JOURNAL OF NEUROPHYSIOLOGY
Vol. 54, No. 1, July 1985. *Printed in U.S.A.*

Inferior Olivary Neurons in the Awake Cat: Detection of Contact and Passive Body Displacement

REUBEN GELLMAN, ALAN R. GIBSON, AND JAMES C. HOUK

Department of Physiology and Neuroscience Program, Northwestern University Medical School, Chicago, Illinois 60611

SUMMARY AND CONCLUSIONS

1. We have recorded from 306 neurons in the inferior olive of six alert cats. Most of the cats were trained to perform a simple task with the forelimb. We observed the neural responses to a wide variety of cutaneous and proprioceptive stimuli, as well as responses during spontaneous and learned active movements.

2. Neurons responsive to somatosensory stimulation were found in all parts of the inferior olive, and they were roughly evenly divided between those responsive to cutaneous stimulation and those responsive to proprioceptive stimulation. In the dorsal accessory olive all neurons were responsive to somatosensory stimulation. In the medial accessory nucleus 88% and in the principal olive 74% of cells were responsive to somatosensory stimulation.

3. Cells responsive to cutaneous stimulation usually had small receptive fields, commonly on the paw. These cells had low-threshold responses to one or more forms of cutaneous stimulation and typically fired one spike at the onset of the stimulus on 80% or more of stimulus applications.

4. Cells responsive to proprioceptive stimulation most commonly responded to passive displacements of a limb. These cells were often very sensitive, responding to linear displacements of <1 cm in one specific direction.

5. No cells in our sample responded reliably during active movement by the animal. Only 21% of cells responding to passive proprioceptive stimulation showed any modulation during active movement, and the modulation was weak. Likewise, cells responsive to cutaneous stimulation generally failed to respond when a similar stimulus was produced by an active movement by the animal. Exceptions to this were stimuli produced during exploratory movements or when the receptive field unexpectedly made contact with an object during active movement.

6. Electrical stimulation applied in the inferior olive failed to evoke movements or to modify ongoing movement.

7. Our results are consistent with the hypothesis that inferior olivary neurons function as somatic event detectors responding particularly reliably to unexpected stimuli.

INTRODUCTION

Two major afferent systems provide somatosensory input to the cerebellar cortex: the climbing fiber system and the mossy fiber system. Mossy fibers originate from many parts of the central nervous system such as the spinal cord, cuneate nucleus, and pontine nuclei, whereas all climbing fibers stem from the inferior olive (19). Climbing fiber activity has traditionally been studied by recording complex spikes generated in Purkinje cells, and such studies have revealed responses to both cutaneous (23, 24, 52) and proprioceptive (30, 31, 33) stimuli. Ebner et al. (22) have shown that climbing fiber activity in a Purkinje cell is accompanied by an increased responsiveness in that cell to parallel fiber input, whether inhibitory or excitatory. This finding emphasizes the important role of

climbing fibers in modulating cerebellar activity. The size and complexity of the cerebellum has resulted in a concentration on limited areas of the cerebellar cortex, primarily lobules III–VI of vermal and intermediate cortex, and a few portions of the lateral hemispheres.

In a previous study (25), we recorded from the inferior olive (IO) with the objective of surveying somatosensory responses from all parts of this complex. A surprisingly large percentage (70%) of cells responded to some form of somatosensory stimulation. In one olivary subdivision, the dorsal accessory olive (DAO), most cells were activated by light cutaneous stimuli. In the medial accessory olive (MAO) and principal olive (PO), squeezes and taps were most effective, whereas very few cells responded to light cutaneous stimulation. Cells in the DAO commonly had small restricted receptive fields and showed a fine somatotopic organization. Such an organization was not apparent in the MAO and PO where receptive fields were generally large and complex. Our results supported and extended those of Robertson and Rushmer and their collaborators (49, 52) who recorded climbing fiber activity in the cerebellar cortex. Likewise, we confirmed the presence of units responsive to light cutaneous stimuli, such as puffs of air, reported by Eccles and collaborators (23), units responsive to taps, as reported by Oscarsson and colleagues (45, 47) and units responsive to squeeze of deep structures previously reported by Thach (59).

Almost all the above studies were carried out in anesthetized or decerebrate animals, and it is not clear whether similar responses are present, absent, or substantially modified in the awake animal. Because of the absence of complex spike activity associated with active movement in the monkey (39, 60), it is not known what information is transmitted to the cerebellum by the inferior olive. In this paper we report on a broad survey of sensory properties of olivary cells in the alert cat and contrast these with our earlier results in the anesthetized animal (25). Briefly, the present findings support our earlier results, which suggest that the inferior olive functions as a specialized sensory system. The results in the awake animal further demonstrate an increased responsiveness to all forms of somatosensory stimulation and the presence of a subset of cells that are very sensitive to natural proprioceptive stimuli. Our findings also suggest that the sensitivity of olivary cells to a stimulus is attenuated during certain phases of active movement.

METHODS

Experiments were carried out on six adult cats, three of which were trained on the behavioral task described below. Of the remaining three cats, two were trained to press a bar for a food reward, and one was simply fed during each recording session. In the behavioral task the animal was required to move one forepaw back and forth between two copper plates ("touch plates") (Fig. 1*A*) to obtain food; baby food mixed with water and cod liver oil was delivered through a tube for every successful trial. The touch plates were capacitative devices that produced an output every time contact was made with glabrous skin but did not respond when only hairs made contact.

When the animals performed the task consistently they were surgically prepared for recording. A head holder and recording cylinder were implanted on the skull under aseptic conditions and general anesthesia (iv sodium pentothal). The cylinder was cemented with dental acrylic over a symmetrical opening in the skull overlying the cerebellum and was placed so that the approach to the IO resembled that used in our earlier acute experiments (25), namely at an angle of about 15° to the vertical. Beginning one day before surgery, and continuing for about a week thereafter, the animals were treated with chloramphenicol (Chloromycetin, Parke-Davis) or procaine-penicillin G dihydrostreptomycin sulfate (Combiotic, Pfizer) injected intramuscularly. The wound and inside of the chamber were kept clean with hydrogen peroxide and povidone-iodine.

Recording began about a week after surgery, and sessions lasting 3 h were held 4–6 days a week. During recording the animal was restrained in a bag, with its limbs protruding and resting on two separate platforms (Fig. 1, *A* and *B*). The head was attached to the frame by a thick felt pad, which allowed small heavily damped movements. This flexible mount reduced the torque on the headholder and appeared to be more comfortable for the animal but did not impair recording stability. Recordings were made with tungsten microelectrodes (impedance 0.8–2 MΩ). The inferior olive was localized by first identifying the fourth ventricle and the hypoglossal nucleus. The olive is typically 3–4 mm below the dorsal surface of the brain stem, and the hypoglossal nucleus is approximately coextensive with the IO mediolaterally and rostrocaudally. Penetration of the elec-

trode into the inferior olive was marked by a characteristic low frequency discharge, as described in our earlier paper (25). Individual olivary neurons were identified by their action potentials, which often were followed by one or more wavelets (4, 20, 37), and by their low levels of spontaneous activity, which rarely exceeded 2 spikes/s. A recording was judged to be from a single unit if the spike could be reliably discriminated, the waveform remained relatively constant, the unit respected the refractory period of olivary cells by not firing more than one spike in intervals of <100 ms, and variations in spike amplitude were no greater than the noise level (typically 50 μV). To allow precise localization of recording sites, small marking lesions were placed at selected sites in the IO by passing current (−10 μA for 10 s) through the recording electrode. After completion of all recording, each animal was killed, and the tissue was processed histologically. Recording tracks and lesions were identified, and only cells that were clearly located in the IO are considered in this paper. The locations of cells were plotted on standard unfolded dorsal views of the individual olivary nuclei (after Brodal, Ref. 15).

When an olivary cell was isolated, a variety of sensory stimuli were applied in an attempt to activate it. We chose flexible methods of stimulation that could readily be applied to almost all parts of the body. Stimuli consisted of light taps delivered by hand, light touch with an esthesiometer, puffs of air controlled by a solenoid, stroking, pinches, squeezes, and passive displacement of a limb or pair of limbs. The displacement was achieved by manipulating the limb or by displacing the platform on which the animal was standing. Figure 1*B* shows that the entire limb could be displaced by moving the platform up and down (range of 10 cm) or laterally (range of 7 cm). The position of the platform was monitored by appropriately mounted potentiometers. The mechanical delay between the input to the solenoid air valve and the delivery of a puff of air was determined by applying the puff to a microphone. The delay between the electronic pulse and delivery of the puff was 15 ms, and this value was used in computing response latencies for cells responsive to this stimulus. Vibration of the resting surface was produced by a sudden tap with a finger. Although contact was maintained for about 100 ms, the mechanical transient decayed much more rapidly.

Action potentials, the pulse inputs to the puffer, the outputs of the potentiometers (indicating dis-

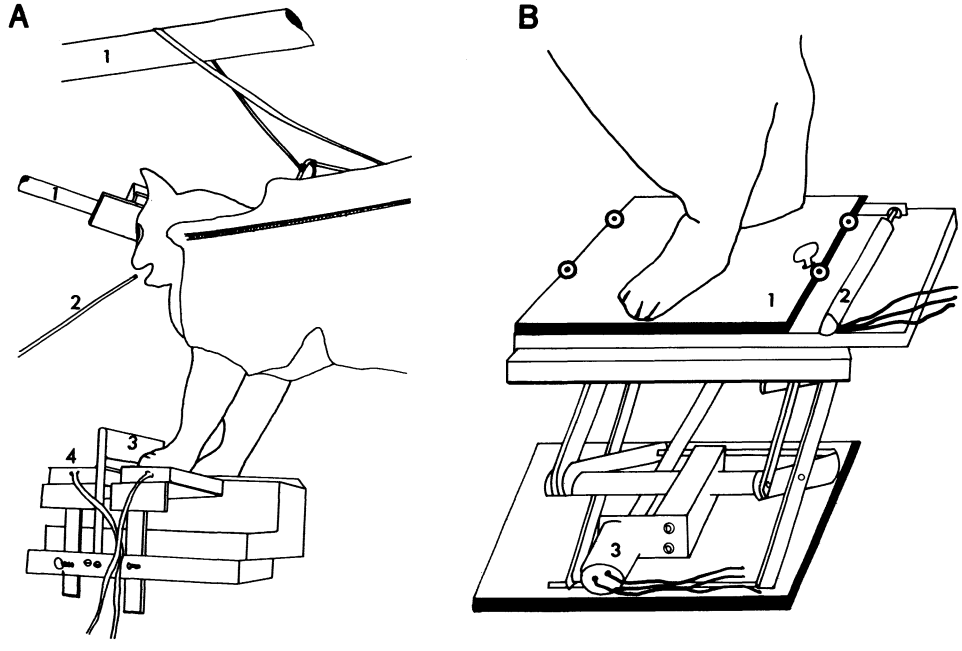

FIG. 1. Experimental apparatus. *A*: cat was restrained in a bag that was supported from a frame (*1*) by sturdy elastic bands. The head was attached to the frame by a thick felt pad, which provided a flexible mount. Baby food was provided through the feeder tube (*2*). Right forepaw is shown resting on one of two touch plates; animal was trained to move its paw over a barrier (*3*) to a second touch plate (*4*), and back again. *B*: hindlimbs are shown resting on a device used for proprioceptive stimulation. The platform (*1*) could be displaced laterally, its position being monitored by a linear potentiometer (*2*). The limbs were displaced vertically by cranking the jack up and down; a rotary potentiometer (*3*) signaled vertical position.

