Behavioral Thermosensitivity After Lesions of Thalamic Target Areas of a Thermosensory Spinothalamic Pathway in the Cat

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Norrsell, U. and A. D. Craig. Behavioral thermosensitivity after lesions of thalamic target areas of a thermosensory spinothalamic pathway in the cat. J. Neurophysiol. 82: 611–625, 1999. The ability of 17 cats to discriminate floor temperatures 2–4°C below the ambient temperature was tested before and after unilateral electrolytic thalamic lesions. The lesions were made contralateral to the paws showing better performance in the temperature discrimination task. They were aimed at one or more of the three main target areas of thermoreceptive-specific lamina I spinothalamic neurons [i.e., the nucleus submedius, the dorsomedial aspect of the ventral posterior medial nucleus, and the ventral aspect of the basal ventral medial nucleus (vVMb)], following microelectrode mapping of somatosensory thalamus. The thermosensory consequences of each lesion were measured in postoperative testing, beginning 6–8 days after the final preoperative test session. A mild but definite thermosensory deficiency was found in five cats, in which the response behavior on the contralateral side was reduced below the 69% criterion level for several sessions. Histological analysis indicated that these cats differed only by the inclusion in the lesion of all or part of vVMb. Consequently this area appears to be important for cats’ thermosensory behavior. Nevertheless even large lesions of virtually all of the thermoreceptive lamina I spinothalamic projection areas produced only this mild thermosensory deficit in stark contrast with the massive defect observed previously after spinal lesions of the middle of the lateral funiculus, where lamina I axons ascend. Accordingly such spinal lesions were added at the C4 level, on the same side as the thalamic lesions, in six cats 3 mo after the thalamic surgery. These lesions caused severe contralateral defects (i.e., chance level performance). Thus the present findings are taken to indicate that contralateral ascending projections to vVMb in the thalamus participate in cats’ thermosensory discrimination but that ascending projections to the brain stem must play an important role in their behavioral thermosensitivity.

INTRODUCTION

It has been known since the beginning of the 20th century that a restricted unilateral lesion of the spinal cord in man may cause an overt contralateral thermosensory deficiency. From the beginning, this was attributed to interruption of a crossed, ascending spinothalamic pathway. Historically there was some uncertainty regarding the location of the pathway (Foerster and Gagel 1932; Stookey 1929), but in recent decades several reports have confirmed a location in the middle part of the lateral funiculus (Gildenberg 1972; Moffie 1975; Nathan 1990; Nathan and Smith 1979; Nathan et al. 1986; Norrsell 1979, 1989a).

Crossed spinothalamic fibers that ascend in this location in cat and monkey originate mainly in lamina I of the spinal dorsal horn (Craig 1991b; Ralston and Ralston 1992). The physiological properties of these neurons are consistent with the effects of cordotomy. There are three types of lamina I spinothalamic neurons: thermoreceptive-(cold)-specific, nociceptive specific, and polymodal nociceptive (Craig and Kniffki 1985; Dostrovsky and Craig 1996a; Han et al. 1998). Thermoreceptive-specific lamina I neurons are the only identified spinal projection neurons that respond linearly to innocuous temperatures, and their activity can be related directly to human cold perception (Craig and Bushnell 1994; Davies et al. 1983). In primates, these neurons project to the posterior ventral medial nucleus (VMpo) (Craig et al. 1994), where thermoreceptive-specific neurons are found in monkeys and humans and where cold sensation can be evoked by microstimulation in humans (Davis et al. 1999; Dostrovsky et al. 1992; Lenz et al. 1993a,b). VMpo neurons terminate in the insular cortex, where clinical lesions can cause thermoanesthesia (Bassetti et al. 1993; Biemond 1956; Horiuchi et al. 1996; Schmahmann and Leifer 1992). Recent positron emission tomographic (PET) functional imaging data confirm that innocuous cool stimuli activate the insula but not primary somatosensory cortex in humans (Craig et al. 1996). In cats, antergrade Phaseolus vulgaris leucoagglutinin (PHA-L) tracing studies (Craig 1987, 1991a) and antidromic mapping studies of the projections of single, identified lamina I neurons (Craig and Dostrovsky 1991; Dostrovsky and Craig 1993) indicate that thermoreceptive-specific lamina I spinothalamic fibers terminate mainly in three parts of the contralateral thalamus, the nucleus submedius (Sm), the dorsomedial aspect of the ventral posterior medial nucleus (dmVPM), and the ventral aspect of the basal ventral medial nucleus (vVMb). The functional significance of this tripartite termination is unknown.

Prior experimental studies in cats showed that spinal transections cause severe, permanent disturbances of contralateral thermosensitivity only if the lesions incorporated the middle of the lateral funiculus (Norrsell 1979, 1983, 1989a) where lamina I thermoreceptive-specific spinothalamic fibers ascend (Craig 1991b). Lesions located more ventrally, where other spinothalamic fibers ascend (Jones et al. 1987; Stevens et al. 1991), did not produce a comparable deficiency nor did lesions of more dorsal parts of the spinal cord. We now have studied the consequences for the cat’s behavioral thermosensitivity of lesions of the thermosensory lamina I pathway’s three main thalamic termination sites. It will be shown that only lesions involving vVMb, a region not traditionally regarded as somatosensory, cause significant thermosensory disturbances. It will also be shown that large lesions including all three thalamic regions do not produce the massive thermosensory behavioral consequences of spinal lesions, which suggests that sites in the brainstem may be of major importance for cats’ thermosensory
behavior. A preliminary report was published (Norrsell and Craig 1993).

METHODS

Seventeen adult cats of both sexes were trained for an appetitive, operant, thermal discriminatory, two-choice task before electrolytic lesions were made unilaterally in one or more thalamic nuclei. The body halves were tested in alternate sessions before and after the thalamic surgery, and six of the cats, in addition, had a surgical lesion made in the cervical spinal cord on the same side 3 mo after the thalamic operation. The testing lasted 1–1.5 yr for the different cats with testing sessions on average every second day but never >5 days in a row. Regulated amounts of extra food were portioned out immediately after sessions and on weekends to prevent underfeeding. The experiment was sanctioned by an ethical jury in accordance with Swedish law.

