Responses of Cat Cerebellar Purkinje Cells to Convergent Inputs from Cerebral Cortex and Peripheral Sensory Systems

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THE PURKINJE CELLS provide the only output from the cerebellar cortex (17). Their responses to different inputs might, therefore, provide valuable clues to understanding how afferent information is processed by the cerebellar cortex. Compared with the wealth of recent literature concerning the anatomy (13, 28–30, 43, 58) and basic neuronal circuitry of the cerebellar cortex (6, 20, 21), relatively little is known about Purkinje cell unit activity in response to different physiological stimuli (4, 5, 15, 41, 46, 48, 50, 53–57). In this study, the temporal activity of individual Purkinje cells in the posterior vermis of the cat was studied in response to different inputs from the periphery and from the cerebral cortex. There were two main experimental objectives. The first was to study the distribution of sources of afferent activity at the single-unit level in order to characterize the functional inputs to different cells. This relates directly to the branching patterns of mossy fibers and the distribution of climbing fiber afferents to the cerebellar cortex. Is afferent information conveyed by these two classes of input fibers spatially segregated and distributed to particular groups of Purkinje cells (possibly lying along the same "beam" of parallel fibers (9)), or is it distributed in such a way that many Purkinje cells receive similar inputs? The second objective was to study the mechanisms of encoding of afferent information from specific peripheral inputs.

Experiments based on gross evoked potentials have shown that the posterior vermis receives auditory, tactile, and visual inputs from the periphery (1, 19, 42, 52) as well as a considerable afferent input from the cerebral cortex (2, 11, 12, 38, 51). It also receives inputs from other parts of the central nervous system (13, 17, 29). The detailed distribution of these different inputs to individual Purkinje cells is unknown. It is evident that some principles of sensory integration performed by the cerebellar cortex might be definable by interactions between different inputs.

In the work to be reported here, Purkinje cells in lobules VI and VII were found to receive a multiplicity of convergent inputs subserving different sensory modalities (somesthetic, auditory, and visual) from the periphery and from the cerebral cortex. Responses evoked by stimulaton of any one of many different inputs were very similar and consisted of a short burst of spikes followed by a long period of spike suppression. Specific information conveyed by a particular peripheral input or sequence of inputs did not appear to be preserved either by being distributed to a particular set of Purkinje cells or by producing any specific pattern of spikes. In this sense there appeared to be no obvious spatial or temporal coding mechanism relating the activity of Purkinje cells to different peripheral events. On the other hand, a facilitatory convergence between peripheral and cerebrocortical inputs in the same sensory modality was discovered. The probability of response of a Purkinje cell to a particular peripheral input was selectively increased by a concurrent input from that part of the primary sensory receiving area of the cerebral cortex

Received for publication February 6, 1970.

which received inputs from the same peripheral source. These results suggest that the posterior vermis processes afferent information according to a probabilistic rather than a spatial or temporal coding mechanism. The ability to distinguish subtle characteristics of different inputs which such a "tunable-filter" mechanism might produce are discussed.

METHODS

Sixty-four adult cats were used. Several initial experiments were directed at choosing the most suitable method of anesthesia. The use of spinal or decerebrate preparations was precluded because of the necessity of preserving inputs from both the spinal cord and from higher centers. Somnolence-producing lesions in the reticular formation proved to be unacceptable for the same reason. Several barbiturate preparations (Nembutal, 35 mg/kg intraperitoneally; Surital, 20 mg/kg intrathoracic; Thiopental, 60 mg/kg intraperitoneally) were tried. They severely reduced and, in many cases, completely abolished the responses of Purkinje cells to peripheral stimulation. Moreover, they greatly reduced the areas from which surface responses to different stimuli could be obtained. Similar difficulties with the use of barbiturate anesthesia have been reported previously (7, 16, 18, 52). Alpha-chloralose (50 mg/kg intravenously) produced neither of these difficulties, and was used in the experiments to be described.