placement) and the output of the touch plates were recorded on a HP3968A instrumentation recorder and analyzed off line. For analysis, the raw data was plotted on a Gould ES1000 electrostatic chart recorder. Response latencies were measured from these plots with 2 ms resolution. We further constructed peristimulus histograms, using bin widths of 50 ms, to quantify neuronal responses to stimuli. This choice of bin widths was determined by the low firing rates of olivary cells; narrower bins would have been too small for statistical analysis. For analysis of firing during active movement, histograms were centered on lift off and touch down on the two touch plates. The low firing rates encountered during movements necessitated the use of wider bins, and data were analyzed using bin widths of both 100 and 200 ms. To compare the responses of a neuron to different stimuli the response probability of the neuron to each stimulus was calculated by dividing the number of spikes in each bin by the number of trials. Since a given neuron could fire no more than once in one bin on one trial (because of the 100-ms refractory period, Ref. 37), a response probability of 1 indicates that the unit fired one spike to every presentation of the stimulus. Occasionally, two or three units were recorded simultaneously and could not be discriminated reliably. Since these units often fired together, possibly due to electrotonic interactions (as documented by Llinas and his colleagues; Ref. 37), we analyzed them as we did single units but noted that the data represented the activity of more than one unit.

We further attempted to assess the function of the IO in the control of movement by examining the effect of olivary microstimulation on movement. Cathodal stimuli were delivered with a Grass S88 stimulator and a PS-IU6 constant-current unit. Parameters were similar to those employed by other investigators in the cat (14) and the rabbit (7), namely 10–60 μA, 0.1- to 0.2-ms pulses for 0.5–5 s, at a rate of 10–60/s. Stimuli in this range have been shown to elicit climbing fiber responses in the cerebellum (14).

The results of these experiments are contrasted with earlier experiments (25) in which we recorded from the inferior olive in 18 cats anesthetized with pentobarbital sodium and 2 decerebrate cats. We have previously noted that responses in the decerebrate were similar to those in the anesthetized animal.

RESULTS

Almost 85% of olivary cells (n = 306) recorded in 90 tracks throughout the inferior olive were responsive to somatosensory stimuli. A small proportion (4%) responded to visual stimuli, and 11% were unresponsive to the stimuli we employed. The responsive cells were located in all olivary subdivisions, namely the rostral and caudal divisions of the dorsal accessory olive, the medial accessory olive, and the ventral and dorsal lamellae of the principal olive.

A wide range of stimuli was found to be effective in activating olivary cells. Cells responsive to light touch, puffs of air, vibration, stroke, slip, or pinching a fold of skin were classified as cutaneous. Those responsive to linear displacement of a limb, joint rotation, sharp taps near the tendon or on the muscles, or squeeze of a muscle were classified as proprioceptive. Since proprioceptive stimulation was invariably accompanied by activation of cutaneous receptors (e.g., the skin being stretched or hairs being bent), the many cells that responded to both stimulus categories were classified as cutaneous although a deep component may have been present. The presence of a deep component in such cells is suggested by our earlier finding in anesthetized animals (25) that some cells responding to cutaneous input are also activated by deep input when the skin is removed. We were unable to classify 33 neurons into the above categories. Cells responsive only to taps or pokes in the receptive field (17 cells) were classified as "undefined" since it was uncertain whether the response to these stimuli was due to activation of high-threshold cutaneous receptors or proprioceptors. Also included in this category were cells that were lost before their response properties were adequately characterized. Table 1 lists the major categories of cells and provides the number in each category.

The great majority of cells in both categories had exclusively contralateral input; 25 cells with bilateral input and 3 cells with strictly ipsilateral input were encountered (i.e., 11% noncontralateral). Furthermore, most cells had simple contiguous fields; only 4% had noncontiguous fields. In contrast, our earlier study on anesthetized animals revealed that a substantial percentage (34%) of somatosensory cells had noncontiguous fields or received bilateral input.

Localization within olivary subdivisions

DORSAL ACCESSORY OLIVE. We were able to localize 289 neurons to specific subdivi-

TABLE 1. *Categories of cells in chronic experiments*

	Fore	Hind	Face	Fore + Hind	Fore + Face	Trunk	Total
Cutaneous	54	38	14	5	8	4	123
Proprioceptive	62	34	1	5	0	1	103
Undefined	16	6	5	1	0	5	33
Somatosensory	132	78	20	11	8	10	259
Visual							12
Unresponsive							35
Total							306

Breakdown of all cells recorded in the IO of awake animals according to the major categories used in this paper as well as of somatosensory cells by receptive field. Note the predominance of cells with input from the forelimb. Table includes cells with contralateral, bilateral, and ipsilateral input.

sions of the inferior olive. Analysis of these revealed several patterns of organization, which we described for anesthetized animals, as well as some new features. As in the anesthetized animals, the DAO of the awake cat had the largest proportion of responsive cells (100% of 92). The pattern of organization that we found in the DAO in these experiments was very similar to that which we described for anesthetized animals. Under both conditions a mediolateral somatotopy was evident (Fig. 2), with the face represented most medially, followed by the forelimb and the hindlimb. As in the acute experiments, cells with cutaneous input predominated in rostral parts of this subnucleus (71% cutaneous vs. 16% proprioceptive; $n = 69$), whereas those with proprioceptive input were more common caudally (52% proprioceptive vs. 39% cutaneous; $n = 23$). Cells with input from both the forelimb and the hindlimb were fairly common in the anesthetized animals (13%), whereas only one such cell (i.e., 1%) was found in the DAO of awake cats.

The forelimb and hindlimb were represented approximately equally in the DAO (39 forelimb, 41 hindlimb), but for both limbs there was a very strong emphasis on the paw. Of 69 cells for which the extent of the receptive field was clearly defined, 44 cells received input from the paw only, 9 had receptive fields that included the paw, and 16 received no paw input. We found only 2 cells with input from the trunk and 9 repre-

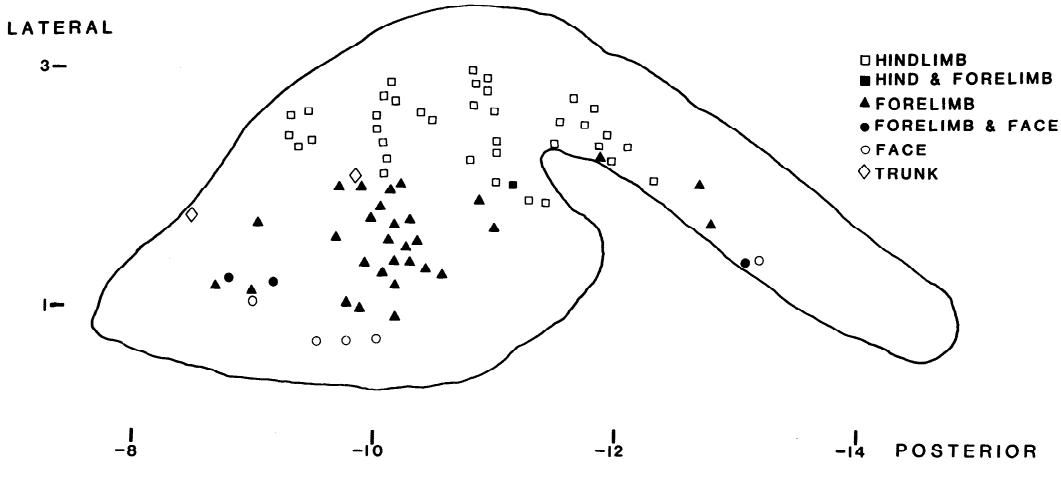

FIG. 2. Receptive fields of cells recorded in the dorsal accessory olive are shown in this dorsal view of the DAO (after Brodal, Ref. 15). In this and subsequent figures, each *symbol* indicates the receptive fields of all cells recorded on one penetration. The dorsal accessory olive is organized in a somatotopic fashion; forelimb cells are located medially, hindlimb laterally. A number of cells with input from the face are located medial to the forelimb region.

senting the face. Of the latter, 4 received input from the forelimb as well. Overall, 88% of cells in the DAO represented exclusively the limbs.

MEDIAL ACCESSORY OLIVE. The vast majority of cells in the MAO (88% of 132, including cells in the dorsomedial cell column, the ventrolateral outgrowth, and the dorsal cap) were responsive to sensory stimulation. This represented an increase over the proportion in the anesthetized animal, where only 66% of cells studied were responsive. In addition, most cells in the awake animals had low thresholds, whereas strong squeeze of deep structures was often necessary to activate cells in the MAO of anesthetized animals.

A minor difference between receptive fields in the MAO and those in the DAO was that bilateral receptive fields were more common in the MAO (15% vs. 2%), as were receptive fields representing both forelimb and hindlimb (8% vs. 1%). As in the DAO, the paw was heavily represented. Of 45 cells for which we precisely defined the extent of the receptive field, 38% received input from the paw only, 35% included the paw, and 27% received no input from the paw. An additional emphasis in the MAO was on the forelimb; 68% of cells received forelimb input only, 24% received hindlimb input only, and 8% received mixed input (n = 93). Subsequent reexamination of our data from anesthetized animals (25) has revealed a similar preponderance of input from the forelimb (76% forelimb cells, 24% hindlimb cells, n = 33). Cells with forelimb input were found throughout the mediolateral extent of the MAO, whereas those with hindlimb input were found only laterally, as indicated in Fig. 3.

The most common classification of cells in the MAO was proprioceptive (49% of somatosensory cells), with 35% responding to cutaneous stimulation. Cells of both categories appeared to be distributed evenly throughout both rostral and caudal parts of the MAO. Likewise, cells classified as unresponsive were located in all parts of the MAO (Fig. 3).