Training and testing procedures

The cats were kept without food for 24 h before each testing session, which consisted of 32 trials. The testing was made with a computer-controlled, modified T maze, shown in Fig. 1. The cat waited in the starting chamber between trials. A trial started when the sliding door (Fig. 1B, top center) lifted, giving access to two narrow testing alleys (Fig. 1B, top, left and right of center) with thermode floors. In each alley, a barrier protruded 7 cm upward along the middle, between the two parallel thermodes, that kept the cats’ noses away and restricted the paws of each body half to one thermode only. The cat was free to enter either alley repeatedly. The cat made its decision and finished the trial by moving through one of the two testing alleys completely and nudging the hanging door at the end (Fig. 1C). A push on one of the hanging doors caused the sliding door behind the cat to close immediately. The starting chamber’s food-tray advanced one step and presented a piece of food if the decision had

FIG. 1.  A: oblique view of the right testing alley of the T maze. Arrows show airflow between holes in the roof and slots in the thermode. Barrier running along the alley center, which prevents contact between nose and thermode, is not shown. B: sketch of the T maze seen from above. C: 6 sequential photographs of cat 392 from a single trial. Sequence should be read from left to right, top to bottom: 1) trial begins with the opening of the sliding door, 2) cat enters the left (“correct”) alley, 3) cat switches to the right (“wrong”) alley, 4) cat re-enters the correct alley, 5) cat makes a decision by pushing open the hanging door at the end of the alley, 6) cat collects a reward. Durations of sequences involving this number of changes for this cat varied between 10 and 12 s.
been effected in the alley carrying the positive cue. A push on the hanging door of the alley with the negative cue caused the sliding door to close, but no food was served, and the cat had to wait for a new opportunity in the following trial. The countdown for the next trial (60 s) started when the cat had returned to the starting chamber, whether food had been presented or not. Cues were switched between the two alleys according to a pseudorandom series. The thermodes were polished to minimize cues from thermal radiation, and the air-flow inside the testing alleys was kept moving downward through slots in the thermodes (Fig. 1A) to prevent cues based on thermal convection. Adjustable surface covers were used to restrict the access to only one of the two parallel thermodes during a session. The testing technique has been used and described in previous publications (e.g., Norrsell 1974, 1983).

In a typical trial, a cat might decide straight away what to do on the basis of experience or it first might compare the floors of the two alleys, as in the single testing trial shown in the sequence of six photographs in Fig. 1C. Contact between paws and the thermodes were recorded electromagnetically, and the cat’s presence in an alley was recorded photo-electrically. These records permitted the calculation of each cat’s correct performance (percent correct responses per session); effort (mean number of entries into the alleys per trial); positive decision quotient (PDQ) = number of contacts with positive cue + number of correct responses - number of trials)/number of contacts with negative cue; negative decision quotient (NDQ) = number of contacts with positive cue - number of correct responses)/number of contacts with positive cue; efficiency = PDQ - NDQ; strategy (percent initial entries in left or right alley per session); and paw preferences (mean number of times each forepaw was put down first when the right and left alleys were entered). In addition, the cats’ behaviors were recorded with a video camera for all trials of all sessions. These records were used to spot behavioral aberrations and equipment errors indicated by the computer data. Most of the video records were discarded after a short time except for those from the immediate pre- and postlesion periods. The criterion for discriminatory competence for a given set of cues was 69% correct trials (P < 0.05 by chance) for at least three consecutive sessions (Finger and Norrsell 1974).

Transfer effects (Eninger 1952; Sutherland and Holgate 1966; cf. also Mackintosh 1974) from an additional acoustic cue were used to supplement the thermal discriminatory performance under certain conditions. A white noise [89 dB(A)] was produced continuously inside the testing alleys in all sessions, and this was used for secondary reinforcement; i.e. a correct decision immediately caused a 10 dB attenuation of the noise that lasted while the food tray was being moved forward. In addition, mechanical contact between a cat’s paws and the thermode with the positive cue also could generate a 10 dB attenuation of the background white noise, so that a cat received an additional cue whenever touching the thermode with the ‘correct’ temperature. This auxiliary acoustic cue was used together with the thermal cue during the initial training. The cues were altered successively after the cats had satisfied the above-described criterion. First, the auxiliary acoustic cue was diminished stepwise. It was discontinued after a cat had produced a satisfactory criterion response (≥69% correct finish) for thermal cues alone in sample sessions. This occurred on average when the acoustic cue had been diminished to attenuation levels ≥3 dB. If the auxiliary acoustic cue had to be added again at a later stage to assist an unsustainable thermal discriminatory performance, it was reintroduced at the attenuation level at which it had been discontinued.

The testing was performed at a controlled ambient temperature of 25°C. The cats first were trained to use the T maze without hesitation in the absence of differential cues before the introduction of the thermal and acoustic stimuli. Training with the acoustic cue followed, and the temperatures of the floors of the two testing alleys were set at a difference of 20°C, straddling the ambient temperature equally on either side, when the auxiliary acoustic cue was discontinued. The higher of these temperatures (“warm”) was used as a positive cue. Access to the thermodes was restricted to one body half for each session. Afterward, if a cat had produced ≥69% correct responses for one body half at one session, then it was allowed to use the other side at the next session. After six consecutive successful sessions, i.e., three for each side, a control session was obtained in which the cat was tested with the thermodes completely covered, to guard against inadvertent accessory cues. The cat then was advanced to the next more difficult thermal discriminatory level. At the initial 20°C difference, the positive and negative cues each deviated 10°C from the ambient temperature. In the subsequent levels, first the temperatures constituting negative cues and afterward those constituting positive cues were moved toward the ambient temperature in fixed steps. The successive steps were (in °C): +10 (pos.)/−10 (neg.), +10/−7, +10/−4, +10/−2, 0/−2 (or 0/−4). Thus the cats learned that the way to obtain food was through the alley in which the metal floor did not deviate from the ambient temperature, whereas the alternative route through the other alley, which had a floor temperature below the ambient temperature, was inappropriate.