Four control experiments were performed in which response characteristics of Purkinje cells in locally anesthetized cats (paralyzed with gallamine triethiodide, with 2% Xylocaine infiltrated in all wounds and pressure points) were compared to the responses obtained when the cats were subsequently administered alpha-chloralose, and were found to be substantially similar.

The exposure and preparation of the cerebellar cortex, the primary sensorimotor, auditory, and visual receiving areas of the cerebral cortex, and of the inferior olivary complex were similar to that reported by other investigators (3, 15). Cerebral pulsations were substantially reduced by performing a bilateral pneumothorax, and artificially respirating the animals. Temperature was maintained between 36 and 38 C.

Fine silver-ball electrodes were used to record cortical surface potentials. Extracellular field potentials were recorded with glass micropipettes filled with 4 M sodium chloride (NaCl) having a d-c resistance of 1–5 megohms. Single-unit responses were recorded extracellularly with tungsten microelectrodes (31) having a tip impedance of 1–2 megohms, measured at 1000 Hz. Spike potentials were coupled via a solid-state headstage to conventional recording equipment. A specially constructed spike-height discriminator (35) was employed to select a single unit for subsequent analysis.

In many of the experiments natural stimuli of the following type were presented: *a*) free-field auditory stimuli consisting of clicks, fixed-frequency tone bursts, and frequency-modulated tone bursts; *b*) visual stimuli consisting of light flashes of different intensity and duration (produced by a pulse-width modulated glow modulator tube photic stimulator (33)); and *c*) proprioceptive stimuli consisting of step or sinusoidally varying changes in tension (whose rate of change and amplitude were servocontrolled by a strain-gauge feedback system), delivered to joints and/or muscle tendons. Electrical stimuli, to be subsequently described, were delivered by a photoisolation unit. A specially constructed electronic stimulus-artifact suppressor (34) was employed to abolish unwanted stimulus artifacts. A LINC-8 computer was employed in later stages of the investigation to make a quantitative comparison between the responses of Purkinje cells to different types of stimuli.

RESULTS

Identification of Purkinje cells

Purkinje cells were identified either by *a*) orthodromic activation following stimulation of the inferior olive (21, 22) or *b*) antidromic activation following stimulation of the cerebellar white matter (21, 23). Single-shock stimulation of the inferior olive typically produced a burst of 1–6 spikes after a latency of 3–8 msec; these responses had an all-or-none characteristic similar to that described by Eccles et al. (21). Single-shock stimulation of the cerebellar white matter with a bipolar needle electrode in the region of the fastigial nucleus commonly produced, after a latency of 1–2 msec, a single spike which would follow stimulation frequencies up to 200/sec. Single units responding to stimulation of the inferior olive and/or to the cerebellar white matter were usually encountered at a depth of 350–550 μ beneath the pial surface. They exhibited rather irregular spontaneous activity. Inactivation responses (37) and spontaneously occurring climbing fiber responses (21) were fre-

quently observed in these units. Identification by antidromic activation was used only at the beginning of this investigation in order to avoid injuring incoming fibers in the cerebellar white matter by the stimulating electrode.

Responses of Purkinje cells to peripheral stimulation

The responses of a single Purkinje cell in lobule VI to several different types of natural and electrical stimuli are shown in Fig. 1. Beneath the spike records are shown the potentials recorded simultaneously from the pial surface overlying the recording microelectrode. Responses to two stimuli given several seconds apart are shown for each type of stimulus. Figure 1 shows the responses to brief electrical stimuli of the following structures: *A*, the skin of the dorsal surface of the ipsilateral foreleg; *C*, the forelimb area of the primary somatosensory cortex (SI (60)), and *E*, the skin of the ipsilateral hindleg. Figure 1*B* and *D* shows the responses of the same cell to a click and to a brief flash of light, respectively. The characteristic feature of each response is a short burst of spikes followed by a prolonged period of silence.