Although the emphasis in this study was on cells with somatosensory input, we noted 11 olivary cells responsive to visual stimulation, 9 of which were located in the dorsal cap and the neighboring MAO. (The remaining 2 were not localized with sufficient certainty.) Figure 3 indicates the sites at which these cells (V) were recorded. The most effective stimulus was a moving textured field (a newspaper), although smaller objects were effective in some cases. All the cells activated

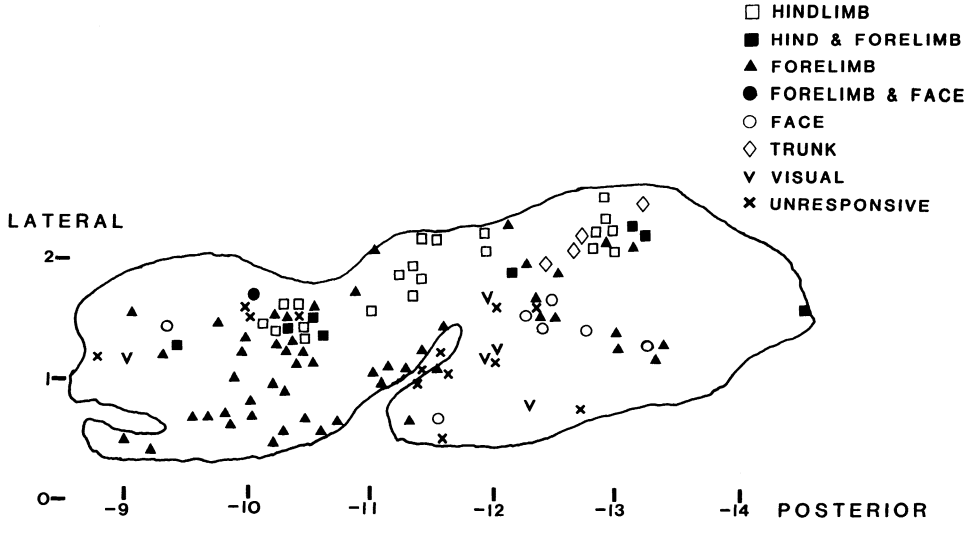

FIG. 3. There is no distinct somatotopic organization in the MAO although all cells with input from the hindlimbs are located laterally. This horizontal projection of the MAO further shows that cells with forelimb input predominate in the MAO. Cells with visual input (V) are located primarily in caudomedial areas. *Symbols* located in the "inlet" of the MAO represent cells recorded in the dorsal cap or ventrolateral outgrowth, which overly this area.

by moving a textured field showed directional selectivity; 3 cells responded to downward movement, 3 to movement away from the animal, 1 to upward movement, and 1 to ipsilaterally directed movement. Two of the former cells and three others unresponsive to moving textures responded to a flash of light, but this response was unreliable.

PRINCIPAL OLIVE. The majority of cells in the PO (74% of 65 vs. 43% in anesthetized animals) were responsive to somatosensory stimuli. Like the MAO, the PO contained few cells with hindlimb input; of 48 somatosensory cells, 26 received input from the forelimb only, 7 from the hindlimb only, and 2 from the hindlimb and forelimb. In contrast to the hindlimb, the face was relatively well represented, with 8 cells (of a total of 20 face cells encountered in the IO) being located in this subnucleus. In addition, 3 cells (of 8 in the IO) with input from both face and forelimb were found in the PO. As in the DAO and MAO, the paws were heavily represented (13 paw only, 5 included paw, 3 no paw). Cells with deep input were slightly more common in the PO than those with cutaneous input (50% vs. 40% of somatosensory cells).

A few differences were noted between the ventral lamella (n = 32 cells) and the dorsal lamella (n = 16 cells) (Fig. 4). First, of the 7 pure hindlimb cells, 6 were located in the dorsal lamella. Second, of the 11 cells with input from the face, 9 were in the ventral lamella, where they concentrated along the medial edge (Fig. 4). Third, the two lamellae differed with regard to the distribution of proprioceptive and cutaneous cells. In the dorsal lamella, 78% of responsive cells (n = 14) were proprioceptive, compared with 14% cutaneous. In the ventral lamella, 40% of responsive cells (n = 25) were classified as receiving proprioceptive input, whereas 52% received cutaneous input.

Nature of sensory responses

CUTANEOUS RESPONSES. Table 1 indicates that 123 units (47% of somatosensory cells), with receptive fields located largely on the limbs, were classified as cutaneous. Many of these cells were remarkably sensitive to the appropriate stimulus. For example, 5 cells (of 10 tested) responded to touch with a von Frey hair exerting a force of only 4.5 mg. (This was the lightest calibrated stimulus available to us.) Other sensitive cells responded to light puffs of air or mild vibration of the surface on which the animal stood.

The response to a cutaneous stimulus generally consisted of one spike. This was true whether the stimulus was maintained for a long time or applied only briefly (typically 5–100 ms). Figure 5*A* exemplifies the response of an olivary neuron to an impulsive stimulus

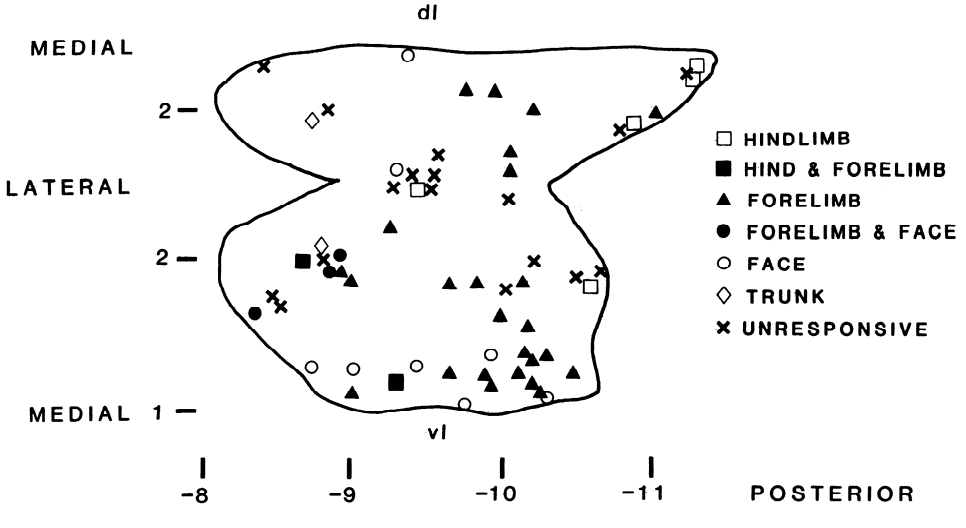

FIG. 4. In the PO, shown here in an unfolded horizontal projection, there is no somatotopy evident, but there are several differences between the dorsal and ventral lamellae. Cells with input from the hindlimbs are located primarily in the dorsal lamella, whereas those with input from the face are concentrated in the ventral lamella.

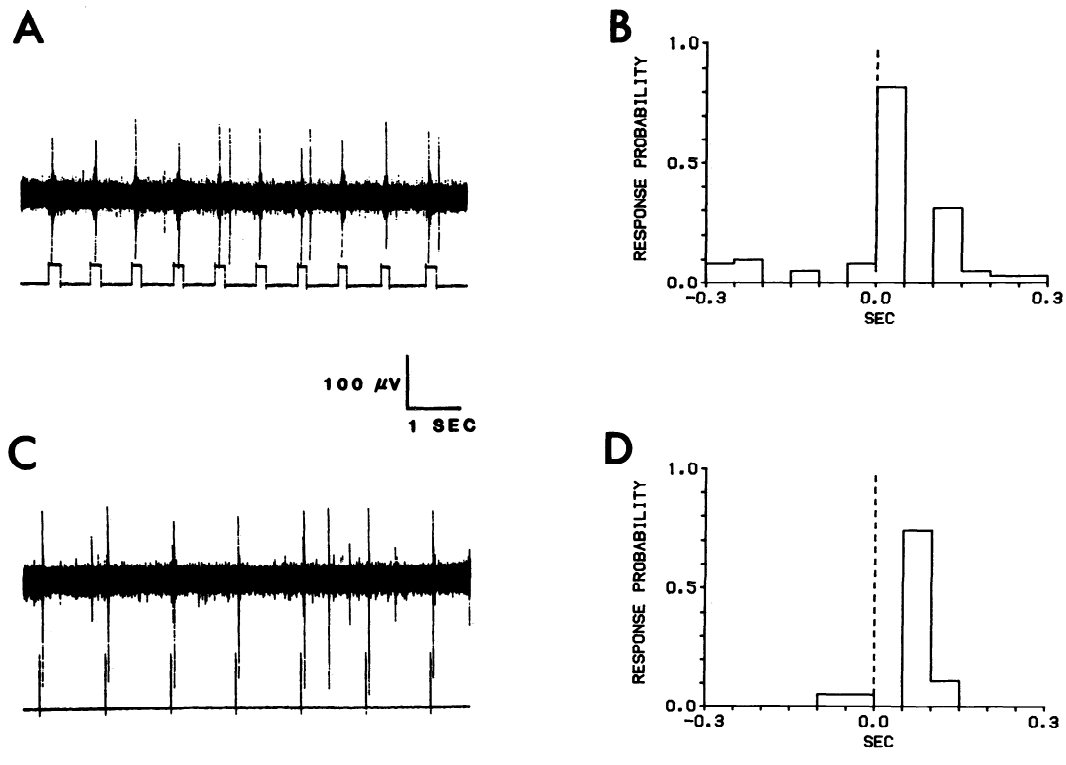

FIG. 5. *A*: upper trace shows the response of an olivary cell to taps (pulses in lower trace) on the platform on which the animal stood. The histogram (*B*) to the right summarizes the data from 39 trials. During this time 60 spikes were recorded; the figure shows that spontaneous activity was very low, although the response probability was high (82% in the first 50 ms). A small secondary peak is seen at 100–150 ms; this is due to an occasional spike produced at the end of the tap (note trials 6, 8, 11). In *C* the response of a different olivary cell to a light puff of air (trigger shown in lower trace) on the lateral surface of the hindlimb is shown. *D*: (19 trials; 18 spikes) shows that the response probability is high and spontaneous activity low.

and shows the response to a tap on the recording table which produced a slight vibration in the carpeted surface on which the hindlimbs rested. The trace showing neuronal activity emphasizes that the response was highly reliable and that it appeared over a background of low spontaneous activity. The histogram to the right of the traces (Fig. 5*B*) documents both the reliability of the response (occurring on over 80% of trials) and the low background activity. Figure 5*C* shows the response of a different cell to a light puff of air in its receptive field; here too the response is highly reliable, a point emphasized by the accompanying histogram (Fig. 5*D*).

We obtained response latencies for 27 cells using puffs, and for 2 cells using taps on the supporting surface as stimuli. Mean latencies were 27 ms for the forelimb, 32 ms for the hindlimb, and 35 ms for the face. These values were 5–20 ms longer than latencies we have described in anesthetized animals, where latencies were obtained by percutaneous shocks. The variability in the latency to a puff (mode 10 ms) for individual cells was much greater than the variability when shocks were used in anesthetized animals (typically 1–2 ms; Ref. 25).

Although most cells classified as cutaneous showed an excitatory response to the application of a stimulus, as in the above examples, 19 cells responded upon termination of a stimulus and often showed a depression of activity while the stimulus was being applied. This set of cells included some with receptive fields on the side of the limbs or on the trunk, but the largest subset consisted of 7 cells that fired on release of light pressure from the footpads. A particularly interesting feature of these cells is that they responded

to a sudden loss of support. Thus, if the experimenter placed his hand under the paw and suddenly removed it, the cell fired. These cells were clearly cutaneous because the response was elicited by release of very light pressure on the pad. For cells with receptive fields on the side of the limbs or the trunk, responses were elicited when a fold of skin was pinched and released without apparent involvement of deep tissue.

