larger number of trials are not being rewarded. However, the overall increase in false hits observed in some of the postinjection testing blocks was small and does not account for or diminish the credibility of the detection deficit.

Retinotopy

When small volume injections of muscimol were made, the target locations at which the detection deficit was most severe were consistent with the anterior–posterior location of SC inactivation based on the known retinotopic organization of the SC. Injections at the rostral cannulae produced deficits that were most severe at the central target locations while caudal injections produced deficits most severe at the peripheral target locations. This was best observed at the earlier postinjection time points, presumably before the muscimol had spread to or affected more distant sites. During the first hour or so postinjection, these deficits often progressed to involve all contralateral target locations.

Data from individual experiments illustrate the retinotopic nature of the detection deficit. Fig. 2a shows an experiment in Bart in which the left caudal SC was inactivated. The deficit at 25 min postinjection was most severe at the peripheral right target locations (24 and 36 deg). By 50 min postinjection the deficit included all right target locations. In contrast, Fig. 2b shows data from an experiment in which Bart's left rostral SC was inactivated. The deficit was initially restricted to the most central target location (12 deg) on the right, and by 70 min postinjection, encompassed all right target locations. Figs. 2c and 2d show analogous results for right SC inactivations in Homer.

To assess the overall effect of the site of SC inactivation on the retinotopic location of the detection deficit, we pooled experiments carried out at each cannula location in the following manner. Only experiments with muscimol injections smaller than 0.5 μl were included since we were trying to assess the effects of *focal* SC inactivation. The average preinjection "score" (percent correct) for all experiments at a given cannula location was computed. For each of these experiments, the first postinjection block of trials in which a significant deficit was observed was used to compute the average postinjection score. The postinjection score was then subtracted from the preinjection score to determine the change in performance, or *deficit*, following SC inactivation.

Fig. 3 shows the *Average Performance* (preinjection and postinjection) and the *Average Deficit* (preinjection minus postinjection performance) for each cannula location in both cats. At all eight cannula locations, the average detection deficit is most severe at the target location that would be predicted based on the retinotopic organization of the SC. These pooled results also demonstrate the severity and reproducibility of the detection deficit even for small (0.1–0.5 μl) muscimol injections. Error bars reflecting the standard error of the mean are small relative to the deficit, especially at the most severely affected target locations. In addition to depicting the change in performance for targets in the *contralateral* visual hemifield, the pooled results also illustrate that performance for targets in the ipsilateral field and on blank trials is not significantly affected by unilateral SC inactivation.

Depth analysis

At six cannula locations, a series of injections were made at depths ranging from above the SC surface to below the deep layers of the SC in 0.5 mm increments and detection data were obtained. In a given series, the volume and concentration of the injections were kept the same for each experiment and each of these injections was made on a separate day. The estimated depth of the SC surface and of the injections was approximately determined based on two considerations. First, guide cannulae were stereotaxically positioned to be 2 mm above the SC surface. Second, the shortest injection needle that consistently produced a behavioral deficit in either detection or perimetry was thought to be just below the SC