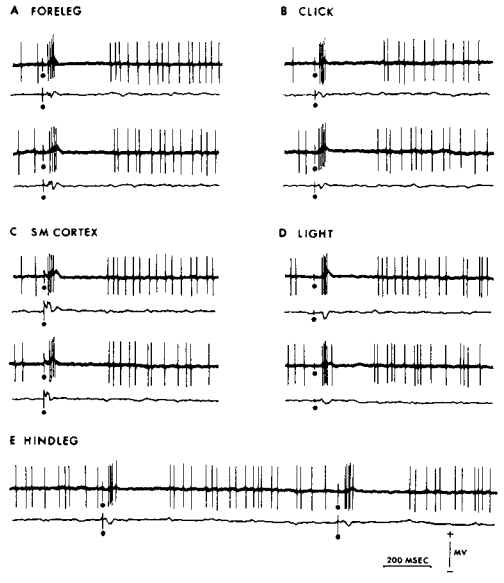

FIG. 1. Responses of a Purkinje cell in lobule VI to different stimuli. Beneath spike records are shown potentials simultaneously recorded from the pial surface overlying the recording microelectrode. Responses to two stimuli given several seconds apart are shown for each type of stimulus (stimulus artifacts marked by dots). *A:* responses to electrical stimulation (1 stimulus/2 sec, stimulus intensity 2 times threshold) of the skin of the dorsal surface of the ipsilateral foreleg. *B:* responses of the same Purkinje cell to repetitive clicks (1 click/2 sec, approximately 2 db intensity). *C:* responses of the same Purkinje cell to electrical stimulation of the forelimb area of the primary somatosensory cortex (SI, 1 stimulus/2 sec, stimulus intensity 2 times threshold). *D:* responses of the same Purkinje cell to brief flashes of light (wide-field illumination of the ipsilateral eye by 2-msec flashes of light of approximately 500 mlm intensity produced by a glow-modulator tube. Stimulus rate 1 flash/4 sec). *E:* responses of the same Purkinje cell to electrical stimulation of the skin of the ipsilateral hindleg (1 stimulus/2 sec, stimulus intensity 2 times threshold).

A more detailed analysis was done to determine quantitative differences between responses of Purkinje cells to different stimuli. The analysis is described in the legend of Fig. 2. The results of this analysis, applied to the same Purkinje cell shown in Fig. 1, are shown in Figs. 2 and 3. Analyses of 50 consecutive responses are shown to electrical stimulation of each of the following structures: the ipsilateral front toepad (Fig. 2*A*); the hind toepad (Fig. 2*B*); the forelimb area of the ipsilateral primary sensorimotor cortex (SI, Fig. 3*A*); the ipsilateral primary auditory cortex (AI (61), Fig. 3*B*); and the ipsilateral visual cortex (area 18, Fig. 3*C*). In addition, responses to the following natural stimuli were analyzed: clicks (Fig. 2*C*), brief flashes of light (Fig. 2*D*), and flexion of the ipsilateral forelimb (Fig. 3*D*). A great similarity in the average response of the cell to the different stimuli is apparent in the PSTs in the left-hand columns of Figs. 2 and 3. The PSTs in the middle columns of Figs. 2 and 3, shown on an expanded time scale, reveal an unexpected similarity between the different responses in terms of the duration of the early burst.

The distribution of interspike intervals during the burst of spikes following each stimulus is shown in the interval histograms in the right-hand columns of Figs. 2 and 3. Each histogram decays from its peak value in an exponential-like fashion, which would be expected if the interspike intervals were randomly distributed (10, 32). Two indexes of the intraburst interval distributions were calculated: the mean (left-hand vertical line) and the time until