Durup’s (1967) pseudorandom series has to be used in multiples of 16 trials. When a cat failed to produce ≥69% correct responses for a certain session (i.e., <22 correct in 32 trials), it was allowed to use the same body half again during the following session(s) with the same temperature stimuli if the performance had been ≥75% for either one of the two subsets of 16 (i.e., ≥12 correct of 16). If lower values had been obtained, then the auxiliary acoustic cue was added to the temperature stimuli in the following session(s), and it was removed again as soon as the cat had produced ≥69% correct responses for 32 trials in its presence. The final preoperative testing consisted of at least three groups of sessions consisting of one session for each body half and one control with completely covered thermodes e.g., left, right, control, right, left, control, left, right, control. The test sessions with access to the thermodes were required to produce satisfactory performance (≥69% correct responses) without the aid of the auxiliary cue. The negative thermal cue was augmented for the cats who were unable to discriminate consistently at the most demanding level. Their final preoperative groups of sessions were run instead at 0/−4°C.

The cats were tested as soon as possible postoperatively (average 8 days), beginning at the final preoperative discrimination level, and the sessions were run according to the same pattern as if a cat immediately produced satisfactory performance (≥69% correct responses) for the sessions with thermal cues. The control sessions with covered thermodes were omitted for at least six sessions, however, if the thermosensory performance was below the criterion level. Training with the auxiliary cue was reintroduced whenever necessary, after the first six postoperative sessions had been completed.

**Surgery**

The surgery was performed aseptically under pentobarbital sodium (Nembutal, Abbott, 20 mg/kg) anesthesia after atropine sulfate (Atropin, ACO, 0.5 mg) premedication. Equal parts oxygen and nitrous oxide were used for inhalation during all surgical procedures, and in the case of spinal lesions, the cats were paralyzed with pancuronium bromide (Pavulon, Organon Teknika, q.s.) and respirated artificially. The thalamic lesions were made after electrophysiological recordings of the somatosensory thalamus with a tungsten microelectrode. The small region in which neurons respond to thermal stimulation of the ipsilateral tongue, which lies along the dorsomedial aspect of the ventroposterior medial nucleus (Auen et al. 1980; Landgren 1960), the ipsilateral tongue, which lies along the dorsomedial aspect of the ventroposterior medial nucleus (Auen et al. 1980; Landgren 1960), was located and used as a reference for positioning the lesions. The thalamic lesions were made after electrophysiological recordings of the somatosensory thalamus with a tungsten microelectrode. The small region in which neurons respond to thermal stimulation of the ipsilateral tongue, which lies along the dorsomedial aspect of the ventroposterior medial nucleus (Auen et al. 1980; Landgren 1960), was located and used as a reference for positioning the lesions. The thalamic lesions were made after passing 500 μA cathodal DC current through the electrode for 10–20 s at 1–96 sites (median 8, 3rd quartile 32). For each cat, the lesions were placed in the thalamus contralateral to the paws with the better thermosensory behavioral results; there were nine operations on the right side and eight operations on the left.

For spinal surgery, the spinal cord was exposed through removal of the dorsal arch of the 4th cervical vertebra, followed by transverse and longitudinal incisions of the dura mater. The spinal cord lesions were made with minute hooks, inserted perpendicularly into the lateral
surface, under visual guidance with the aid of a high-power binocular dissection microscope.

The wounds were closed with separate muscle and skin sutures, and the cats were given procaine penicillin (Penicillinprokain Vettrenium, Novo, 2 ml im) for 3 days postoperatively, and in the case of thalamic lesions hydrocortisone (Solu-Cortef, Upjohn, 33 mg im) as well. Fluid and electrolyte therapy (Ringer-glukos, ACO, 100 ml/12 h) was given by subcutaneous injections until the cats began to drink spontaneously. The cats were returned to their home cages as soon as possible after postoperative recovery, usually after <3 days.

**Histology**

Approximately 3 mo after the thalamic surgery, the cats were anesthetized with pentobarbital sodium (75 mg/kg) and then infused intra-arterially with 1 l warm (37°C) physiological saline followed by 3 l 10% (37°C) buffered formalin solution. The brains were removed in one piece, placed in fresh 10% buffered formalin solution, and shipped immediately from Göteborg to Phoenix for evaluation. Information regarding the behavioral outcome was not shared until after the lesions had been evaluated and documented. In cats with spinal lesions, the cervical segments were removed, placed in 10% buffered formalin solution, and shipped to Phoenix after the appraisals of the thalamic lesions had been made. Before cutting, the tissue blocks were placed in 30% sucrose with 10% formalin for ≥1 wk. Serial 50 μm frozen sections were cut from the thalamus in the coronal plane or from the spinal cord in the transverse plane and then mounted, stained with thionin, and coverslipped. The thalamic lesions were identified by well-defined holes in the tissue surrounded by dense gliosis and neuronal loss, and spinal lesions were similarly outlined. Thalamic nuclei were identified according to Berman and Jones (1982) and Craig and Burton (1985), using the contralateral side as an added guide where lesions were large. Digital images of appropriate sections were made with a Leaf Microlumina (3380 × 2253 pixels) mounted on a Nikon photomicroscope through a ×1 plan objective and then sharpened with Adobe Photoshop. The locations of the lesions were plotted on a standardized coronal series of six sections (taken from 1 of the cats) spaced at 0.5 mm intervals.

**RESULTS**

**Behavioral observations before thalamic surgery**

The cats had been selected from a larger group on the basis of inclination and ability to participate in the behavioral task. The strategies they used when solving the behavioral problem varied between cats as well as between stages of the experiment. Some cats showed a side preference when allowed to enter the testing alleys, others varied their side preference according to undecipherable patterns. Their temperaments were also different. Some cats made their final choice after a minimal examination of the testing alleys, whereas others exhibited hyperactivity, i.e., they made multiple partial or complete entries into each alley in most of the trials. These behavioral variations were recorded faithfully (see METHODS), but they did not appear to complicate the interpretation of the results. There were also no apparent effects of the number of preoperative sessions. The four cats, whose behavior is illustrated in Figs. 2–4, all had ~1 yr of training and testing before the first operation. The criterion for making a lesion was based on the behavioral performance (per cent correct responses) alone.