Olivary cells generally responded only to the transient phase of a stimulus. Thus, repeated stimulation evoked repeated responses, provided the 100-ms refractory period was respected. A maintained tonic stimulus, such as touching the receptive field and maintaining the touch, in contrast, evoked only one spike at the onset of the stimulus. However, stroking the skin sometimes evoked a maintained low-frequency response (10 cells), presumably reflecting repeated transient stimulation of individual hairs or small regions of skin. Another group of cells that exhibited a tonic response consisted of 11 units that were activated by a slow continuous slip of the paw over a surface. Although the response was directionally selective, it was independent of the method of delivery of the stimulus. Thus, for example, one of these cells was activated both by sliding the forepaw backward over a surface and by moving the surface forward under the limb.

In Fig. 6*A* we have mapped the locations in the IO of several types of cells that appear well suited to detect specific somatic events, namely those responsive to slip, vibration, and removal of pressure from the pads. The last mentioned are designated "contact removal" cells (n = 18) in Fig. 6, and fourteen of these were located in the MAO; 10 of these were confined to an area 0.2 × 0.7 mm. Cells responsive to vibration also showed a distinct pattern of organization; all were located in the MAO, and 6 of 7 vibratory cells with hindlimb input were found in a region of 0.5 × 0.7 mm. Figure 6 does not include cells responsive to light touch and puffs of air. These neurons, which may also be described as somatic event detectors, are located in all olivary subdivisions, without any apparent concentration in specific locations.

PROPRIOCEPTIVE RESPONSES. Of 259 cells that we classified as somatosensory, 39%

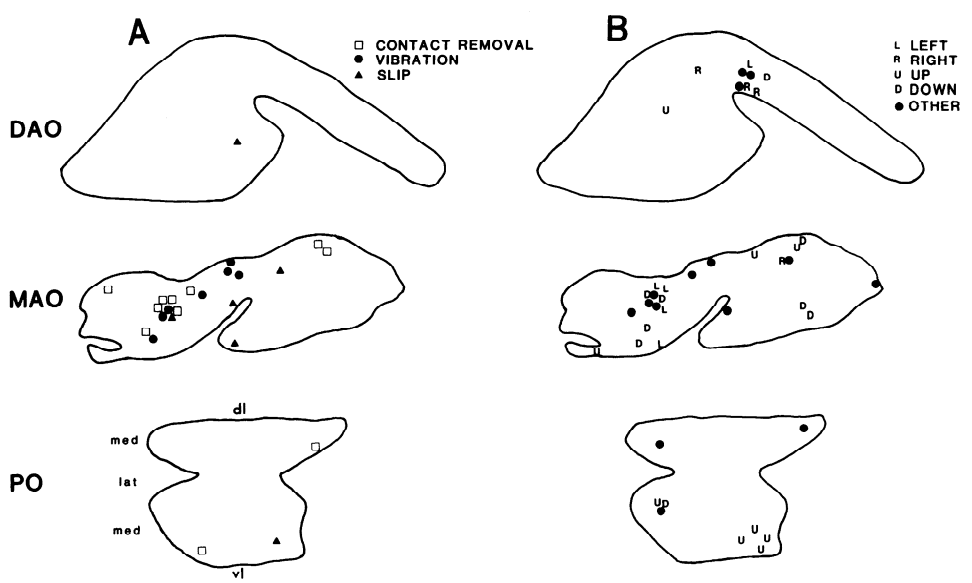

FIG. 6. The locations of several groups of cells that may be viewed as specific somatic event detectors are shown on dorsal projections of the three major olivary subdivisions. *A* shows the locations of cells responsive to several categories of cutaneous stimuli. Note that most of the cells classified as responding to contact removal are concentrated within a relatively small part of the rMAO. *B* shows the location of cells responsive to displacement in specific directions. Left and right displacement refer to the right IO; thus, leftward displacement indicates abduction. Cells with bilateral input responded to displacement of both limbs in the same spatial direction. Cells labeled "other" responded well to displacement in several directions, and the optimal direction was not determined.

responded to proprioceptive stimulation only. Table 1 shows that there is a significant (χ^2, $P < 0.05$) preference for forelimb over hindlimb representation among this group of cells. The majority of proprioceptive cells (91%) showed an excitatory response to a stimulus; the remainder were inhibited by a maintained stimulus such as maintained pressure on a muscle, or fired on termination of the stimulus. At the outset of these experiments stimuli were applied by hand, and cells were encountered that were responsive to manual rotation of a joint, tugging against a contracting muscle, sharp taps on a tendon or muscle, or squeezing a muscle or group of muscles. Because squeeze is an aversive stimulus, it was rarely used; only 10 cells requiring activation by squeeze were noted. Tugging on a limb as the animal withdrew was particularly effective, with some cells responding to brief tugs (<1 cm) with response probabilities in excess of 0.9. Linear displacement by the device shown in Fig. 1*B* was introduced as a regular test in later experiments. Of 50 cells tested with this device, 43 were reliably activated.

Figure 7 provides an example of the response of a proprioceptive cell to displacement of a limb. In this figure, each step had an amplitude of about 1 cm, with a velocity range of 7–14 cm/s. The interval between steps was 1–2 s. This cell responded to downward, but not upward, displacement. Two common features of the response of IO cells activated by displacement are well illustrated in this figure. First, the response is independent of the initial position; although the starting point of the displacement varies over 10.5 cm, the response is apparently invariant. A second common feature of olivary respon-

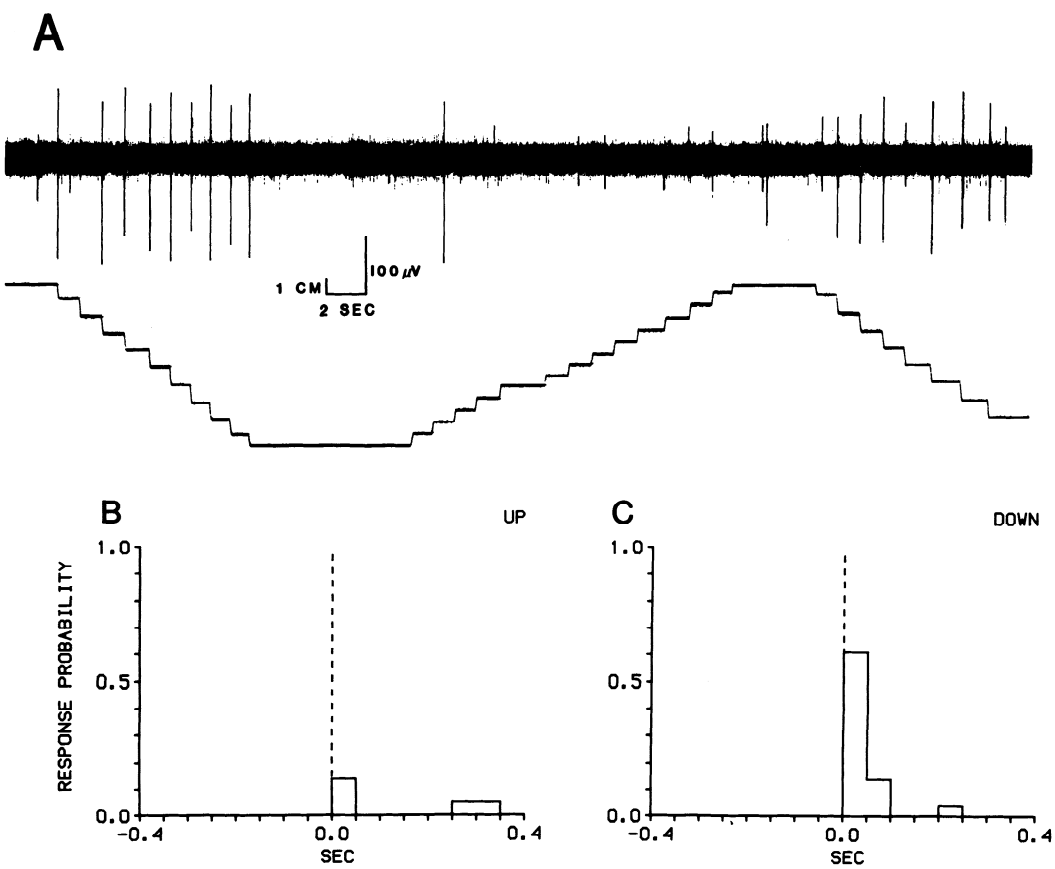

FIG. 7. The response of an olivary cell to passive displacement of the forelimb (lower trace) is shown in *A*. The cell did not respond to upward displacement, but responded reliably to small downward movements. The response consisted of 1 spike, and was independent of initial position. The histograms summarize the data for 32 upward (*B*, 5 spikes) and 36 downward (*C*, 22 spikes) displacements, and emphasize the directional dependence of the response.

ses to displacement is directional selectivity. The preference of the cell in Fig. 7*A* for downward displacement is shown in the histograms of Fig. 7, *B* and *C*. Very little response ($P = 0.14$) is seen to displacement in the direction opposite to the preferred direction. This implies the existence of a distinct axis along which both the best response and a complete lack of response are seen; this seemed to be true for all cells tested. Figure 6*B* shows the location within the IO of cells with preferred displacements in various directions and shows that they are distributed throughout the IO but are found most often in the MAO and PO.

An example documenting directional preference is given in Fig. 8. The entire limb was displaced up and down (typical amplitude 0.8–1.3 cm, velocity 10–20 cm/s) back and forth or laterally (0.9–6.0 cm, 9–20 cm/s). For the cell in this figure downward displacement produced the best response ($P > 0.9$), whereas upward movement produced no increase above spontaneous activity. For this cell, as with all others tested, displacement along the axes orthogonal to the best-/no-response axis produced intermediate responses. Thus, displacing both forelimbs to the left produced a good response ($P > 0.7$), whereas displacements to the right, back, and front gave weaker ($P \cong 0.35$) responses. We normally restricted testing to these 6 directions, but for one cell we noted a best-/no-response axis in the horizontal plane at an angle of about 30° to the anterior-posterior axis. From a sample of 35 cells tested in all 6 directions a total of 14 cells responded best to downward displacement. For eight cells upward displacement was the most effective stimulus. Additional preferences were for adduction (8 cells) and abduction (5 cells). Although backward and forward displacement were also systematically tested, no cells produced an optimal response in either of these directions.