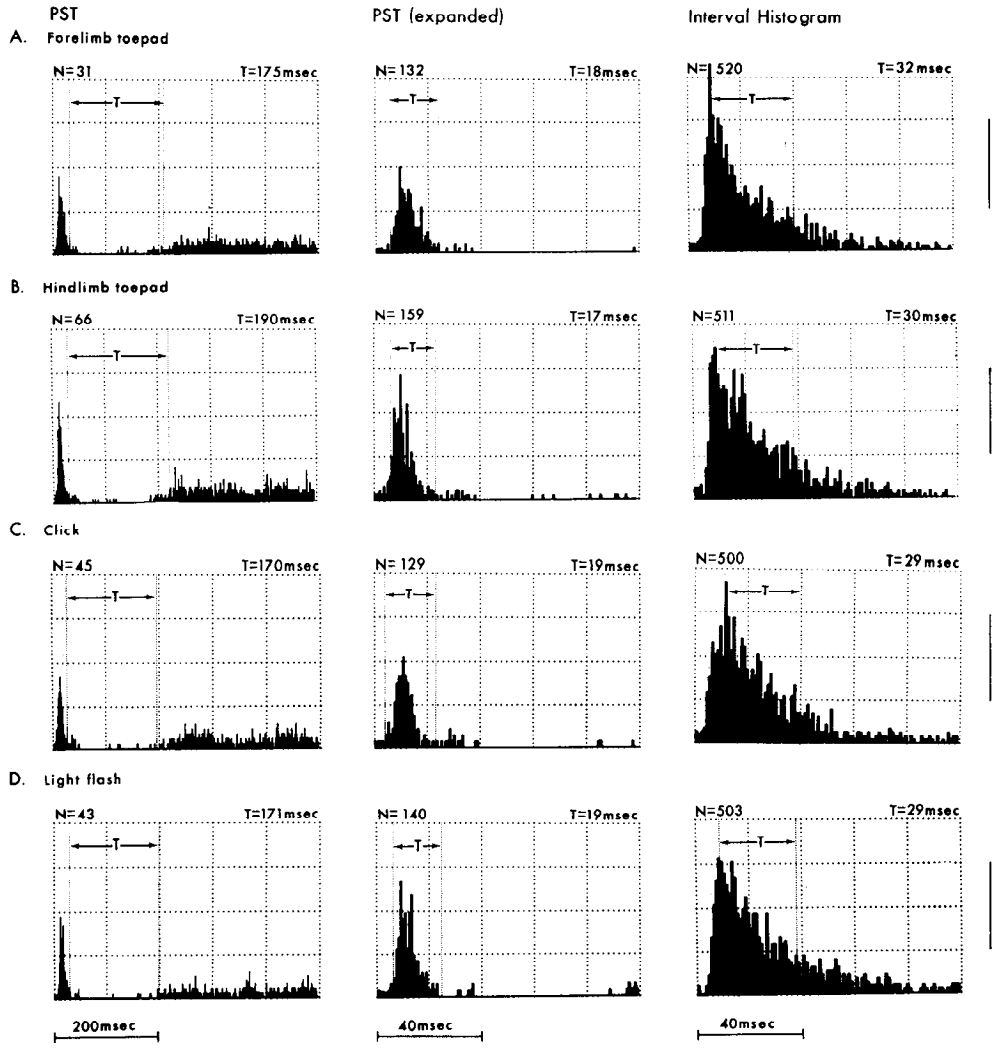

FIG. 2. PST and intraburst-interval histograms of responses of the same Purkinje cell to different stimuli. All histograms shown were computed for the same Purkinje cell shown in Fig. 1, in response to same types of stimuli described in that figure. A LINC-8 computer calculated conventional PST histograms for responses to 50 stimuli. These are shown in the left-hand column (500 points, bin width = 1 msec) and on an expanded time scale in the middle column (500 points, bin width = 0.2 msec). It also calculated a moving spike frequency from which it then computed times of onset and termination of the initial burst of spikes following the stimuli. From this was calculated the duration of the burst and total number of spikes in the burst. These values are shown above records in the middle column, respectively. Similarly, it calculated the duration of the period of inhibition following the burst and total number of spikes during that interval. These values are shown above records in the first column, respectively. Finally, it calculated the distribution of first-order interspike intervals during burst of spikes following each stimulus (shown in third column). Note that heights of the intraburst-interval histograms decay approximately exponentially, which would be expected if the intervals were randomly distributed. The computer calculated the mean interval (first vertical dotted line in records of the third column) and the total number of intervals (N) included in one "time constant" (T, in third column). *A* and *B:* responses of Purkinje cell to single-shock electrical stimulation (1 stimulus/2 sec, 2 times threshold) of the ipsilateral front and hind toepad, respectively. *C:* responses to repetitive clicks (1 click/2 sec, approximately 2 db). *D:* responses to brief flashes of light (wide-field illumination of the ipsilateral eye with 2-msec flashes of light of approximately 500 mlm intensity; 1 flash/4 sec). It can be seen from these records that there was a rather great quantitative as well as qualitative similarity between responses of the cell to different stimuli. Vertical calibration marks: 40 spikes (left-hand column), 30 spikes (middle column), 20 intervals (right-hand column).