**Behavioral observations after thalamic surgery**

After surgery, testing was resumed at the final preoperative conditions, with a median interval between the last preoperative session and the first postoperative session of 7 days (range 6–8). The cats’ general behavior even after the largest thalamic lesions remarkably was unaltered. The thermosensory behavioral consequences of the thalamic lesions could be divided into three categories. Eight cats who did not display any postoperative reduction of thermosensory performance were allocated to category 1. Four cats who showed an unspecified postoperative behavioral disruption were allocated to category 2. Finally, five cats who showed a mild, albeit definite postoperative thermosensory disturbance were assigned to category 3. Table 1 summarizes the data for the different cats according to these classifications, including their preoperative discrimination levels and the thalamic nuclei damaged by their lesions, and it also specifies the six instances of spinal surgery. Sequential displays of the pre- and postoperative thermosensory behavior across test sessions of cats belonging to each of the three categories are illustrated in Fig. 2. The top diagram illustrates the performance of a cat (192) belonging to category 1, the second diagram shows the data for a cat (589) assigned to category 2, and the bottom diagrams show examples of two cats (894 and 594) belonging to category 3. Figure 3 shows quantitative summaries of the pre- and postoperative data for three of these cats (192, 894, and 594) on three different behavioral measures: performance (top) or the percent correct finishes in each session; effort (middle) or the average number of alley visits per trial; and efficiency (bottom) or the difference between the probability of changing from the ‘‘wrong alley’’ to the ‘‘correct alley’’ and the probability of changing from the correct alley to the wrong alley (that is, PDQ minus NDQ).

**CATEGORY 1.** The final preoperative sequence of sessions was repeated postoperatively in the absence of thermosensory disturbance, thus constituting a demonstration of criterion performance. This type of result is illustrated in Fig. 2, top, which shows the criterion series performance of cat 192 before and after the thalamic lesion. Similarly, the seven other cats assigned to category 1 (Table 1) performed satisfactorily during a complete postoperative criterion series of nine sessions without any sign of a change in their ability or propensity to perform the behavioral thermosensory task.

The behavioral data for cat 192 are summarized in Fig. 3 (left). These show clearly that the thalamic lesion produced no change in performance (top) with either the contralateral (black bars) or the ipsilateral paws (white bars). A noticeable decrease in this cat’s efficiency and an increase in effort occurred for both body halves postoperatively, but effort increased also in the control sessions, where performance (checkered bars) was at the 50% chance level and efficiency undulated around zero, as required in the absence of inadvertent auxiliary cues. Thus the reduced efficiency and increased effort in the presence of thermal cues were likely due to temperamental hyperactivity rather than a reduced thermosensory discriminatory capacity.

**CATEGORY 2.** Four cats showed a distinct postoperative behavioral disturbance that interfered with their test results but was not specifically related to their thermosensory abilities. For example, the sequential behavioral performance of one such cat (589) is shown in Fig. 2. This cat initially was disinclined to perform the behavioral task, as shown by the gray shading (indicating the number of completed trials). During the first two postoperative sessions, he finished only four trials. He completed the stipulated 32 trials with the ipsilateral paws in the third session, but with chance level performance and very low effort. His effort reached the preoperative level in the 6th postoperative session, when he
Finally, began to perform above criterion level with the paws contralateral to the lesion, and a full criterion series was completed with the 15th session. Postoperative performance was better with the contralateral paws than with the ipsilateral paws, as it had been preoperatively. Thus it was concluded that the postoperative behavioral disturbance did not indicate a thermosensory deficiency. The three other cats that were assigned to category 2 (Table 1) also satisfactorily completed a full series of nine sessions postoperatively after a similar disinclination to complete the behavioral task (i.e., drastically or totally reduced effort values). Ultimately they performed well without a sign of any change in their ability to achieve criterion performance in the thermosensory task.

### CATEGORY 3

The two cats (894 and 594) whose results are illustrated in Fig. 2, bottom, and in Fig. 3, right and middle, both showed mild but unambiguous postoperative thermosensory deficiencies with their contralateral paws. The summarized results of the intermediate pre- and postoperative periods for cat 894 (Fig. 3, middle) reveal how the performance for the contralateral paws diminished while performance for the ipsilateral paws improved. The cat’s reduced contralateral performance was also evident in the decreased efficiency (Fig. 3, bottom). The sequential presentation of test results in Fig. 2 (2nd from bottom) shows how the cat appeared to recover from this deficit rapidly, and she achieved a stipulated criterion series by session 13. Nonetheless her proficiency with the contralateral paws was significantly worse than the ipsilateral body half during this postoperative criterion series ($P < 0.02, \chi^2$ test). This contrasts with the small (statistically insignificant, $P \geq 0.6, \chi^2$ test) difference in the opposite direction that had existed preoperatively. The relative deficiency in her postoperative performance with the contralateral paws remained statistically significant for >2 mo.

The results for another category 3 cat (594), also summarized in Fig. 3, were superficially more ambiguous, although a marked decrease of contralateral performance (top right) and efficiency (bottom right) was evident. As shown in the sequential display in Fig. 2 (bottom), the cat failed to attain the criterion level with the ipsilateral paws during her first postoperative session, but this was her only failure with the ipsilateral paws during the next three months. The performance with the contralateral paws commenced just above criterion level, but this level was not maintained in subsequent sessions. Fig. 2 shows how the intermittent subcriterion performance for the contralateral paws required either reiteration of contralateral sessions or recourse to an accessory acoustic cue (cf. METHODS). The figure also shows that it was only with the 32nd postoperative session that she was able to commence a full criterion series. The preoperative difference in thermal discriminative capacity between the body halves (Fig. 3) was statistically significant ($P \leq 0.01, \chi^2$ test), and according to the protocol, the thalamic lesion was placed contralateral to the more proficient body half. The resultant mild thermosensory deficiency caused this difference to disappear and slightly invert. Except for the first postoperative session, the performance with the previously inferior, ipsilateral body half remained persistently above criterion level during the 3 mo before the subsequent spinal lesion. It took 2.5 mo of postoperative training for the performance with the previously superior, contralateral body half to just reach that level (Fig. 2). The preoperative superiority for the contralateral paws did not return.

Three more cats (293, 994, and 593) also were allocated to category 3. They all had postoperative discriminatory problems of thermosensory nature, although even milder than those in cats 894 and 594. Cat 994 performed at only chance level during his first two sessions with the contralateral paws, but his proficiency recovered rapidly, and thereafter he maintained a stable level of satisfactory performance. Cat 293 also failed to produce criterion performance immediately after surgery, but her behavior showed an abrupt increase in the number of alley visits during the fourth session, and her performance recovered rapidly thereafter. Yet she was unable to maintain that level continuously, and she showed frequent, temporary performance lapses, although these were not confined to either body half.