To establish whether the response to displacement involved more than one joint, we occasionally rotated individual joints while observing the response of the unit ($n = 26$). Although most cells ($n = 14$) responded to rotation only around a single joint, a number responded to rotation around several joints. All the possible combinations were seen; responses to rotation of all three joints ($n = 2$); responses to wrist/ankle and elbow/knee ($n = 3$), or elbow/knee and shoulder/hip ($n = 4$). In addition, three cells were seen that responded to rotation about the wrist and the shoulder but not the elbow. The presence of the last mentioned group is indicative of substantial complexity in the afferent input to the IO, because it implies that individual cells may be activated by more than one muscle, which may be some distance apart. This is supported by our occasional observation of cells that did not respond reliably to manipulation of any one joint, but responded well to displacement of the entire

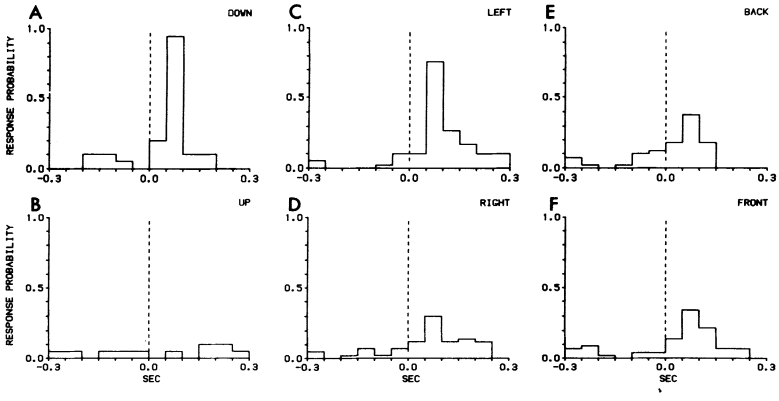

FIG. 8. This set of histograms shows the response of an olivary cell to displacement in six orthogonal directions. The cell responded best to downward displacement of both forelimbs (*A*), and did not respond at all to upward displacement. Displacement in the other directions produced intermediate responses; leftward (*C*) displacement (of either or both limbs), produced a reliable response; while displacement to the right, back, or front (*D, E, F*) produced weaker responses.

limb by the platform. Thus, there appear to be cells that reach threshold for activation only when several joints are moved simultaneously, perhaps in specific combinations. As a striking example of multijoint involvement in the response we noted three cells responding to lateral displacement of both hindlimbs or forelimbs. These cells responded to displacement of both limbs in the same direction in space; that is, if the contralateral limb responded to adduction, the ipsilateral limb responded to abduction.

Our present limited observations indicate that the response is rather independent of the amplitude and the velocity of the displacement through most of the range we tested. There does, however, appear to be a threshold for both of these parameters; below a given velocity and amplitude a particular cell would not respond reliably. For downward displacement, the amplitude threshold was generally less than 1 cm, whereas that for lateral displacements appeared to be in excess of 2 cm. Our methods did not allow the quantitative measurements needed for a careful study of these factors.

Modulation of responsiveness during active movement

During our study of the somatosensory properties of olivary cells we were surprised by the relative silence of these cells while the animals were engaged in active movements such as agitated scrabbling, spontaneous lifting of the limbs, and performance of a simple bar-pressing task. The remarkable sensitivity of olivary cells to somatosensory stimuli, whether cutaneous or proprioceptive, had led us to expect significant modulation of neuronal activity associated with active movement since these movements would seem to be accompanied by a rich array of sensory events.

To study the apparent lack of response to self-produced stimuli, we developed the task requiring alternate placing of a limb onto two touch-sensitive plates as described in METHODS. This task was intended to utilize the common representation of the ventral surface of the paw throughout the IO, since touch down on the plates would provide repeated natural self-produced cutaneous stimulation. We examined the responses of cells with receptive fields in this region to both externally applied and self-produced stimulation. All 32 of the cells included in the sample responded reliably to low-threshold stimulation of one or more of the following types: touch, puffs of air, vibration of the resting surface, slip and light taps. All had receptive fields that included sensitive zones on the ventral surface of the forepaw or the hindpaw.

The results provided strong support for the earlier observation of a lack of response to self-produced stimuli. In all but one of the 32 single-unit recordings the response during active touch down was indistinguishable from spontaneous levels of activity. Figure 9 provides an example of a cell which was one of the most sensitive that we encountered. The cell responded to the mildest touch in the receptive field (shown to the right of the figure). It also responded to light puffs of air (Fig. 9, upper), and even to the slightest vibration of the recording table. The response to vibration disappeared when the hindlimb was lifted from the support surface. (Note the absence of background firing in the upper panel, where the limb was suspended in the air, compared with the lower panel, where the limb was picked up and moved down to the touch plate.) The upper part of Fig. 9 shows that the response probability to a puff of air in the receptive field was 0.85 in 100 ms. When the stimulus was produced by the animal actively contacting the touch plate, after the experimenter lifted the paw and released it, the response probability did not exceed the background level (lower panel).

In another instance we recorded from a cell with a receptive field extending from the ventromedial to the dorsomedial surface of the forepaw (shown to the right of Fig. 10). This cell responded to a 4.5-mg force applied to the receptive field, as well as to slip of the paw over the support surface and puffs of air in the receptive field. The cell responded with a probability of 0.82 to the last mentioned stimulus (Fig. 10*A*). We further obtained recordings from the cell while the animal performed the alternating behavioral task. The results from these recordings are shown in Fig. 10*D*, which shows that no increase in response probability is associated with touch down compared with spontaneous activity of the cell (Fig. 10*B*). Although we have no direct measure of the force exerted

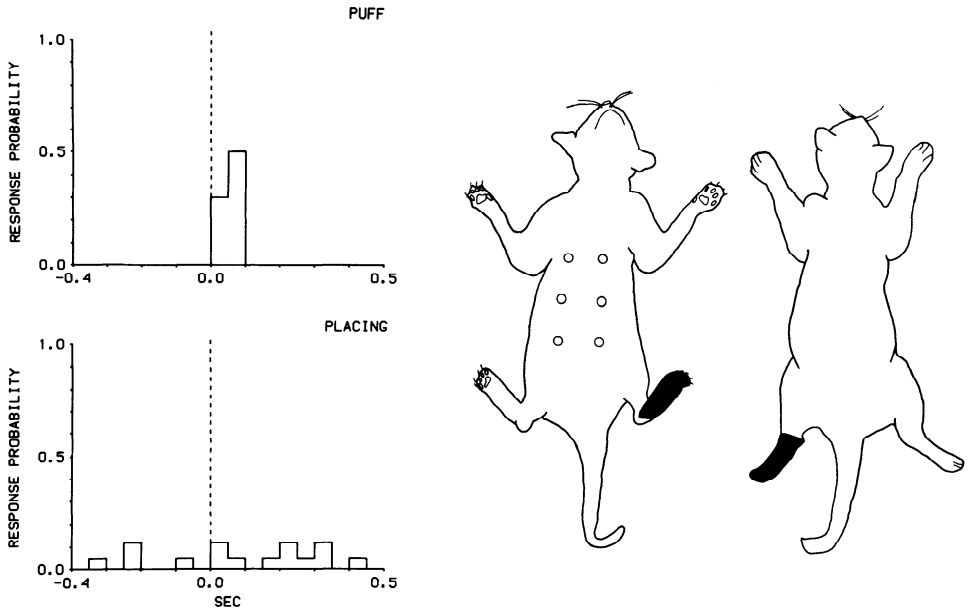

FIG. 9. The upper histogram shows the response of a cell to repeated puffs of air in the receptive field (*right panels*). The cell was also responsive to light touch and mild vibration of the surface on which the animal rested. When the animal placed its paw on the surface (lower histogram, the *broken vertical line* shows the time of contact) no response above background levels was seen. The increased background activity in the lower histogram was due to slight vibrations occurring while the paw rested on the surface and by the experimenter lifting the paw before the animal placed it. The low probability of response prior to touchdown implies that refractoriness of the unit cannot account for the lack of response.

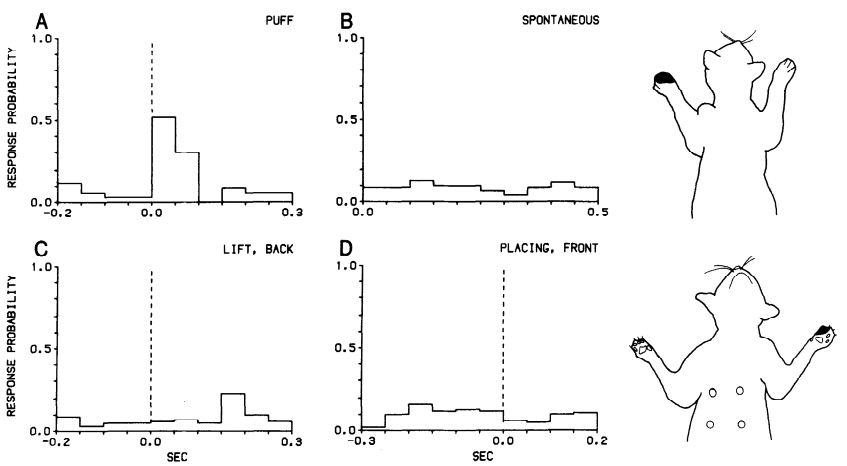

FIG. 10. The reliable (82% in 100 ms) response of an olivary cell to a puff of air in the receptive field (shown *right*) is shown in *A* (33 trials; 42 spikes). The spontaneous activity, sampled over 68 intervals where the limb was not moved, is shown in *B* for comparison (63 spikes). When the animal placed its paw on the surface, making contact with the receptive field, no response was seen (*D*) (94 trials; 90 spikes). In *C* (94 trials, 76 spikes) a small increase in response probability is seen at 150–200 ms; this was apparently due to the limb "bumping" into the barrier (see Fig. 1*A*) on approximately ⅓ of trials.

by the animal on touch down, it is likely that this force exceeded the 4.5 mg that was sufficient to activate the cell in the absence of movement.

On five occasions we recorded from multiple units with receptive fields on the ventral surface of the paw. In all these cases there was a slight increase in response probability just after touch down (mean response probability = 0.35; mean spontaneous probability = 0.12). In two of these instances the response probability exceeded 0.5; one record involved four units that had a combined response probability of 0.73 in 100 ms (spontaneous probability 0.17) for touch down on one of the two touch plates. In the other case, involving two or three units, response probability was 0.56 for touch down, compared with spontaneous probability of 0.08. On a per-cell basis, however, the response was rather small.

The responsiveness of olivary cells to self-produced cutaneous stimuli reappeared under conditions where the stimulus might convey particularly significant information. For example, when the animal encountered an unexpected obstacle, such as an object placed in the trajectory of a descending paw, 9 of 10 cells studied fired when that object made contact with the receptive field. An example of a response to an "accidental" self-produced stimulus is shown in Fig. 10*C* where the increase in probability of discharge above the spontaneous level of activity (to 0.23) that occurs at 100–150 ms was associated with the animal bumping into the barrier that separated the two touch plates on about a third of all trials. Likewise, during exploratory movements with the forelimb cells with appropriately located receptive fields were activated by self-produced contact.