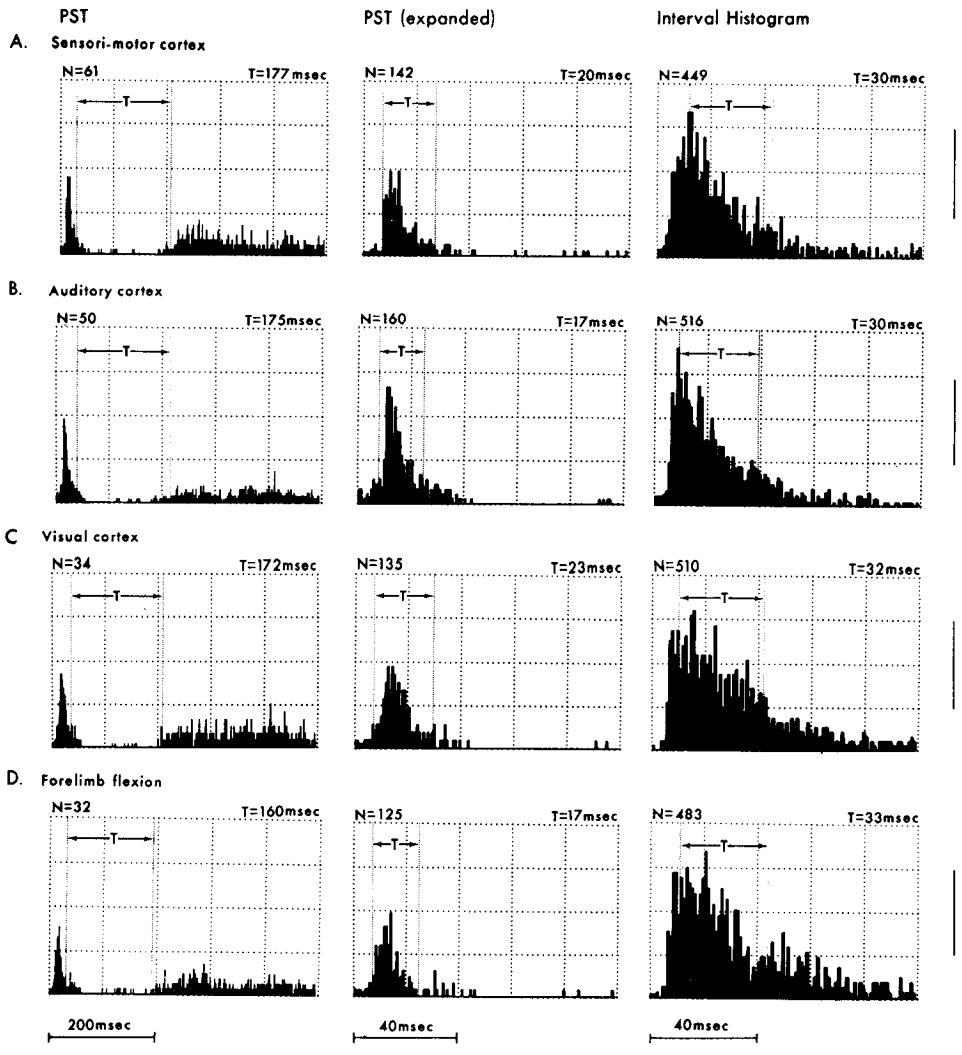

FIG. 3. PST and intraburst-interval histograms of responses of the same Purkinje cell to different stimuli. All histograms shown were computed for the same Purkinje cell shown in Fig. 1 in response to stimuli described in the text. Details of computation of histograms and vertical and horizontal scales are the same as in Fig. 2. *A–C:* responses of Purkinje cell to single-shock electrical stimulation (1 stimulus/2 sec, 2 times threshold) of ipsilateral primary sensorimotor cortex (SI), primary auditory cortex (AI), and visual cortex (area 18), respectively. *D:* responses to flexion of the ipsilateral forelimb (through 30° of arc at a velocity of 100°/sec, and a repetition rate of 1 flexion/4 sec). These records reveal further the great quantitative and qualitative similarity between responses of this Purkinje cell to many different stimuli. Because of the relatively simple structure of the intraburst-interval distributions it is unlikely that the distribution of spikes within a burst contains specific information identifying which particular input gave rise to the burst; e.g., there appears to be no temporal coding of single inputs.

the height of the histogram had decayed to 1/e (i.e., 1 "time constant") of this value (right-hand vertical line).

These histograms point out the similarity of the bursts of spikes following each of the different types of stimuli. Because of their relatively simple shape it is unlikely that the distribution of spikes within a burst contains specific information identifying which particular input gave rise to the burst.

In 36 experiments the responses of a total of 183 identified Purkinje cells were recorded which had characteristics similar to those just described: that is, they could be activated by a great diversity of different

types of stimuli. This was true for those control cats which initially received only local anesthesia as well as for cats which received general chloralose anesthesia.

Twenty-four Purkinje cells receiving convergent somesthetic, auditory, and visual inputs were examined for qualitative differences in the receptive fields in each of these sensory modalities. Peripheral cutaneous receptive fields were diffuse and complicated. Wide-spread convergence made it difficult to map the receptive fields of a cell in the somesthetic, auditory, or visual sensory modality in satisfactory quantitative detail. In these cells, however, there was no preferential response to the direction of lightly stroking the hair with a brush, to the direction of movement of a spot of light across the retina, or to the direction of modulation of the frequency of a brief tone burst. The thresholds of Purkinje cells located in different parts of the same folium and in different folia varied in a nonsystematic way for tone bursts of the same frequency, and in this sense there was no discernable tonotopic organization.