Finally, cat 593 differed in that the deficiency was not immediately evident. He already had performed satisfactorily

### TABLE 1. Different cats’ complete to minor lesions of different structures

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Affiliations to the three results’ categories are indicated in the first column. Subsequent spinal lesions are indicated to the right. +, --++, minor to complete lesions. Sm. n. submedius; dmVPM, dorsomedial aspect of the ventral posterior medial n.; vVMb, ventral aspect of the basal part of the ventral medial n.; VPI, ventral posterior inferior n.; ZI, zona inserta; P +, paracentral n.; Cl +, central lateral n.; CM, central medial; CeM, central medial n.; VL, ventral lateral n.; LP, lateral posterior n.; MD, medial dorsal n. 

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**THERMOSENSITIVITY AFTER THALAMIC LESIONS**
during two sessions with the paws of each body half when his performance deteriorated. Afterward, with the contralateral paws he was unable to maintain thermosensory discriminatory behavior at the preoperative level continuously, and he failed to achieve a full criterion series of nine complete sessions. The preoperative performance of cat 593 had been somewhat better with the contralateral than the ipsilateral paws. It became slightly worse than the ipsilateral performance during the initial postoperative sessions. The differences were not statistically significant in either case. However, postoperatively the cat's tendency to turn back from the correct alley instead of continuing straight through to the reward (NDQ) increased when using the contralateral paws. This increase of erroneous or inefficient behavior with the contralateral paws was signif-

![Graph](http://jn.physiology.org/)

**Fig. 2.** Sequential presentation of behavioral performance (ordinates) during the final preoperative test sessions (negative values, abscissae) and the initial postoperative test sessions (positive values, abscissae) for cats 192, 589, 894, and 594. Numbers of correctly finished trials are shown with vertical bars, and the numbers of completed trials are indicated by the background shading. Results of tests of the paws contralateral to the thalamic lesions are shown with black bars, and those of tests with the ipsilateral paws with open bars. Checkered bars indicate control sessions. The lower, dotted horizontal lines crossing the diagrams indicate the 50% “chance” performance levels, and the upper, solid horizontal lines indicate the 69% “criterion” performance levels. Stars above 3 bars for cat 594 indicate that an accessory acoustic cue was added for these sessions. Empty space for postoperative session 11 of cat 594 represents a control session spoiled by a partial failure of the thermodes' control valves.
significant ($P < 0.04$, $\chi^2$ test) compared with the corresponding preoperative behavior.

**Behavioral observations after spinal surgery**

The weak effects of thalamic lesions on the thermosensory behavior of the present cats contrasted starkly with the previously observed massive effects of spinal lesions involving spinothalamic thermosensory input (Norsell 1979, 1983, 1989a). Thus an elaboration of the experimental protocol was made toward the end of the series. The effect of an additional lesion of the ascending spinothalamic tract was investigated before the final histological appraisal in six cats, essentially as a positive control or reconfirmation of the validity of the experimental paradigm. The cats were retrained (if need be) for 3 mo and brought to a stable level of thermosensory performance, and then the middle of the lateral funiculus was cut at the C4 spinal level, ipsilateral to the lesion, their ability to perform this discrimination dropped to the 50% chance level with the contralateral paws. The task subsequently was made easier for sessions with the contralateral paws by setting the temperatures at the initial training values, i.e., $+10$ (pos.)/$-10^\circ$C (neg.), but contralateral performance remained at the 50% chance level. The ipsilateral performance for both cats 192 and 594 was just below the 69% criterion level in the immediate postoperative period, but it returned to the preoperative level with the most stringent stimulus test ($-2^\circ$C) within the sessions shown in Fig. 4, and it remained there to the very end, in contrast to the permanent deficiency on the contralateral side.

The consequences of the spinal lesion were slightly different for cat 894, the third cat portrayed in Fig. 4 (middle). Performance was below the 69% criterion level for the contralateral paws in the sessions immediately after the lesion and remained below criterion (albeit above chance levels) for the difficult discrimination ($-4^\circ$C to the end. In contrast, ipsilateral performance returned to the preoperative level after one session. When after six postoperative sessions the easiest temperature stimuli were used for the contralateral side [$+10$ (pos.)/$-10^\circ$C (neg.)], contralateral performance increased above the 69% criterion level. Nevertheless the cat’s best results when performing the easy discrimination with the contralateral paws were significantly ($P < 0.02$, $\chi^2$ test) worse than those obtained when performing the more difficult ($-4^\circ$C) discrimination with the ipsilateral paws.

Spinal lesions were made in three more cats (293, 992, and 994) with similar results. Two of them (293 and 992), like cats 192 and 594, performed at chance levels postoperatively with their contralateral paws even for the easiest [$+10$ (pos.)/$-10^\circ$C (neg.)] discrimination of the early training. Cat 994 consistently performed below the criterion level (albeit above chance level) on the difficult ($-4^\circ$C) preoperative discrimination task, like cat 894, and it also failed at the subsequent, easier task [$+10$ (pos.)/$-10^\circ$C (neg.)].
Histological analysis of thalamic lesions

The lesions in each cat were documented first without knowledge of the behavioral results. For the final, global analysis, the lesions in each case were plotted on a series of six standardized coronal levels (taken from cat 894) spaced at 0.5 mm intervals. Lesions in selected cases are illustrated in Figs. 5 and 6. The photomicrographs in Fig. 7 document the damage produced at the numbered thalamic levels in four cats. The degree of damage (graded from 1 to 4) of various thalamic nuclei is compiled in Table 1 for all cats. The reference column at the far right in Fig. 5 indicates the intended targets of the thalamic lesions, Sm, dmVPM, and vVMb, where prior evidence has shown that thermoreceptive lamina I terminations occur.