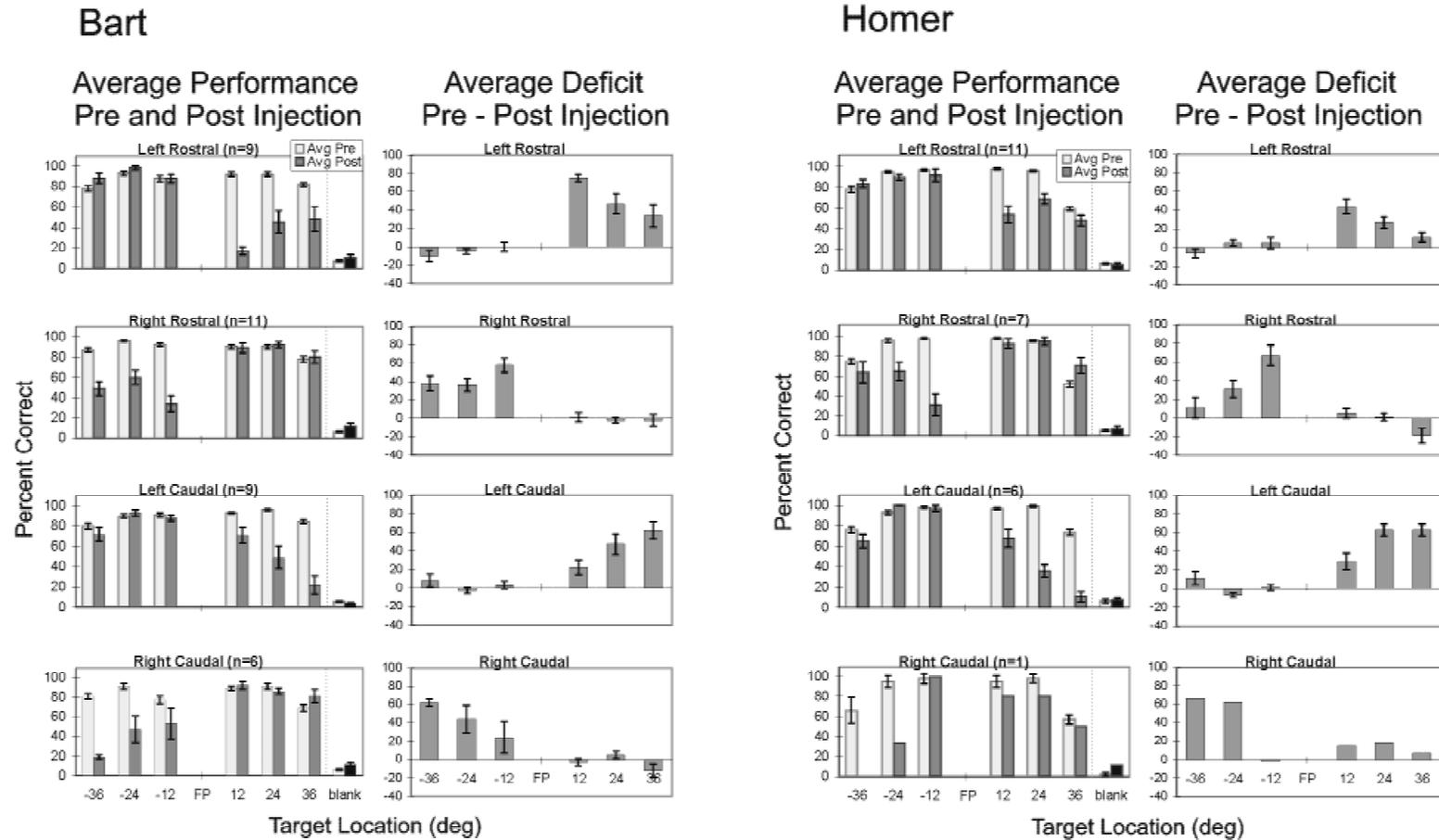


Fig. 3. Pooled retinotopy analysis. Graphs were generated by averaging preinjection and postinjection detection performance for experiments conducted at each cannula location. These graphs are shown in columns above (Bart: Average Performance; and Homer: Average Performance). The difference between the preinjection and postinjection scores was then calculated and plotted on a separate graph to the right of each of these graphs (Average Deficit). For these graphs, a taller bar indicates a more severe deficit at that target location. The average deficit graphs clearly demonstrate that at all cannula locations in both cats the detection deficit follows a pattern consistent with the retinotopic organization of the SC. Error bars depict the standard error of the mean in all graphs.