To determine whether Purkinje cells located in different regions of the folia might differ in some systematic way with respect either to the extent of convergence or to their response characteristics, recordings were made at regularly spaced points along and across different folia in lobules VI and VII in four cats. The threshold of a Purkinje cell for a particular test stimulus was defined as that stimulus intensity which produced a 50% probability of response (i.e., for which the cell responded, in the fashion shown in Figs. 1, 2, and 3, an average of 50 times out of 100 stimuli). A quantitative comparison of the thresholds of different Purkinje cells to several different test stimuli was made by determining the probability of response as a function of stimulus intensity (described below): *1)* responses from each of 54 cells could be elicited by natural cutaneous, auditory, and visual stimuli, and by electrical stimulation of the primary sensory receiving areas of the cerebral cortex; *2)* there was a sixfold variation in threshold of response to a particular stimulus, between the least and the most responsive Purkinje cell; *3)* there was no systematic variation of the threshold of the Purkinje cell to a particular test stimulus with respect to the position of the cell in the folium; *4)* the relative variations of thresholds for different test stimuli as a function of position of the cell within the folium was not constant from cat to cat.

Evidence will be presented in a subsequent paper that both mossy fibers and climbing fibers participate in the genesis of the Purkinje cell response to different test stimuli. Mossy fibers branch extensively on entering the cerebellar white matter, with the result that afferent activity conveyed to the cerebellar cortex by the mossy fiber input is spread over a wide area. Differences in Purkinje cell thresholds for similar test stimuli show that, despite the widespread branching of mossy fibers and the further divergence of afferent activity introduced by the granule cell-parallel fiber distribution, afferent activity in the mossy fiber input is not spread homogeneously over the entire width of the folium. However, because all the Purkinje cells tested responded to a great diversity of different stimuli, the classical concept of a "topographical map" (e.g., based on degeneration studies and on evoked cortical potentials) does not obtain at the Purkinje cell level.