Proprioceptive cells also were surprisingly unresponsive to self-produced stimuli. When the animal performed a movement that superficially mimicked an externally applied stimulus that reliably activated a cell, no response was seen in 79% of 75 cells for which an adequate passive stimulus was defined. In the remaining 21% there appeared to be weak modulation of the response, as judged by listening to the neuronal activity over the audio monitor. This dichotomy between the responses to active and passive stimuli existed in the face of apparent similarity between the two conditions. In the behavioral task the animal moved the limb 2–3 cm upward, then 6–8 cm back or forth, and finally 2–3 cm downward. Movement time was 300–600 ms, yielding velocities in the range of 15 to 50 cm/s. For the passive stimulus we typically displaced the limb 0.5–8.0 cm, using a comparable velocity range (typically 20 cm/s). We were able to collect sufficient data during performance of the alternating task for seven cells. These were selected as good candidates because listening to the unit activity on the audio monitor seemed to show some modulation with movement. Although none of these fired reliably during any phase of the movement (the greatest response probability that we observed was 0.33 in 100 ms, compared with values of 0.8 or greater for passive stimuli), two of the cells showed a weak, but statistically significant, modulation during movement. One example is that of a cell responsive to passive retraction of the shoulder. The number of spikes occurring during 64 200-ms periods preceding touch down and following lift-off, on the back and front touch plates, respectively, was 14, 22, 16, and 2. Spontaneous activity over a similar period (64 periods, 200 ms each) of standing quietly generated 11 spikes. When these five values were compared for significant deviations by means of a χ^2 test, the modulation was found to be significant ($P < 0.01$), although the probability of response during any 200-ms period was never greater than 0.34.

ELECTRICAL STIMULATION. In an attempt to define possible motor consequences of olivary activity, we applied microstimulation (see METHODS) at 25 sites in the inferior olive. These sites were distributed through all olivary subdivisions: 8 in the DAO, 13 in the MAO (including the ventrolateral outgrowth and dorsomedial cell column), and 4 in the PO. We stimulated in regions where forelimb cells, hindlimb cells, or unresponsive cells were recorded. We looked for effects of microstimulation by observing the animals' limbs or by supporting the limbs by hand in an attempt to feel subtle movements that might not have been visible. In no instance did we detect any movement being produced

or modified, whether the animal was quiescent or actively moving, by the stimulation. Low-intensity stimulation in the adjacent lateral reticular nucleus and in the hypoglossal nerve produced distinct well-defined movements.

DISCUSSION

A remarkably high percentage of cells in the inferior olive was found to be responsive to natural somatosensory stimulation (85%), and the responses observed generally exhibited high sensitivity and specificity for modality and spatial features. High sensitivity for discrete tactile stimuli has been reported previously for cells in the rostral dorsal accessory olive (rDAO) (25) and for climbing fiber responses in parts of the cerebellum that receive projections from the rDAO (52). The remaining subdivisions of the inferior olive have been described as weakly responsive or unresponsive by most previous authors. On the basis of evoked responses to electrical stimulation of peripheral nerves, Oscarsson (46) concluded that spinoolivary pathways generally require activation of high-threshold afferents (the FRA, or flexor reflex afferents), lack modality specificity, and are spatially diffuse. He suggested that the main function of the spinoolivary pathways is to forward information about activity in central motor centers rather than to signal peripheral events. However, we found no clear cases in which olivary discharge occurred in relation to the animal's movements. Our results suggest that spinoolivary pathways transmit information from well-defined receptive fields. Each cell appears to respond best to a limited set of somatosensory stimuli and not to information about central motor activity.

Several factors may have contributed to the high degree of responsiveness found in the present study. One is the use of natural as contrasted with electrical stimulation. The discharge of olivary cells may require the activation of particular combinations of sensory receptors readily produced by natural stimulation but difficult to reproduce with nerve stimulation. The extensive search we made for the receptive field of each cell may also be an important factor. This search was facilitated by the design of our apparatus since most of the body parts were accessible to manipulation. Finally, the present recordings were made in awake animals. The importance of the latter factor can be assessed by comparison with a recent study in which we used essentially the same methods for stimulation and for mapping receptive fields, but the cats were either anesthetized or decerebrated (25). While the percentage of responsive cells was only slightly less in rDAO (96% vs. 100% in the present study), the responsive percentage was appreciably less in the other olivary subdivisions (61% vs. 83%). Another indication that responsiveness was depressed in the anesthetized and decerebrate animals is that stronger stimuli were frequently required in these preparations as contrasted with the awake animal.

Origin of sensory responsiveness

A number of spinoolivary pathways have been demonstrated with electrophysiological techniques (44, 45, 47), although only 2 have been traced anatomically (13). This is because several pathways involve polysynaptic linkages. One of the anatomically demonstrated pathways relays in the dorsal column nuclei, and the other is a direct tract traveling in the ventral funiculus.

The dorsal column and the ventral funiculus pathways send somatotopically organized projections to the contralateral DAO and a less organized crossed projection to cMAO (12). These observations agree well with the physiological representations in these regions (RESULTS; Ref. 25) which demonstrate a strict somatotopic map in the DAO (Fig. 2) and a less organized representation in cMAO (Fig. 3). In the DAO, the hindlimb, forelimb, and face are represented in a lateral-to-medial progression. The medial face area corresponds to a region receiving terminals from the spinal trigeminal nucleus (11). A polysynaptic pathway traveling in the dorsolateral funiculus appears to be organized in conformity with the rostral portion of the same DAO map (34). Thus, three distinct spinoolivary pathways are in somatotopic register; they combine to yield a single detailed map of the contralateral body surface in rDAO.

The receptive fields we find in rDAO are similar in modality and size to those described for dorsal column cells (cf. Ref. 65) and also for the indirect pathway via the dorsolateral funiculus (34). For example, many rDAO cells are responsive to gentle air puffs that

bend hairs corresponding to the frequent sensitivity to hair bending reported for dorsal column cells. Both small and large receptive fields are found for both dorsal column cells and rDAO neurons. In both cases the small fields occupy only the distal limb. The low percentage of rDAO cells that are responsive to proprioceptive stimuli may obtain their input from those dorsal column cells that receive projections from muscle spindles (50). Alternatively, these proprioceptive signals may be transmitted by the ventral funiculus pathway, which also receives projections from muscle afferents (44).

The predominance of cutaneous cells in rDAO reverses to a predominance of proprioceptive cells in cDAO and MAO. Perhaps this relates to the fact that the caudal regions receive a less prominent input from the dorsal columns (cf. Ref. 13). If so, this would suggest that the ventral funiculus pathways are important for transmitting proprioceptive signals. There is a medial region of cMAO adjacent to the dorsal cap where we rarely encountered somatosensory cells (Fig. 3); this particular region is also spared by the projections of the ventral funiculus and dorsal column pathways (13).

We did not find any significant difference between the somatosensory responsiveness of the rostral and caudal halves of MAO. In contrast, the anatomic data indicate a striking difference in the distribution of terminals from the dorsal column and ventral funiculus pathways; these terminals are prominent in cMAO and apparently absent in rMAO (13). Evidently the somatosensory input to the rMAO is transmitted entirely by a polysynaptic pathway. There is a lateral funiculus pathway, demonstrated by Larson et al. (35) using electrophysiological techniques, which projects to a sagittal zone in intermediate cerebellar cortex (the C2 zone) that is known to receive climbing fibers from rMAO. This lateral funiculus pathway is the likely origin of the somatosensory signals that we recorded in rMAO. The latter pathway is dominated by input from the forelimb (35), an observation that fits well with our finding that most cells in rMAO have forelimb receptive fields.

The requirement of stronger stimuli in anesthetized animals is particularly well illustrated by cells responsive to proprioceptive stimuli. In the awake cat many olivary cells were responsive to small displacements of a limb and to passive joint rotation. Our percentage estimate, based on results in the later phases of this study, is about 30% of olivary neurons. In marked contrast, we noted no cells that responded reliably to joint rotation in our study with anesthetized and decerebrate cats. Instead, we encountered cells categorized as "deep" that were responsive to squeeze or sharp taps applied to limb muscles; the latter are strong stimuli that were generally not required in the present study. Taps and muscle squeeze are effective stimuli for eliciting massive discharge from muscle proprioceptors, particularly from primary spindle receptors. Massive activation of these receptors presumably was required to overcome depressant effects of anesthesia or decerebration on transmission through spinoolivary pathways.

Stretch of a single forelimb muscle in regionally anesthetized cats produces climbing-fiber spikes in Purkinje cells of intermediate cerebellar cortex (42). The responsive cells were located in a large patch in lobule V that clearly included the C2 projection zone innervated by rMAO as well as the C1 and C3 zones innervated by rDAO. These responses were attributed to input from primary and secondary spindle receptors in some combination. The proprioceptive cells encountered in the present study may derive their sensitivity to limb displacement in a preferred direction as a consequence of convergent input from spindle receptors of several muscles. The presence of cells responsive to stimulation at widely separated joints supports this suggestion. The depressed state of many spinoolivary pathways in anesthetized or decerebrate cats apparently translates the high sensitivity to limb displacement characteristic of the awake animal into a weak responsiveness to squeeze of deep structures and a responsiveness to electrical stimulation of high-threshold afferents, namely the FRA, that converges from several peripheral nerves. Evidently an awake animal is required to obtain interpretable responses of these proprioceptive neurons to natural stimulation.

Like the rMAO, the PO receives practically no direct somatosensory input. Ekerot and Larson (24) found short-latency (10- to 20-ms) responses to peripheral nerve stimulation

in the D2 zone of anterior cerebellum, which receives input primarily from the PO; they speculated that these responses might stem from the DAO, since the PO was not known to receive somatosensory input. Our results suggest an alternative explanation, namely that these responses are transmitted through the PO. In our study ~75% of the cells in the PO were responsive to somatosensory stimuli.

Somatic event detection

The binary nature of the response of an olivary cell has fostered the notion that these neurons serve as event detectors (29, 42, 51; for an alternative view, see Ref. 33). A typical neuron responsive to cutaneous stimulation fires a single spike in response to contact with an external object independent of the intensity and duration of contact (RESULTS; Ref. 51). The failure of the response to grade with intensity and duration derives from a biophysical limitation peculiar to IO neurons; these cells produce a prolonged action potential that is followed by a refractory period lasting about 100 ms (37, 38). In the awake cat the threshold for evoking a one-spike response is typically extremely low, and the response above threshold is highly reliable. Thus, it is unlikely that significant sensory events would be missed. Since the receptive fields of these cells occupy different locations on the body surface, discharge of a particular cell provides specific information concerning the site of contact. Thus, although intensity and duration appear not to be important parameters, location on the body surface clearly is.

Several other categories of cutaneous neurons found in this study are also excellent candidates for somatic event detectors. Cells sensitive to slip respond when the support surface slides under the footpad in a given direction, or when the footpad slides across the support surface in the opposite direction. The event detected is a slip having a particular direction. Other cells sensitive to removal of pressure on the footpads detect loss of contact between the foot and the support surface. Cells sensitive to vibration detect trembling of the support surface.

A typical proprioceptive neuron fires a spike when a limb is passively displaced. Since different cells are sensitive to displacements of different limbs in different directions, something analogous to the location code of cutaneous neurons is preserved. Parameters that appear to be less important are the amplitude and velocity of displacement and the initial position of the limb. Another category of proprioceptive neuron is responsive to tugs on muscle and appears suitable for the detection of abrupt mechanical loads.