Bart Injection Series: Left Caudal SC Cannula

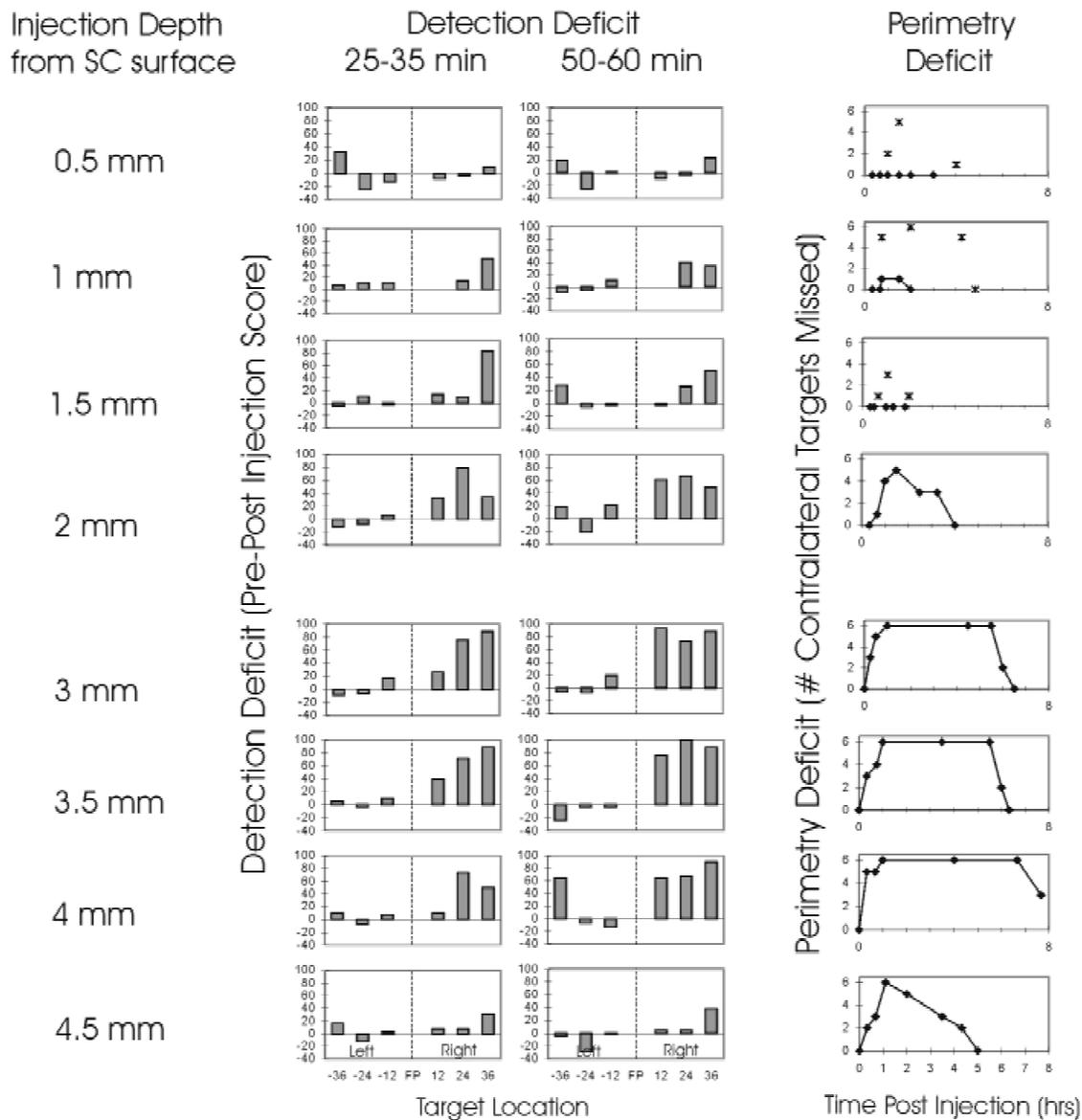


Fig. 4. Injection series for Bart's left caudal cannula. This figure shows the detection and perimetry data for the series of experiments conducted at Bart's left caudal cannula location. Injection depths ranged from the surface of the SC to 4.5 mm below the surface. All injections were 0.1 μ l of muscimol at a concentration of 4 mg/ml. The first column shows the estimated depth below the SC surface of the muscimol injection made in that experiment. Detection performance at 25–35 and 50–60 min postinjection is shown in the next two columns. In each detection graph, the detection deficit (or difference between preinjection and postinjection performance) is plotted for each target location. Performance in the perimetry task is shown in the fourth column. The perimetry-deficit graphs show the number of *contralateral* targets missed at various times postinjection. In this task, there are six targets in each hemifield, so six is the maximum number of targets that can be missed. The perimetry data is shown to indicate the severity of the deficit. It does not show the retinotopic pattern of those data. The three graphs in a given row are all from the same experiment. Because there was little to no perimetry deficit for the most superficial injections, data from experiments in which larger (0.3–0.5 μ l) injections were made are shown with asterisks.

surface. This injection was estimated to be 0.5 mm below the SC surface and other injection depths were determined in relation to this injection. In most cases, the shortest needles that produced detection deficits were those that protruded 1.5–2 mm from the guide cannulae, roughly consistent with our stereotaxic placement.

At all six cannula locations in both cats, detection deficits were most severe following injections centered in the intermediate and

deep layers of the SC. For some cannula locations there was a gradual increase in the severity of the detection deficit over the first 1–2 mm of penetration, with the most dramatic detection deficits occurring 2–4 mm below the SC surface. An example of this is shown in Fig. 4, an injection series from Bart's left caudal cannula. Detection data are presented as the "Detection Deficit," the difference between the preinjection and postinjection scores, as

defined earlier. In this series, there is a gradual increase in the severity of the detection deficit as injection depth increases for both postinjection time blocks. The most severe deficits were seen following injections centered approximately 3.0–3.5 mm below the SC surface.

At other cannula locations there was a more abrupt increase in the severity of the detection deficit at depths 1.5–2.0 mm below the SC surface. For example, in the injection series from Homer's left rostral cannula, no detection deficit was observed for the first three injections depths (estimated depths 0.5–1.5 mm below the SC surface) at either 30 or 60 min postinjection. At depths 2–3.5 mm below the SC surface, however, a detection deficit was observed. The rather abrupt transition from no deficit to deficit occurred at 2 mm below the SC surface.

As injection depth increased, both cats had increasing difficulty with fixation and in some cases were unable to perform the detection task to complete the depth series. In four of the six depth series, however, the deepest injections, which were estimated to be below the deep layers of the SC, produced no detection deficit or a much less severe deficit. The detection data from the deepest injections in Fig. 4 illustrate this result. Bart's deficit was less severe at the 25–35 min test following the injection made 4 mm below the SC surface, and at 4.5 mm the deficit was minimal for both postinjection time blocks. The considerable perimetry deficits observed after these deeper injections confirmed that these injections had indeed inactivated some SC tissue, so the lack of detection deficit cannot be attributed to an unsuccessful injection.

Response latency analysis

As another parameter of detection performance, response latency for target detection was assessed in a small number of experiments. Response latency was defined as the time between stimulus onset and depression of the response pedal. The preinjection and postinjection response latencies were calculated from two experiments at each cannula location for both cats. Experiments were chosen that had a large number of postinjection trials and in which a moderate to severe detection deficit was observed. The average preinjection response latency and standard deviation for all targets was 525 ± 70 ms and 535 ± 64 ms for Bart and Homer, respectively. Following SC inactivation, the response latencies increased slightly to 541 ± 78 and 567 ± 73 ms. Both cats had slightly but significantly ($P < 0.005$) longer response latencies and slightly increased variance in the response latency following SC inactivation.