Influence of interactions between different stimuli on probability of Purkinje cell response

In asking the question: "Is there a temporal coding of spikes for a particular afferent input?" one would expect that such a code, if it exists, would be manifested in the responses of a Purkinje cell to different peripheral inputs by either a change in the frequency, the interval distributions, or the duration of bursts of spikes. No evidence of this is seen in the histograms of Figs. 2 and 3. Moreover, it is unlikely that the Purkinje cell responds with a unique, coded sequence of action potentials for each of the different inputs which it receives because of their great number and the great complexity of temporal spike sequences which such a coding scheme would necessitate. These considerations, and the fact that information enters the cerebellar

cortex continuously and not as discrete, isolated events, lead to the question whether a Purkinje cell might respond differently to two or more concurrent inputs.

The effect of the interaction of a pair of stimuli, i.e., a click and a single-shock stimulus of the primary auditory cortex (AI) is shown in Fig. 4. The times of occurrence of Purkinje cell spikes are represented by dots (59). The times of presentation of stimuli are represented by the two vertical columns of dots marked by arrows. Those dots which lie on a given horizontal line represent the response of the cell to a given stimulus; the dots which lie along the next row down represent the response of the cell to the next stimulus, etc. The response of this cell to five consecutive clicks and to five consecutive shocks to the ipsilateral primary auditory cortex (stimulus artifact marked by heavy dots) presented 50 msec later, are shown in Fig. 4*A* and *B*, respectively. In Fig. 4*C*, both stimuli were presented in sequence. The intensity of the cortical stimulus was held constant while the intensity of the click was gradually increased from below to above threshold. Above threshold a sharp transition occurred: the cell responded to the click but not to the cortical stimulus. In Fig. 4*D*, *E*, and *F*, the order of stimulus presentation was reversed. When the intensity of the cortical stimulus was increased to above threshold, the cell responded to it but not to the click. Increasing the intensity of the cortical stimulus to greater than 20 times threshold failed to overcome the inhibition caused by the preceding click stimulus in Fig. 4*A*. Conversely, increasing the intensity of the click stimulus to greater than 20 times threshold failed to overcome the inhibition caused by the preceding cortical stimulus shown in Fig. 4*D*.