At least 85% of olivary cells respond to an appropriate somatosensory stimulus and can be considered somatic event detectors. We saw little evidence that the somatosensory cells respond to other sensory modalities, and other modalities seem to be relatively poorly represented. Possible exceptions to this are vestibular cells and visual cells. We did not test for vestibular responsiveness though it is known that portions of the IO receive a dense input from the vestibular nuclei (54). Cells responding to vestibular input would be sensitive to body movement and can be considered as another type of somatic event detector. Cells responsive to visual input are also found in portions of the IO, particularly the dorsal cap, in both the rabbit (6) and the cat (RESULTS; Ref. 25). Visual IO cells are specialized for particular types of stimuli, mainly large fields moving at low velocities (6). These properties contrast strongly with the properties of visual cells in the cerebral cortex or superior colliculus (27), or even other sources of visual input to the cerebellum (5, 41). The stimuli to which visual olivary cells respond are appropriate for eliciting optokinetic nystagmus and, when viewed, produce a powerful sensation of body movement. Thus, it seems that even the visual cells in the IO may be characterized as somatic event detectors.

Behavioral modulation

Several investigators have reported that complex spike activity in Purkinje cells in the monkey is only poorly, if at all, correlated with active movement under normal circumstances (39, 60). Our results seem to provide an explanation for this observation; olivary cells carry almost exclusively sensory signals, and these are substantially reduced or absent during active movement. Recently Bauswein et al. (8) made a direct comparison of Purkinje cell activity during active versus passive limb movements in the monkey. Climbing fiber responses were seen in both cases though

they were typically weaker or absent during active movement. Judging from their illustrations, passive movements usually produced response probabilities of ~0.3, which is low compared with responsiveness in our study and provides a less-than-ideal reference for evaluating behavioral suppression. In one illustrated case (Ref. 8, Fig. 4), response probability to passive movement was particularly high (~0.8 according to our calculation), and in that case the response during active movement was markedly depressed.

What mechanism might underlie the apparent absence of olivary response to self-produced stimuli, given the great sensitivity of these cells to externally applied stimuli? It seems unlikely that a difference in stimulus quality accounts for the observed dichotomy. First, we have noted that passive and self-produced proprioceptive stimuli lie in the same velocity and amplitude range. Second, no response to self-produced stimulation is seen in cutaneous cells, whether they are best activated by light touch, taps, puffs of air, vibration, or slip. The possibility that none of these stimuli is present during active touch down in the movement task seems unlikely.

Modulation of proprioceptive sensitivity could occur peripherally or centrally. Evidence reviewed earlier suggests that primary endings of muscle spindles may contribute importantly to the high sensitivity of proprioceptive cells. If so, the changes in sensitivity seen in the olive could result from modulation of spindle intrafusal muscle contraction controlled by activity in gamma motor fibers. Data on spindle activity in freely moving cats suggests that primary ending sensitivity may be reduced during stepping, an effect attributed to static gamma activity (48). However, the differences in responsiveness are not great and may be inadequate to explain the observed depression of proprioceptive responses in the olive.

Modulation of tactile sensitivity is likely to occur centrally since peripheral cutaneous receptors are not known to be under efferent control. Prior studies have demonstrated a 20% depression in medial lemniscus potentials for 100–200 ms before and after an active movement (18, 26), and a corresponding elevation in tactile threshold has been shown for humans (21). However, the time course of the former process appears to be inappropriate to explain our results with cutaneous IO cells. We found that cells unresponsive to touchdown are exquisitely sensitive to objects encountered in the course of movements. The modulation of sensitivity we found for cutaneous IO cells is more analogous to that reported for a subpopulation of cells in the sensory cortex of the rat (16, 17). Although the cortical effects might be attributed to a mechanism operating at the level of the dorsal column nuclei, Chapin and Woodward (16, 17) favored a mechanism operating in the sensory cortex. The modulation of olivary response we observed may likewise occur at the level of the dorsal column nuclei, which are known to receive cortical input (64), or at the level of the spinal cord. It is tempting, however, to speculate that the modulation occurs in the IO itself, and that it is produced by one or more of the many inputs to this region from the cerebellar nuclei (9, 12, 62), the brain stem (55, 56, 57), and the cerebral cortex (13, 53, 55, 58, 63). Modulation by the cerebellum is a particularly intriguing idea, since efference copy of a hypothetical motor command from the cerebellum may well carry the timing information needed to produce the timed reduction in sensitivity displayed by olivary cells responsive to cutaneous stimulation. The reported presence of a (presumably inhibitory) GABAergic projection from the cerebellar nuclei to the inferior olive (43) in the rat lends credence to this suggestion.

Bell (10) reviewed three functional categories of effects that motor commands may have on sensory inflow, providing several examples of each. One effect is a simple inhibition or depression of responsiveness that prevents self-produced stimuli from activating a sensory channel. The second is an efference copy mechanism in which a negative image of expected reafference is used to cancel self-produced responses without impairing responses to unexpected inputs. The third is a facilitatory mechanism that serves to enhance responsiveness during exploratory movements. We are not yet certain which of these categories applies best to the gating found for olivary neurons. A simple inhibitory process could explain the absence of tactile responses during touchdown and the absence of proprioceptive responses during the whole duration of active movement. However, one

needs to postulate that the inhibitory gating is timed to occur just at the end of the movement in order to account for the responsiveness of cutaneous cells to contacts that interrupt a movement. It would be interesting to test proprioceptive cells for responses to perturbations delivered during movement, since a positive result would argue for an efference copy mechanism. This would support the error signal hypothesis of Oscarsson (46). Finally, the high responsiveness of tactile cells during exploratory movements may indicate sensory enhancement. Further studies will be required to distinguish between these alternatives.

Functional consequences of olivary discharge

The present results indicate that the IO provides a signal to the cerebellum when a part of the body is passively displaced or contacted. Displacement or contact resulting from self-produced movements ordinarily do not activate olivary cells, although contact during exploratory movements or contact that interrupts a movement part way through its trajectory produces a reliable response. In other words, the IO appears to signal unexpected (i.e., externally imposed) somatic events. What could be the functional consequences of such a signal for the cerebellum?

One possibility is that this discharge is used to trigger corrective responses or reaction-time movements (29, 36). In this view, the unexpected somatic events that fire IO cells would signal that a problem has arisen, and climbing fiber input to the cerebellum would trigger a corrective movement. Given the somatic emphasis of IO signals described here, the trigger theory does not explain how movements can be initiated by small visual targets or by auditory cues. Furthermore, the lack of motor consequences from olivary stimulation and lack of movement relations seems to argue against a trigger function.

Another possibility is that olivary discharge functions to produce long-term adaptive changes in the cerebellum that then mediate learned motor responses (1, 32, 40, 61). The theories proposed by Marr (40) and Albus (1) postulate that those particular parallel fiber synapses that are active at the time of a climbing fiber spike, are either strengthened (40) or weakened (1) as a basis for the learning. More importantly from the standpoint of the present results, both models assume that the IO cells transmit representations of higher motor commands; Purkinje cells then learn to initiate movements automatically without the involvement of higher centers. These theories would have to undergo appreciable revision to be compatible with our observation that IO cells are reliably driven by sensory stimuli and not by motor events. A subsequent model proposed by Albus (2, 3) postulates that the learning input to a cerebellar model transmits error information about the differences between actual (sensory signal) and desired (efference signal) movements; output cells then learn to produce improved movement commands. While the unexpected contact detectors described here might be appropriate error signals for this model, a comprehensive theory should also take account of the reliable responses of IO cells to contact or passive displacement in the absence of movement.

A third possibility is that the olive provides the cerebellum with a signal that body position is no longer accurately represented by efference copy. It has often been suggested that the central nervous system uses efference copy, rather than afferent input, in its internal representation of body position (e.g., Ref. 28). However, when a limb is displaced passively, for example if it slips, afferent information must be used to correctly update this internal representation. Olivary neurons would be activated in such circumstances and thus might provide a signal to the cerebellum to take afferent information into account when next updating the representation of body position.

All of these possibilities warrant further testing, and the work on olivary signals presented here should help to focus upon critical tests of specific functional hypotheses.

ACKNOWLEDGMENTS

The authors thank Dannie Hansma for assistance with artwork and histology.

This work was supported by Grant PO1-NS17489 from the National Institutes of Health.

Received 24 May 1984; accepted in final form 17 January 1985.