The damage in two category 1 cats with particularly large lesions (992 and 192) is illustrated in Fig. 5, far left. The lesions in these two cases included all of the intended portion of Sm and all or nearly all of dmVPM. Photomicrographs of the lesions at levels 2 and 4 in cat 192 are presented in Fig. 7. In cat 992 there was also massive gliosis and neuronal loss along the electrode penetrations through the intralaminar nuclei [paracentral n. (Pc), central lateral n., and centre médian] and medial dorsal n. The lesions in the remaining category 1 cats damaged Sm and dmVPM to lesser and varying degrees (Table 1), along with portions of various neighboring nuclei. In one category 1 cat (588), the lesion was in the rostral mesencephalic tegmentum just lateral to the periaqueductal gray. In three category 1 cases (992 192, and 392), there was damage in dorsal and anterior portions of VmB and in the anterior portion of VPI (Fig. 5), but in no category 1 case was there any damage to vVMb.

The damage in two category 2 cats with large lesions (189 and 589) is illustrated in Fig. 5. In both cases, there was nearly complete destruction of the appropriate portion of Sm, as well as considerable damage to midline and intralaminar nuclei (CeM and Pc). Photomicrographs of the lesion in cat 589 at levels 3 and 4 are shown in Fig. 7. In another category 2 cat (690), a smaller lesion was made that included less damage to Pc and no damage to CeM. In the remaining category 2 cat (889), the lesion was in the mesencephalic tegmentum, similar to that in cat 588.

The lesions in all five category 3 cats are illustrated in Fig. 6. These differ from the previous cases in that they all include damage to vVMb. The lesions in cats 594 and 894 destroyed the entire extent of vVMb, and significantly, these are the two cats that had the most unambiguous thermosensory deficiencies. The lesion in cat 594 also included nearly all of Sm and dmVPM; however, in cat 894 there was no damage to Sm or dmVPM. Photomicrographs of the lesion in cat 894 at levels 1 and 2 are shown in Fig. 7.

The lesions in the other three category 3 cats damaged part, but not all, of vVMb. In cat 994, the lesion damaged most of dmVPM, a large part of Sm, and most of vVMb, but the caudal aspect of vVMb at level 1 remained intact. In cat 593, the lesion was centered in the most caudal aspect of vVMb, yet the medial half of vVMb at the more rostral levels 2 and 3 was not damaged, and there was little or no damage in Sm and dmVPM. Photomicrographs of the lesion in cat 593 at levels 1 and 2 are shown in Fig. 7. Last, in cat 293, the lesion damaged Sm and dmVPM and, in particular, the lateral aspect of vVMb at its border with posterior VPI at the middle and rostral levels (2 and 3), but it did not involve the most posterior aspect of vVMb (level 1) or its medial half more rostrally. Thus the common feature in these three cats was the partial, but incomplete destruction of vVMb. The thalamic lesions of all five category 3 cats included the posterolateral aspect of vVMb at level 2. There was also variable damage more laterally in posterior VPI and the ventral aspect of VPL (where nociceptive lamina I terminations occur) in many of these cases, without any apparent correlative consequences. Finally, inclusion of damage to Sm and dmVPM in the lesions had no consequence for the category 3 cats’ behavioral thermosensitivity, consistent with the category 1 cases.
Histological analysis of spinal lesions

The spinal lesions in each of the six cats who received additional spinal surgery were documented without knowledge of the behavioral results. Each lesion was signified by clear destruction and dense gliosis that was concisely delimited. The lesions in each case (Fig. 8) destroyed the middle of the lateral funiculus and extended as deep as the spinal gray matter, like correspondingly efficacious lesions in prior studies (Norrsell 1979, 1983, 1989a). The damage extended slightly into the ventral funiculus in cats 192, 992, and 594. There was no observable damage on the opposite side in any cat. There were no apparent correlations between the extent of the lesions and their behavioral effects, other than an inconclusive relationship with the size of the lesions. Thus of the four cats in which thermosensory discrimination with the contralateral paws was reduced to chance level for even the easiest task, three (192, 992, and 594) had relatively larger lesions, but one (293) had a restricted lesion. Of the two remaining cats (894 and 994), one (894) had a restricted lesion and the other (994) a larger lesion, but both showed similarly massive defects in thermosensory behavior, with a slight, yet detectable discriminatory capacity remaining in their contralateral paws.

FIG. 5. Thalamic lesions in selected cats belonging to categories 1 (992 and 192) and 2 (189 and 589). Standardized levels in each column progress from caudal to rostral (bottom to top). Shading illustrates the extent of the damage in each cat. Cytoarchitectonic designations and level numbers are shown in the reference column at the far right, which also shows the regions targeted by the lesions.

Histological analysis of spinal lesions
DISCUSSION

The aim of the present study was to answer an ostensibly straightforward question. In previous experiments (Norrsell 1979, 1983, 1989a), severe thermosensory impairments were found after unilateral damage to the middle of the lateral funiculus of the cervical spinal cord but not after even large lesions dorsal or ventral to this region. On the basis of salient evidence from cats, monkeys, and humans (Craig 1991b; Craig and Kniffki 1985; Gildenberg 1972; Kuru 1949; Moffie 1975; Nathan 1990; Nathan and Smith 1979; Ralston and Ralston 1992), it seemed reasonable to presume that the impairments had been caused by interruption of thermosensory spinothalamic axons originating in lamina I. Prior anterograde tracing and antidromic mapping data had indicated that thermosensitive lamina I neurons terminate in three regions in the cat thalamus: Sm, dmVPM, and vVMb (Craig 1987, 1991a; Craig and Dostrovsky 1991; Dostrovsky and Craig 1993). Hence it could be asked if all three thalamic target areas were equally involved in overt thermosensory behavior or if lesions involving a particular nucleus might cause more pronounced disturbances. The results provide a credible, yet partial, answer to that question.

In general, even the largest thalamic lesions caused remarkably few changes in behavior. Of the 17 cats, 8 were able to reproduce their preoperative performances immediately after surgery (category 1, Table 1). Two of these cats (192 and 992)
had very large thalamic lesions. Four cats (category 2) failed to go through the motions of the behavioral task immediately after the thalamic lesion, but their behavior soon normalized without any sign of difficulties in thermal sensibility. It was inferred that transient postoperative distress of a general nature had occurred, probably of no direct relevance to thermosensory behavior.1

Nevertheless five cats did show definite, albeit mild, postoperative defects in thermosensory discrimination (category 3). Three of these showed strictly contralateral defects, and two showed bilateral effects that may have been a general behavioral thermosensory deficiency due to a perceptual ambiguity. These moderate thermosensory deficiencies lasted throughout the postoperative period for three of the cats, though they receded with time.