Average response latencies were separately calculated for each cat for right and left SC inactivation and for ipsilateral and contralateral targets. A small but significant increase in response latency occurred for contralateral targets following inactivation at all locations. In addition, a significant increase in response latency occurred for ipsilateral targets following right SC inactivation in Homer. Overall the increases in latency were slight and resulted in responses that occurred well within the response time limit of 800 ms.

To ensure that any increase in response latency did not account for the deficit observed in postinjection detection scores, we analyzed missed target trials in these same experiments for pedal presses that occurred after the response time limit and within 4 s of stimulus presentation. Pedal presses during this block of time could represent delayed responses to the target presentation. We calculated the percentage of target presentations in which the cat pressed the pedal after the response time limit. Both cats showed an increase in late pedal presses on contralateral, but not ipsilat-

eral, target presentations following SC inactivation (Bart: 4% preinjection, 12% postinjection. Homer: 0% preinjection, 3% postinjection). However, as cats detected most targets preinjection and most ipsilateral targets postinjection, they had fewer opportunities for late pedal presses in these trials. When the percentage of late pedal presses was calculated as a function of missed trials rather than all trials, both cats had fewer late pedal presses following contralateral misses postinjection (Bart: 25% preinjection, 16% postinjection. Homer: 7% preinjection, 6% postinjection). Overall, late pedal presses were not observed in the majority of missed target trials following SC inactivation. It is therefore unlikely that the cats detected the target but had a very delayed response.

Perimetry task

Perimetry deficit

All three cats were tested in the perimetry task. Under normal conditions cats oriented briskly to targets presented throughout their visual field. It was extremely rare for cats to miss a target during preinjection testing. The most commonly missed targets under control conditions were those located 90 deg to the left or right of midline. These missed targets may have been presented just outside the cats' visual field if the animals' fixation was slightly off center.

During unilateral inactivation of the SC with microinjections of muscimol, animals failed to orient to some or all targets presented in the visual hemifield contralateral to the side of SC inactivation. Impaired animals would maintain central fixation while the peripheral target was displayed for approximately 2 s. When they were released by the investigator, they would continue to ignore the peripheral food target and would move forward to retrieve the central (fixation) food reward. This deficit was quite robust. Waving the peripheral target around for several seconds or bringing it closer to the cat in an effort to make it more salient did not improve performance. The cats rarely gave any indication of stimulus detection, such as a startle or hesitation to approach the fixation target. In contrast, ipsilateral targets prompted a brisk and accurate orienting response. Injections of muscimol ranging from 0.1 μ l to 1 μ l in volume and 1–4 mg/ml concentration could produce orienting deficits throughout the contralateral visual hemifield that began as early as 5–10 min after injection and lasted as long as 8 h postinjection. Cats always made a complete recovery of visual orienting within 24 h of the injection.

The first time point at which an orienting deficit was observed following SC inactivation ranged from 5 min to 90 min postinjection. At this time, the deficit often involved a restricted region of the contralateral visual hemifield so that the cat would orient to some contralateral targets but not others. Within the first 1–3 h the deficit would expand to its maximum extent. In many experiments, this would include all contralateral targets. In some experiments, particularly with superficial or relatively small injections, the cat never missed targets at more than one or two locations. Larger or more concentrated injections produced more severe deficits resulting in loss of a larger region of the contralateral visual hemifield at earlier postinjection time points. Several hours following the injection, the orienting deficit would eventually begin to decrease until the animal recovered the ability to orient to all contralateral visual targets.

Fig. 5 shows perimetry data from five experiments in the three cats. For each experiment, five postinjection testing sessions are shown. Fig. 5a shows the perimetry performance following a left