REFERENCES

1. ALBUS, J. S. A theory of cerebellar function. *Math. Biosci.* 10: 25–61, 1971.
2. ALBUS, J. S. A new approach to manipulator control: the cerebellar model articulator controller (CMAC). *J. Dyn. Syst. Meas. Control* Sept.: 220–227, 1975.
3. ALBUS, J. S. Data storage in the cerebellar model articulator controller (CMAC). *J. Dyn. Syst. Meas. Control* Sept.: 228–233, 1975.
4. ARMSTRONG, D. M. AND HARVEY, R. J. Responses in the inferior olive to stimulation of cerebellar and cerebral cortices in the cat. *J. Physiol. London* 187: 553–574, 1966.
5. BAKER, J., GIBSON, A., GLICKSTEIN, M., AND STEIN, J. Visual cells in the pontine nuclei of the cat. *J. Physiol. London* 255: 415–433, 1976.
6. BARMACK, N. H. AND HESS, D. T. Multiple-unit activity evoked in dorsal cap of inferior olive of the rabbit by visual stimulation. *J. Neurophysiol.* 43: 151–164, 1980.
7. BARMACK, N. H. AND HESS, D. T. Eye movements evoked by microstimulation of dorsal cap of inferior olive in the rabbit. *J. Neurophysiol.* 43: 165–181, 1980.
8. BAUSWEIN, E., KOLB, F. P., LEIMBECK, B., AND RUBIA, F. J. Simple and complex spike activity of cerebellar Purkinje cells during active and passive movements in the awake monkey. *J. Physiol. London* 339: 379–394, 1983.
9. BEITZ, A. J. The topographical organization of the olivo-dentate and dentato-olivary pathways in the cat. *Brain Res.* 115: 311–318, 1976.
10. BELL, C. C. Effects of motor commands on sensory inflow, with examples from electric fish. In: *Comparative Physiology of Sensory Systems,* edited by L. Bolis, R. D. Keymes, and S. H. P. Maddrell. Cambridge: Cambridge Univ. Press, 1984, p. 637–646.
11. BERKLEY, K. J. AND HAND, P. J. Projections to the inferior olive of the cat: II—comparisons of input from the gracile, cuneate, and spinal trigeminal nuclei. *J. Comp. Neurol.* 180: 253–264, 1978.
12. BERKLEY, K. J. AND WORDEN, I. G. Projections to the inferior olive of the cat: I—comparisons of input from the dorsal column nuclei, the lateral cervical nucleus and the spino-olivary pathways, the cerebral cortex and the cerebellum. *J. Comp. Neurol.* 180: 237–252, 1978.
13. BLOEDEL, J. R. AND COURVILLE, J. Cerebellar afferent systems. In: *Handbook of Physiology. The Nervous System.* Bethesda, MD: Am. Physiol. Soc. 1981, sect. 1, vol. 2, pt. 2, chapt. 16, p. 735–829.
14. BOYLLS, C. C. Contribution to locomotor coordination of an olivo-cerebellar projection to the vermis in the cat: experimental results and theoretical proposals. In: *The Inferior Olivary Nucleus: Anatomy and Physiology,* edited by J. Courville, C. de Montigny, and Y. Lamarre. New York: Raven, 1980.
15. BRODAL, A. Experimentelle untersuchungen ueber die Olivo-cerebellare lokalisation. *Z. Gesamte Neurol. Psychiatr.* 169: 1–153, 1940.
16. CHAPIN, J. K. AND WOODWARD, D. J. Somatic sensory transmission to the cortex during movement: gating of single cell responses to touch. *Exp. Neurol.* 78: 654–669, 1982.
17. CHAPIN, J. K. AND WOODWARD, D. J. Somatic sensory transmission to the cortex during movement: phasic modulation over the locomotor step cycle. *Exp. Neurol.* 78: 670–684, 1982.
18. COULTER, J. D. Sensory transmission through lemniscal pathway during voluntary movements in the cat. *J. Neurophysiol.* 37: 831–845, 1974.
19. COURVILLE, J. AND FARACO-CANTIN, F. On the origin of the climbing fibers of the cerebellum. An experimental study in the cat with an autoradiographic tracing method. *Neuroscience* 3: 797–809, 1978.
20. CRILL, W. E. Unitary multiple-spiked responses in cat inferior olive nucleus. *J. Neurophysiol.* 33: 199–209, 1970.
21. DYHRE-POULSON, P. Perception of tactile stimuli before ballistic and during tracking movements. In: *Active Touch,* edited by G. Gordon. New York: Pergamon, 1978, p. 171–176.
22. EBNER, T. J., YU, Q-X., AND BLOEDEL, J. R. Increase in Purkinje cell gain associated with natural activation of climbing fiber input. *J. Neurophysiol.* 50: 205–219, 1983.
23. ECCLES, J. C., SABAH, N. H., SCHMIDT, R. F., AND TABORIKOVA, H. Cutaneous mechanoreceptors influencing impulse discharges in cerebellar cortex. III. In Purkinje cells by climbing fiber input. *Exp. Brain Res.* 15: 484–497, 1972.
24. EKEROT, C. F. AND LARSON, B. The dorsal spino-olivocerebellar system in the cat. I. Functional organization and termination in the anterior lobe. *Exp. Brain Res.* 36: 201–217, 1979.
25. GELLMAN, R. S., HOUK, J. C., AND GIBSON, A. R. Somatosensory properties of the inferior olive in the cat. *J. Comp. Neurol.* 215: 228–243, 1983.
26. GHEZ, C. AND LENZI, C. L. Modulation of sensory transmission in cat lemniscal system during voluntary movement. *Pfluegers Arch.* 323: 273–278, 1971.
27. GIBSON, A., BAKER, J., MOWER, G., AND GLICKSTEIN, M. Corticopontine cells in area 18 of the cat. *J. Neurophysiol.* 41: 484–495, 1978.
28. GUTHRIE, B. L., PORTER, J. D., AND SPARKS, D. L. Corollary discharge provides accurate eye position information to the oculomotor system. *Science* 221: 1193–1195, 1983.
29. HOUK, J. C. Motor control processes: new data concerning motoservo mechanism and a tentative model for SR processing. In: *Posture and Movement,* edited by R. E. Talbot and D. R. Humphrey. New York: Raven, 1979.
30. ISHIKAWA, K., KAWAGUCHI, S., AND ROWE, M. J. Actions of afferent impulses from muscle receptors on cerebellar Purkinje cells. I. Responses to muscle vibration. *Exp. Brain Res.* 15: 177–193, 1972.
31. ISHIKAWA, K., KAWAGUCHI, S., AND ROWE, M. J. Actions of afferent impulses from muscle receptors on cerebellar Purkinje cells. II. Responses to muscle contraction: effect mediated via the climbing fiber pathway. *Exp. Brain Res.* 16: 104–114, 1972.
32. ITO, M., SAKURAI, M., AND TONGROACH, P. Climbing fibre induced depression of both mossy fibre responsiveness and glutamate sensitivity of cerebellar Purkinje cells. *J. Physiol. London* 324: 113–134, 1982.

33. KOLB, F. P. AND RUBIA, F. J. Information about peripheral events conveyed to the cerebellum via the climbing fiber system in the decerebrate cat. *Exp. Brain Res.* 38: 363–373, 1980.
34. LARSON, B., MILLER, S., AND OSCARSSON, O. Termination and functional organization of the dorsolateral spino-olivocerebellar path. *J. Physiol. London* 203: 611–640, 1969.
35. LARSON, B., MILLER, S., AND OSCARSSON, O. A spinocerebellar fibre path activated by the flexor reflex afferents from all four limbs. *J. Physiol. London* 203: 641–649, 1969.
36. LLINAS, R. Neuronal operations in cerebellar transactions. In: *The Neurosciences: Second Study Program,* edited by F. O. Schmitt. New York: Rockefeller Univ. Press, 1970.
37. LLINAS, R., BAKER, R., AND SOTELO, C. Electronic coupling between neurons in cat inferior olive. *J. Neurophysiol.* 37: 560–571, 1974.
38. LLINAS, R. AND YAROM, Y. Electrophysiology of mammalian inferior olivary neurons in vitro. Different types of voltage-dependent ionic conductances. *J. Physiol. London* 315: 549–567, 1981.
39. MANO, N. I. Simple and complex spike activity of the cerebellar Purkinje cells in relation to selective alternate movement in intact monkey. *Brain Res.* 70: 381–393, 1974.
40. MARR, D. A theory of cerebellar cortex. *J. Physiol. London* 202: 437–470, 1969.
41. MOWER, G., GIBSON, A., AND GLICKSTEIN, M. Tectopontine pathway in the cat: laminar distribution of cells of origin and visual properties of target cells in dorsolateral pontine nucleus. *J. Neurophysiol.* 42: 1–15, 1979.
42. MURPHY, J. T., MACKAY, W. A., AND JOHNSON, F. Differences between cerebellar mossy and climbing fibre responses to natural stimulation of forelimb muscle proprioceptors. *Brain Res.* 55: 268–289, 1973.
43. NELSON, B., BARMACK, N. H., AND MUGNAINI, E. A Gabaergic cerebello-olivary projection in the rat. *Soc. Neurosci. Abstr.* 10: 539, 1984.
44. OSCARSSON, O. Termination and functional organization of the ventral spino-olivocerebellar path. *J. Physiol. London* 196: 453–478, 1968.
45. OSCARSSON, O. Termination and functional organization of the dorsal spino-olivocerebellar path. *J. Physiol. London* 200: 129–149, 1969.
46. OSCARSSON, O. Functional organization of olivary projection to the cerebellar anterior lobe. In: *The Inferior Olivary Nucleus: Anatomy and Physiology,* edited by J. Courville, C. de Montigny, and Y. Lamarre. New York: Raven, 1980.
47. OSCARSSON, O. AND SJOLUND, B. The ventral spino-olivocerebellar system in the cat. I. Identification of five paths and their termination in the cerebellar anterior lobe. *Exp. Brain Res.* 28: 469–486, 1977.
48. PROCHAZKA, A. Muscle spindle function during normal movement. *Neurophysiology* 25: 47–90, 1981.
49. ROBERTSON, L. T., LAXER, K. D., AND RUSHMER, D. S. Organization of climbing fiber input from mechanoreceptors to lobule V vermal cortex in the cat. *Exp. Brain Res.* 46: 281–291, 1982.
50. ROSÉN, I. Afferent connexions to group I activated cells in the main cuneate nucleus of the cat. *J. Physiol. London* 205: 209–236, 1969.
51. RUSHMER, D. S., ROBERTS, W. J., AND AUGTER, G. K. Climbing fiber responses of cerebellar Purkinje cells to passive movement of the cat forepaw. *Brain Res.* 106: 1–20, 1976.
52. RUSHMER, D. S., WOOLACOTT, M. H., ROBERTSON, L. T., AND LAXER, K. D. Somatotopic organization of climbing fiber projections from low threshold cutaneous afferents to pars intermedia of cerebellar cortex in the cat. *Brain Res.* 181: 17–30, 1980.
53. SAINT-CYR, J. A. The projection from the motor cortex to the inferior olive in the cat. *Neuroscience* 10: 667–684, 1983.
54. SAINT-CYR, J. A. AND COURVILLE, J. Projection from the vestibular nuclei to the inferior olive in the cat: An autoradiographic and horseradish peroxidase study. *Brain Res.* 165: 189–200, 1979.
55. SAINT-CYR, J. A. AND COURVILLE, J. Projections from the motor cortex, midbrain, and vestibular nuclei to the inferior olive in the cat: anatomical organization and functional correlates. In: *The Inferior Olivary Nucleus: Anatomy and Physiology,* edited by J. Courville, C. de Montigny, and Y. Lamarre: New York: Raven, 1980.
56. SAINT-CYR, J. A. AND COURVILLE, J. Sources of descending afferents to the inferior olive from the upper brain stem in the cat as revealed by the retrograde transport of horseradish peroxidase. *J. Comp. Neurol.* 198: 567–581, 1981.
57. SAINT-CYR, J. A. AND COURVILLE, J. Descending projections to the inferior olive from the mesencephalon and superior colliculus in the cat. *Exp. Brain Res.* 45: 333–348, 1982.
58. SOUSA-PINTO, A. AND BRODAL, A. Demonstration of a somatotopical pattern in the cortico-olivary projection in the cat: An experimental anatomical study. *Exp. Brain Res.* 8: 364–386, 1969.
59. THACH, W. T., JR. Somatosensory receptive fields of single units in cat cerebellar cortex. *J. Neurophysiol.* 30: 675–696, 1967.
60. THACH, W. T. Discharge of cerebellar neurons related to two maintained postures and two prompt movements. II. Purkinje cell output and input. *J. Neurophysiol.* 33: 537–547, 1970.
61. THOMPSON, R. F., CLARK, G. A., DONEGAN, N. H., LAVOND, D. G., MADDEN, J., MAMOUNAS, L. A., MAUK, M. D., AND MCCORMICK, D. A. Neuronal substrates of basic associative learning. In: *Neuropsychology of Memory,* edited by L. Squire and M. Mutters. New York: Guilford, 1983.
62. TOLBERT, D. L., MASSOPUST, L. C., MURPHY, M. G., AND YOUNG, P. A. The anatomical organization of the cerebello-olivary projection in the cat. *J. Comp. Neurol.* 170: 525–544, 1976.
63. WALBERG, F. Descending connections to the inferior olive. *J. Comp. Neurol.* 104: 77–174, 1956.
64. WEISBERG, J. A. AND RUSTIONI, A. Differential projections of cortical sensorimotor areas upon the dorsal column nuclei of cats. *J. Comp. Neurol.* 184: 401–422, 1979.
65. WILLIS, W. D. AND COGGESHALL, R. E. *Sensory Mechanisms of the Spinal Cord.* New York: Plenum, 1978.