These findings indicate one portion of the thalamus that has a discernible role in cats’ behavioral thermosensitivity. Histological analysis revealed that the category 3 cats were the only ones in which vVMb had been damaged. The lesions completely damaged this region in both cats (594 and 894) that showed unambiguous contralateral defects. Partial, incomplete lesions of vVMb were present in the other three cats, who showed even milder deficits. The posterolateral aspect of vVMb may possibly be of particular importance because all of the five cats with thermosensory defects had lesions that damaged this region. Consequently our findings demonstrate that thermosensory transmission via vVMb plays a special role in the cats’ temperature discrimination in the T maze.

These findings provide several functional anatomic insights. First, they indicate that dmVPM is not critical for discriminatory thermosensory function. This is somewhat surprising, because antidromic mapping indicates that only lamina I spi-

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1 Medial thalamic lesions are known to cause disturbances of vigilance and memory in humans (Bentivoglio et al. 1997; Macchi 1997) and reportedly can disturb vigilance and attention in cats (Bouyer et al. 1992). Two of the four cats in category 2 had medial thalamic lesions, yet another cat (992) with considerable damage in medial thalamus did not show any behavioral disturbance in the present context.
nothalamic neurons that are thermoreceptive specific project to this region (Craig and Dostrovsky 1991; Dostrovsky and Craig 1993). Neurons in dmVPM may respond selectively to thermal stimulation of the ipsilateral tongue, yet few have been observed that respond to contralateral stimulation (Auen et al. 1980; Langgren 1960; A. D. Craig and J. O. Dostrovsky, unpublished data; U. Norrsell, unpublished results). Our findings have not clarified the role of dmVPM in thermal sensation, but they indicate that it has minimal, if any, involvement in thermal discriminatory behavior using the paws.

Second, these results similarly indicate that Sm is not involved in cats’ behavioral thermosensitivity. In the cat, Sm receives a dense, topographic input from lamina I that includes both nociceptive and thermoreceptive lamina I spinothalamic neurons (Craig 1987; Craig and Burton 1985; Craig and Dostrovsky 1991; Dostrovsky and Craig 1993; Dostrovsky et al. 1987), but nearly all Sm units that have been recorded are nociceptive specific (Craig 1991a; Dostrovsky and Guilbaud 1988; Kawakita et al. 1993; Miletic and Coffield 1989), and innocuous thermal (cold) stimulation can inhibit Sm neurons (Craig 1991a). This interaction has been conjectured to contribute to the well-known attenuation of pain by cool stimuli (Craig 1991a, 1996; Ericson et al. 1996), and this role would not have been revealed by the present experiment.

Third, these findings indicate that vVMb does have a role in cats’ behavioral thermosensitivity. We infer that vVMb contains neurons responsive to innocuous thermal stimulation of the paws. Only nociceptive neurons have been reported in this region (Vahle-Hinz et al. 1987), but antidromic mapping in the cat indicates that nearly all lamina I spinothalamic axons, both nociceptive and thermoreceptive, have collaterals in vVMb (Craig and Dostrovsky 1991; Dostrovsky and Craig 1993). This supports the view that vVMb is a primordial homologue of the posterior ventral medial nucleus (VMpo) in primates and humans (Craig 1996), which is a dedicated lamina I spinothalamic relay nucleus that contains topographically organized nociceptive- and thermoreceptive-(cold)-specific neurons (Craig et al. 1994). Recent findings in the nocturnal owl monkey directly implicate this pathway in discriminative thermosensory function (Craig and Dostrovsky 1991b; Dostrovsky and Craig 1996b), and the cat’s vVMb also projects to insular cortex in parallel with the adjacent parabrachial projection pathway (Clasica et al. 1997; Vahle-Hinz and Oertle 1993). In cats and monkey, the role of insular cortex in thermosensory behavior has not been specifically studied; experiments in the monkey indicate a contralateral cortical participation in thermosensory function (Ebner and Myers 1962), but no involvement of the first and second somatosensory areas (Cragg and Downer 1967; Porter and Semmes 1974). In humans, lesions of the posterior thalamus (Boivie et al. 1989; Bowsher 1996; Lenz and Dougherty 1997) or the insular cortex (Bassetti et al. 1993; Biemond 1956; Horiiuchi et al. 1996; Schmahmann and Leifer 1992) cause massive contralateral thermosensory defects (although a role of the neighboring second somatosensory area has not been excluded), whereas lesions of parietal somatosensory areas do not (Knecht et al. 1996). Recent PET imaging data in humans similarly indicate significant activation of the insula but not the postcentral somatosensory cortex by innocuous cooling (Craig et al. 1996).

Thus the production of a discernible thermosensory deficiency by damage to vVMb corroborates substantial evidence suggesting a role of vVMb in discriminative thermosensory function in the cat and is congruent with the essential role of VMpo in the primate thermosensory pathway. Yet our findings indicate that the role of vVMb in discriminative thermosensory function, though discernible, is not irreplaceable. This contrasts strikingly with the evidence that lesions of posterior thalamus in humans can produce major, lasting deficits in thermal sensation.

Indeed an unexpected finding of this study was that thalamic lesions did not produce massive behavioral thermosensory defects resembling those caused by spinal lesions (Norrsell 1979, 1983, 1989a,b), even after virtually complete destruction of the thalamic target areas of the lamina I thermosensory component of the spinothalamic pathway. Accordingly, during the course of this study, we extended the protocol so that secondary spinal lesions were made in the middle of the lateral funiculus in six cats that had been retrained for 3 mo subsequent to thalamic lesions. In all instances and in contrast to any of the thalamic lesions, these spinal lesions caused massive contralateral thermosensory defects, reproducing the effects observed previously and providing unequivocal validation of the behavioral testing paradigm.