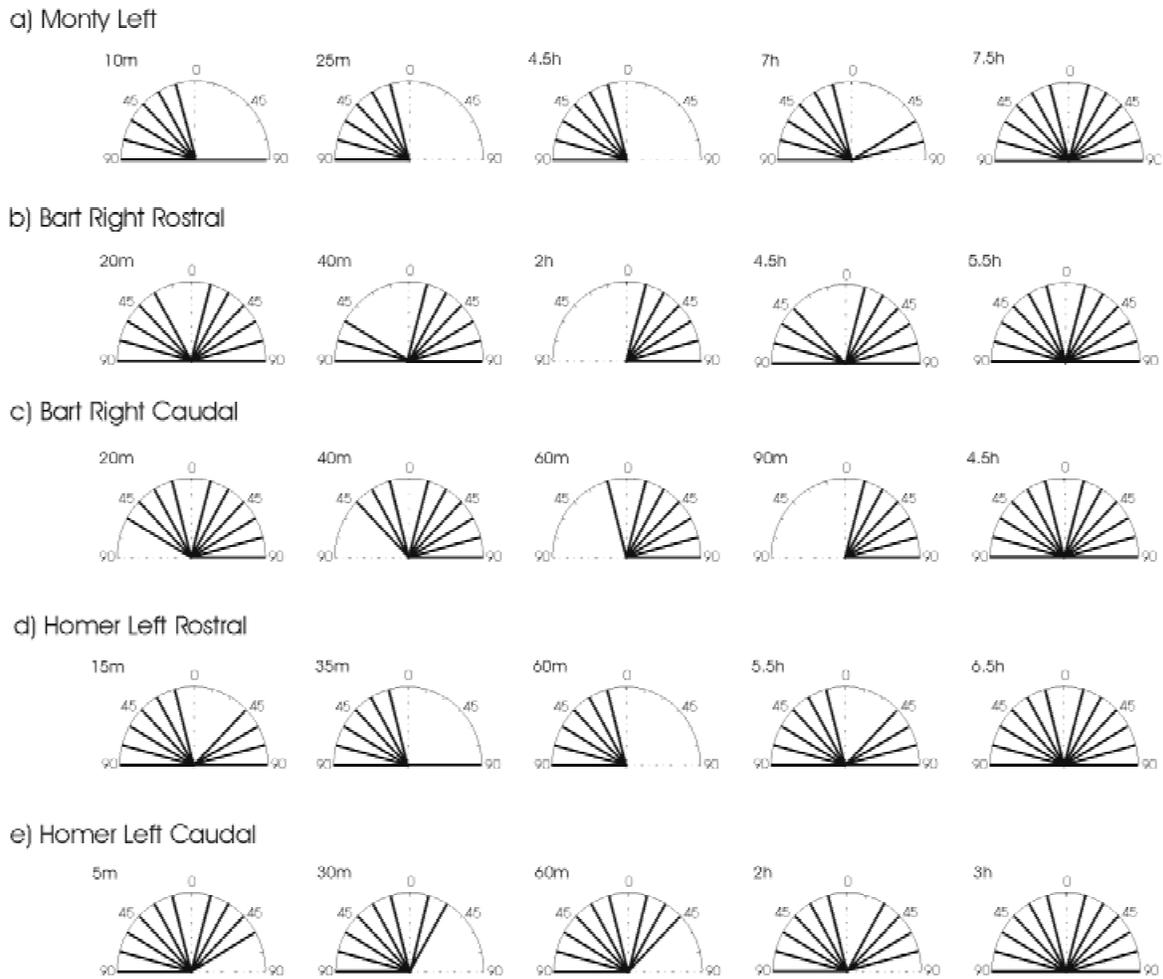


Fig. 5. Perimetry deficits following SC inactivation with muscimol. Each row shows data from one experiment. Five postinjection testing sessions are shown for each experiment. Each testing session is depicted by a schematic of the visual field. A radial line from the center of the semicircle to a given target location indicates intact orienting at that target location.

SC injection in Monty. Inactivation of the SC resulted in a failure to orient to almost all of the target locations in his right visual field within 10 min of the muscimol injection. An orienting deficit was observed for 7 h following the injection with a full recovery of visual orienting at 7.5 h.

Retinotopy

Two of the three cats in this study, Bart and Homer, had cannulae located over the rostral SC (see Fig. 1B). Even relatively large ($1.0 \mu\text{l}$) injections at these cannula locations produced orienting deficits that began at the central target locations, consistent with the retinotopic organization of the SC. The perimetry deficits resulting from rostral SC inactivation in Bart and Homer are shown in Figs. 5b and 5d. In both experiments, the initial deficit was restricted to the most central target locations and developed over the course of 1–2 h to involve the entire contralateral visual hemifield. The recovery of orienting in these experiments also followed this retinotopic pattern beginning with the peripheral target locations (see Fig. 5b: 4.5 h; and Fig. 5d: 5.5 h).

Bart and Homer also had cannulae located over the caudal SC. Larger injections at these locations often produced orienting deficits that involved most of the contralateral hemifield even at the

earliest postinjection time points. Deficits restricted to the peripheral visual field were observed only with smaller, more focal injections. This can be seen in Fig. 5c which shows the perimetry deficit in Bart after an $0.1\text{-}\mu\text{l}$ injection of muscimol in the right caudal SC. At 20 min postinjection, he missed only the targets at 75 and 90 deg to the left. Over the course of 90 min, the deficit increased to include the entire left hemifield. Fig. 5e shows a similar example from a left caudal SC injection in Homer.

Depth analysis

As for the detection performance, perimetry performance was tested following inactivation of the SC at systematically varying depths. In many cases, these data were obtained in conjunction with detection data for comparison. Perimetry data were obtained at eight cannula locations for a series of injections made at depths ranging from above the SC surface to below the SC in 0.5-mm increments. The fourth column of Fig. 4 shows the perimetry deficits for the depth series depicted in that figure. Each graph shows the number of contralateral targets missed as a function of time postinjection.

In all eight injection series, the perimetry deficit that followed superficial injections was much less severe in terms of duration

and number of targets missed than those resulting from deeper injections. This can be seen clearly in Figs. 4: little to no perimetry deficit occurred with injections centered 0.5–1.5 mm below the SC surface. Asterisks on these three graphs show the perimetry deficit resulting from larger injections, demonstrating that these injection sites were within the SC. An injection 2.0 mm below the SC surface produced a more substantial perimetry deficit that resolved at 4 h and at its maximum extent affected orienting at five of the six contralateral target locations. Injections centered from 3.0 mm to 4.0 mm below the surface produced the most dramatic perimetry deficits, lasting 6–7 h and affecting all contralateral target locations. At 4.5 mm, below the deepest layers, the perimetry deficit is less severe.