These findings clearly indicate that thermosensory processing at other sites can supplant spinothalamic lamina I thermoreceptive-specific activity after the destruction of its thalamic target structures. One possibility involves targets of somatosensory mechanoreceptive neurons that are activated phasically by cooling, which have been described in spinal laminae III–V and the dorsal column nuclei (Cliffer et al. 1992; Darian-Smith 1984; Iggo and Ramsey 1976; Perl et al. 1962; Price and Browe 1975; see also Kanosue et al. 1998; Simon et al. 1986) as well as in the somatosensory thalamus (Burton et al. 1970; Bushnell et al. 1993; Martin and Manning 1971; Poulos 1981), and which some have suggested might conceivably provide indication of contact with a cool stimulus. However, the response properties of such ‘‘T + M’’ or ‘‘mechano-cool’’ neurons reflect the nonlinear, weak cooling sensitivity of slowly adapting Type I mechanoreceptors and cannot explain discriminative thermal sensation (Darian-Smith 1984; Iggo and Ramsey 1976). In addition, the axons of such neurons, which ascend in the dorsal columns, the dorsolateral funiculus, or the
antrolateral funiculus (Mann et al. 1971; Rustioni and Kaufmann 1977; Stevens et al. 1991), would be severed by spinal lesions that do not cause any thermosensory deficiency (Nathan 1990; Nathan et al. 1986; Norrsell 1979). Further, if this hypothesis was valid, then the secondary spinal transection of the ascending lamina I pathway in the middle of the lateral funiculus would not be expected to cause any further thermosensory deficiency, contrary to our observations.

A more tenable hypothesis is that the maintained thermosensory competence after thalamic lesions is due to processing of ascending lamina I thermosensory information at structures other than Sm, dmVPM, and vVMb. Such substrates must be located below the level of the thalamus, because almost no thermoreceptive-specific lamina I cells have been antidromically activated from thalamic lamina I projection targets other than these three regions (Dostrovsky and Craig 1993). Thus the present results strongly suggest that contralateral thermosensory lamina I projections to sites in the brain stem may be of major importance for cats’ utilization of thermal information in the T-maze.

Ascending lamina I terminations in the brain stem are bilateral in the medulla and become contralateral in the pons and mesencephalon (Craig 1995a). Lamina I terminations in the periaqueductal gray (PAG) and the intercollicular nucleus are almost entirely contralateral, and spinal lamina I input to the parabrachial nucleus is predominantly contralateral (Bernard et al. 1995; Blomqvist and Craig 1991; Craig 1995a; Feil and Herbert 1995; Wiberg and Blomqvist 1984). The brain stem projections of thermoreceptive-specific lamina I neurons have not been studied yet in detail, but a few have been antidromically activated from the parabrachial nucleus (Light et al. 1993), and thermoreceptive-specific neurons have been recorded there (Menendez et al. 1996; Slugg and Light 1990). The parabrachial nucleus is a major visceral (enteroceptive) integration site, whose projections to VMb and interconnections with the insular cortex (Allen et al. 1991; Moga et al. 1990) parallel those of the lamina I spinothalamic pathway. It is also heavily interconnected with the PAG (Krout et al. 1998; Mantyh 1983b), and significantly, both the parabrachial nucleus and the PAG are interconnected with the hypothalamus and the amygdala (Bernard et al. 1993; Mantyh 1983a; Rizvi et al. 1992), thereby forming part of a forebrain (limbic) network involved in the control of the well being of the animal (or homeostasis; cf. the so-called “emotional motor system,” Holstege et al. 1996). The probable importance of the parabrachial nucleus in the present appetitive behavioral task is underscored by the demonstrated role of its connections with the amygdala and the insular region in gustatory associative learning (Bielavska and Roldan 1996; Grigson et al. 1998; Yamamoto et al. 1994). Further, the probable importance of the PAG for behavioral thermosensitivitiy in the present experiment is emphasized by Bandler and Carrive’s (1988) finding that the motivational (affective) value, or the behavioral relevance, of contralateral nonnoxious somatosensory stimuli can be altered by chemical excitation of the lateral column of the PAG, the portion that receives lamina I input. These considerations are consistent with the idea that evolution produced a hierarchically segmented refinement of thermosensory processing (Satirnoff 1978).

Like people, cats appear to experience cool and warm as part of a perceptual continuum, i.e., warm stimuli are at the same time less cold and vice versa (Norrsell 1984). Nevertheless cold stimuli have a greater behavioral signal value; cold stimuli are always preferable for the early training of cats’ discriminative behavior, even if the final objective is a pure warm discrimination (Finger and Norrsell 1974; Norrsell 1984). Cats do not like water, and “as a rule, the ordinary house cat will avoid even the smallest puddle” (Burger 1980). The physical consequences of poking the paw into a shallow water puddle are not very different from touching the cold negative stimulus in the present behavioral experiment. Thus it seems necessary to suggest that the signal value of our cold stimulus was augmented by an inherently adverse sensory quality. It has long been recognized that thermoreception has both enterceptive (affective, motivational, thermoregulatory) and exteroceptive (discriminative, perceptual) aspects (Darian-Smith 1984; see Craig et al. 1999). Human psychophysical findings indicate that the affective (pleasent/unpleasant) aspect of thermal stimuli is independent of the discriminative (cool/warm) sensory percept, but significantly, that the affective aspect is dependent on thermoregulatory processing (Cabanac 1969; Mower 1976). Therefore the adverse quality of cold stimuli may be dependent on the integration of ascending thermosensory lamina I activity at homeostatic sites in the brainstem. If so, then thalamic lesions of the lamina I spinothalamic pathway would interfere with only part of the forebrain thermosensory integration by leaving the input to the upper brain stem intact. The cats in the present experiment were not required to discriminate perceptually between cool and warm; rather, they were required only to distinguish between two temperatures, regardless of the sensation. Notably, the distinction between affective and discriminative aspects of thermal sensation is pertinent to the thermosensory dysesthesia experienced by human stroke patients. Some patients who have lost the ability to perceive cold and warm due to spinal or thalamo-cortical lesions nonetheless can distinguish warm or cool objects by the distinctly different feelings they evoke (Boivie et al. 1989; Davison and Schick 1935; Kinnier Wilson 1927; Norrsell 1988). Thus the apparent contrast between the mild effects observed after lesions of the cat’s thalamus in this study and the unmistakable thermosensory defects of patients with thalamic lesions may be at least partially illusory.

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REFERENCES