Other behavioral deficits

Other behavioral deficits were observed but not rigorously tested during the course of experiments in all three cats. These deficits included difficulty with fixation and failure to orient to auditory stimuli.

Inactivation of the SC produced an ipsilateral fixation bias in most experiments. Following rostral injections the bias was severe and was usually observed within the first half-hour of injection. Following caudal injections, the fixation bias was less severe and was usually not observed until later time points after the orienting deficit had encompassed the central target locations, that is, after the muscimol has inactivated the rostral SC. This finding is consistent with other studies implicating the rostral SC in fixation of visual targets (Peck, 1989; Munoz & Guitton, 1991b; Werner, 1993). In some cases, when large or concentrated injections were made in the deep SC, fixation biases progressed to ipsilateral circling behavior that precluded testing.

The ability to orient to auditory stimuli was tested in some experiments by scratching under the table at a central (30 deg) and peripheral (75 deg) target location. Deficits in orienting to auditory stimuli were often observed following deeper injections but not after superficial injections. The depth at which auditory deficits began to occur ranged from 1.5 mm to 3.0 mm below the SC surface, varying for different cannulae. The location of the auditory orienting deficit (i.e. central or peripheral) usually corresponded with the location of the visual orienting deficit. These findings are consistent with the observed correspondence of visual and auditory receptive fields in multimodal neurons in the deep layers of the cat SC (Stein & Meredith, 1993).

Discussion

The detection deficit

General

The experiments described in this paper reveal that a dramatic deficit in visual detection occurs in the cat following inactivation of the superior colliculus. In these experiments, cats that were trained and highly proficient at performing a pedal press in response to the presentation of peripheral visual targets were clearly impaired in performing the same task following unilateral inactivation of the SC. This deficit was specific for visual stimuli contralateral to the side of SC inactivation, with no consistent impairment observed for ipsilateral targets. Thus, a generalized motivational or attentional impairment due to the muscimol injection cannot account for the deficit. Because the detection response (a right paw pedal press) was identical for all targets, and because

inactivation of both right and left sides of the SC produced equally severe deficits, this failure to respond to contralateral targets cannot be interpreted as a specific motor deficit related to the pedal press response. The most reasonable explanation for the deficit observed in these experiments is that the SC plays a critical role in (1) processing the relevant information regarding the occurrence of a visual event, and/or (2) relaying that information to the region or regions of the brain that generate the appropriate motor command, that is, a pedal press. The SC could easily play a role in one or both of these processes since it receives visual input from retina, visual cortex and other visual nuclei and projects to several brain regions that could be involved in representing the visual target or generating the motor response, including the lateral geniculate nucleus, LP-pulvinar, basal ganglia, and cerebellum (Altman & Carpenter, 1961; Graham, 1977; Berson & Graybiel, 1978; Mower et al., 1980; Torrealba et al., 1981; Harting et al., 1991, 2001).

Retinotopy

The pooled retinotopy data as well as data from many individual experiments demonstrate that the region of visual space most affected by SC inactivation roughly corresponds to the region of visual space represented at the site of SC inactivation. The retinotopic organization of the SC has been demonstrated in a number of experiments (Feldon et al., 1970; Berman & Cynader, 1972; Gordon, 1973; Peck et al., 1980). Neurons in both the superficial and deep layers of the SC are organized such that the contralateral central visual field is represented in the rostral SC and the contralateral peripheral visual field is represented in the caudal SC (see Fig. 1B). In our experiments, injections centered at more rostral locations in the SC produced the most severe deficits at the central target locations while injections centered in the caudal SC produced more severe deficits at peripheral targets. No other nuclei in the vicinity of the SC are organized in a manner that would produce the retinotopic pattern of the deficit revealed by the pooled retinotopy data. This argues strongly against the possibility that the deficit occurs due to spread to other brain nuclei. These data also point to the visual nature of the detection deficit. A deficit in the ability of the cat to perform the motor response, a pedal press, should not produce a retinotopically patterned deficit.

Response latency

In both cats in the detection study, small but significant increases in response latency occur following inactivation of the SC. Significant increases in response latency were observed consistently for targets presented in the contralateral (impaired) visual hemifield in both cats. This increase may reflect the decreased salience of these targets since response latency can covary with stimulus intensity (for review, see Moody, 1970). However, since these cats were not rigorously trained to respond as quickly as possible, we cannot interpret the data in the context of a reaction time task.

Overall, the increases in response latency are small relative to the normal latencies (3–6% increase) and fall well within the response time limit. This argues against a motor explanation for the deficit. If cats were impaired in generating the pedal press response, one might expect to see a large increase in response latency or even responses beyond the response time limit. However, an analysis of the occurrence of late pedal presses in the intertrial interval following missed trials reveals no increase in late pedal presses.

In addition, no specific trends were observed to support a theory that SC inactivation interfered specifically with the required motor response. This is important since the SC has been implicated

in forelimb reaching behavior in the cat and monkey. Lesion of the SC in the cat produces a deficit in cats hitting a moving lever with their paw (Vievard et al., 1986), and activity in the SC of monkeys has been shown to correlate with visually guided reaching behavior (Werner, 1993; Werner et al., 1997; Stuphorn et al., 1999). If SC inactivation produced a motor deficit in the cats that made the pedal press response difficult, one might expect to see a different pattern in the response-latency data such as an equal increase in both contralateral and ipsilateral target latencies after SC inactivation, or an increase only after inactivation of the left SC since the required response is a right-sided pedal press. No such patterns were observed. The only pattern seen in both cats was an increase in response latency for contralateral targets. This trend is based on the location of the target in the visual field, a sensory parameter.

The visual orienting deficit

The perimetry data confirm and extend previous findings that unilateral inactivation of the SC in the cat results in a striking deficit in visual orienting to targets in the contralateral visual hemifield. This effect was observed with relatively small injections of muscimol spanning a range of locations and depths throughout the SC.

The dramatic nature of the behavioral effect observed in the perimetry task suggests that the deficit is not restricted to visual orienting, as the cats do not give any indication that they are aware of the target's presence. One might expect that if the cats were aware of the peripheral visual target, they would hesitate to approach the fixation target or act confused when released. However, cats never hesitated to approach the fixation target when the peripheral target was in the affected region of the hemifield. These observations from the perimetry testing combined with those from the Detection Task suggest that the deficit observed during SC inactivation is more than just a motor or orienting deficit. It may be a failure to register the occurrence of a visual stimulus for a number of possible behavioral responses.

Effect of injection depth on detection and perimetry performance

The deficits observed in the detection and perimetry tasks following SC inactivation were compared within each experiment. A general correlation in the severity and time course of the perimetry and detection deficits was observed for a given injection location. For example, a large or concentrated injection that produced a relatively severe detection deficit would also produce a severe perimetry deficit. In addition, both deficits followed a retinotopic pattern consistent with the known retinotopic organization of the SC. Finally, a comparison of the detection and perimetry performance as a function of injection depth revealed striking similarities between the two behavioral deficits.

At all cannula locations tested with injections at systematically varying depths, both perimetry and detection deficits were most dramatic following injections centered in the intermediate and deep layers of the SC. As injection depths continued to increase, both perimetry and detection deficits began to decrease or even resolve at injection depths estimated to be below the deep layers of the SC (see Fig. 4). These results suggest that the neurons mediating the detection and perimetry deficits are located within the SC and appear to be located at the same depth within the SC, most likely in the intermediate and/or deep layers. This finding is no surprise with respect to the perimetry deficit, since the intermedi-

ate and deep layers are well known to play a critical role in visual orienting behavior. However, this is the first experimental evidence that inactivation of these layers contributes to a visual detection deficit in a nonorienting behavioral task.

Two findings in the perimetry data provide compelling evidence that the injections targeting the superficial and deep SC were indeed inactivating those layers. First, in this study, dramatic ipsiversive motor biases were often observed following *deep* SC inactivation but not after superficial SC inactivation. Payne et al. (1996) observed a contralateral visual orienting deficit but no dramatic motor biases when they used cooling probes to selectively inactivate the superficial layers of the SC. Since our superficial injections produced a visual orienting deficit without motor biases, similar to the effect documented by Lomber and Payne after superficial inactivation of the SC, it is likely that these injections were largely restricted to the superficial layers of the SC, while our deeper injections were clearly inactivating additional neuronal populations, producing the observed motor biases. These motor biases were similar to those that occur following SC lesions that damage the deep as well as the superficial layers of the SC (Sprague & Meikle, 1965), suggesting that the deep layers are responsible for these motor deficits. Second, in those experiments where auditory orienting was tested, only deep injections resulted in auditory orienting deficits. The deep layers of the SC contain neurons that are responsive to both visual and auditory stimuli while the superficial layers are exclusively visual (Sparks & Nelson, 1987; Stein & Meredith, 1991, 1993; Peck & Baro, 1997). SC lesions that extend into the deep layers produce deficits in auditory as well as visual orienting (Sprague & Meikle, 1965). Thus, our finding that only deep injections produce auditory deficits is consistent with the electrophysiological and behavioral data from those layers, and suggests that our deep injections were indeed inactivating the deep layers of the SC, while our superficial injections were not.

It is also possible that our depth results are simply an artifact of the method of inactivation used in these experiments. When the injection needles are inserted through the guide cannula, they first push down the surface of the SC to some extent before penetrating. A brief amount of time was given to allow the SC tissue to return to its normal shape. However, we cannot be sure that the tissue compression had completely resolved. Shorter needles designed to inject just below the SC surface are less likely to penetrate the surface and may just indent it so that injections would not be as effectively delivered to the superficial layers. In addition, when the injection is actually made, the fluid does not diffuse from the injection site in the shape of a sphere centered at the tip of the needle, but rather some of the fluid leaks back up the shaft of the needle to be absorbed by overlying tissue (see Mize & White, 1989). With deep injections, the fluid that leaks up the shaft is more likely to get absorbed by the overlying SC tissue resulting in a greater amount of tissue inactivation and perhaps a more dramatic behavioral effect. With superficial injections, some of that fluid may leak out of the SC entirely.

Because the injected muscimol solution undoubtedly leaked back up the shaft of the needle to some extent, it is impossible to state with certainty whether inactivation of the superficial or deep layers (or both) is responsible for the detection deficit observed in these experiments. Our results do not exclude the possibility that inactivation of the superficial layers contributes to the detection deficit. However, the trends observed in the depth series data suggest that the intermediate and/or deep layers play a significant if not predominant role in the observed visual detection deficit.

Anatomic substrates

The idea that the intermediate or deep layers play an important role in visual detection is intriguing and unexpected. One might expect the superficial layers would be more likely to be involved in visual detection. The superficial SC layers receive extensive visual input from retina and visual cortex, and make numerous ascending projections to the pretectum, pulvinar and lateral geniculate nucleus (LGN), that project in turn to many visual cortical areas (Huerta & Harting, 1984). In addition, the superficial layers have been shown to have increased activity during a visual detection task in the cat (Vanduffel et al., 1997). To date, no clear function has been attributed to the superficial layers of the SC, and so it would be interesting to identify what role they play in visually guided behavior. Our results, however, suggest that inactivation of the intermediate or deep layers are at least partially if not largely responsible for the visual detection deficit observed in these experiments.

The intermediate and deep layers of the SC are well known to be involved in visual orienting and saccadic eye movements in a number of animals including cats and monkeys (review, see Wurtz & Albano, 1980; Sparks & Hartwich-Young, 1989; Stein & Meredith, 1991). Recent studies suggest that these layers of the SC also play a role in visually guided reaching (Werner, 1993; Werner et al., 1997; Stuphorn et al., 1999). However, a sensory or detection function has never been ascribed to these layers. Deficits in orienting or eye movements following deep SC inactivation have been primarily interpreted in a motor context (for example, see Hikosaka & Wurtz, 1985*b*; Lee et al., 1988).

The intermediate and deep layers of the SC have connections that could conceivably allow them to mediate the detection task. First, these layers receive substantial visual input from extrastriate visual cortical areas and sparser input from the ventral lateral geniculate nucleus (Huerta & Harting, 1984; Sparks & Hartwich-Young, 1989), retina (Berson & McIlwain, 1982; Beckstead & Frankfurter, 1983), and possibly the overlying superficial layers of the SC (Behan & Appell, 1992). Thus, many of the neurons in the intermediate and deep layers of the SC are visually responsive (Sparks & Hartwich-Young, 1989; Stein & Meredith, 1991). Second, the deep layers project to brain regions that could contribute to the generation of the required pedal press response, including the basal ganglia *via* the pulvinar/supragenulate complex (Harting et al., 2001) and the cerebellum *via* the dorsolateral pontine nucleus (Mower et al., 1980).

Both the basal ganglia and cerebellum are involved in learning (for review, see Doya, 2000) and could therefore be involved in a task such as our detection task which is not an innate behavior. The basal ganglia are reciprocally connected to the SC and play an important role in visual target selection for saccadic eye movements *via* connections with neurons in the deep layers (Hikosaka et al., 2000). Activity in the basal ganglia is modulated by reward expectation, supporting the hypothesis that the basal ganglia play an important role in sensorimotor learning (Graybiel et al., 1994; Schultz et al., 1998). In addition to projecting to the SC, the basal ganglia can modulate motor activity in the red nucleus and cortical motor pathways, and could therefore effect the required pedal press response *via* several efferent pathways (Stein & Glickstein, 1992).

In a different learning context, the cerebellum plays a critical role in calibrating and automatizing movements and is involved in the visual guidance of a number of behaviors including saccadic and smooth pursuit eye movements, reaching, reaction time tasks, and eye-blink conditioning (Stein & Glickstein, 1992). In addition to receiving visual information from the SC (as well as from visual cortex and other visual nuclei), the cerebellum projects to the red

nucleus in the brainstem and to cortical motor areas *via* the ventrolateral thalamic nucleus and could also initiate the pedal press response *via* one of these efferent pathways (Stein & Glickstein, 1992). The detection task requires the animals to make an association between a visual stimulus and an arbitrary motor response, a pedal press, using food as a reward. The pathway by which this behavior is carried out could even involve both the basal ganglia (on the reward association side) and the cerebellum (on the motor response side).

The deep layers of the SC contain a diverse population of neurons that demonstrate a variety of sensory and motor-related activities (Wurtz & Albano, 1980; Sparks & Hartwich-Young, 1989; Werner, 1993). Unfortunately, the current study does not provide evidence to speculate on which neuron populations may play a role in the detection of peripheral visual targets.

Conclusion

The experiments described in this paper demonstrate that a dramatic visual detection deficit occurs following inactivation of the SC in the cat. This deficit occurred in animals with intact geniculocortical visual pathways. We conclude that the SC plays a critical role in detecting the visual stimuli used in this detection task, either by providing the visual input directly to the appropriate motor channels or by modulating visual activity in the geniculocortical pathway. This finding establishes a new function for the SC in the sensory processing of visual targets. The mechanism by which the SC mediates the detection response remains to be elucidated but may involve the cerebellum, basal ganglia, or thalamo-cortical pathways.

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