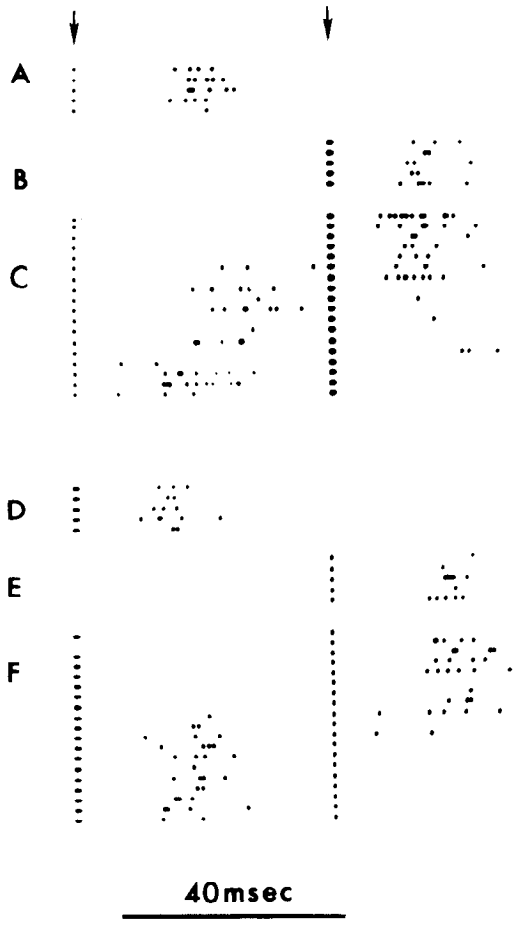

FIG. 4. Inhibitory interaction between two inputs which converge on the same Purkinje cell. Times of firing of the Purkinje cell are represented by dots. Dots on each horizontal row represent a stimulus (column of dots marked by arrows) followed by response of the cell. *A:* responses to five consecutive clicks (from top down), given at the rate of 1/2 sec. *B:* responses to five consecutive shocks to the primary auditory cortex presented at a time delay of 50 msec with respect to the click stimulus. *C:* both the click and the cortical stimulus were presented together. The intensity of the cortical stimulus was held constant while the intensity of the click was gradually increased from below to above threshold. Above threshold, a sharp transition occurred: the cell responded to the click but not the cortical stimulus. *D, E, F:* order of stimulus presentation was reversed. When the intensity of the cortical stimulus was increased to above threshold, the cell responded to it but not to the click. In both cases, the first effective stimulus inhibited a response to the second stimulus.

To test whether the kind of inhibition demonstrated in Fig. 4 was input specific, different pairs of inputs were systematically interacted in 51 Purkinje cells in lobules VI and VII. In every case, if the conditioning stimulus elicited a response, the test stimulus, regardless of its intensity or of its origin, failed to elicit a response or, in any discernible way, to alter the time course of the response to the first stimulus.

The duration of this period of inhibition was investigated for different pairs of inputs in 31 Purkinje cells. In Fig. 5*A* single-shock stimuli were applied to the skin of the ipsilateral foreleg at a fixed time, t_0, and to

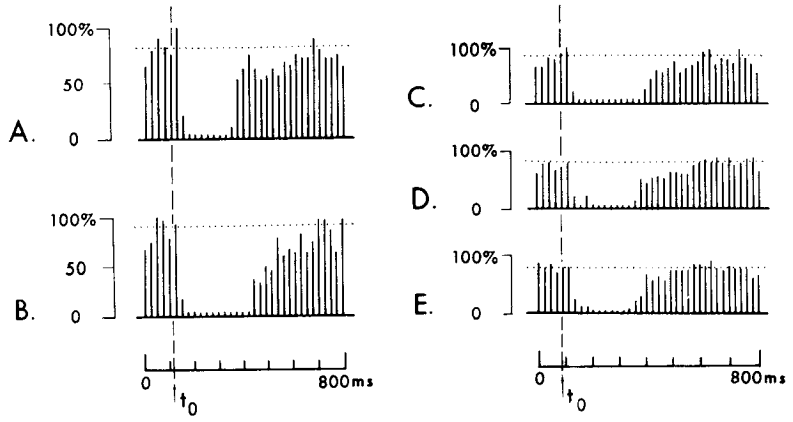

FIG. 5. Duration of inhibition of Purkinje cell response to the second of two paired stimuli. Conditioning stimuli were applied at time t_0 (marked by dashed vertical lines), and test stimuli were presented at the times indicated by the horizontal position of vertical lines. The height of each vertical line is proportional to the total number of spikes in the burst of spikes produced by the Purkinje cell in response to 10 test stimuli. (Details of stimuli are described in text.) *A:* single-shock stimuli were delivered to the skin of the ipsilateral foreleg (conditioning stimuli) and to the ipsilateral somatosensory cortex (test stimuli. *B:* somatosensory cortex stimulus was presented at a fixed time while the time of the skin stimulus was delayed. *C, D,* and *E:* results of a similar experiment on another Purkinje cell. Each pair of stimuli consisted of a click (test stimuli in *C* and *D,* conditioning stimulus *E*) and a shock to the ipsilateral primary auditory cortex. In each record the response to the conditioning stimulus was inhibited for a period beginning at approximately 30 msec after the test stimulus and lasting approximately 250 msec. This inhibition was not input specific.

the ipsilateral primary somatosensory cortex (SI) at a delay which was increased after every 10th stimulus. The responses to the cortical stimuli were completely inhibited for a period beginning at approximately 30 msec and lasting approximately 200 msec after the skin stimuli. In Fig. 5*B* the cortical stimulus was presented at a fixed time, while the time of presentation of the skin stimulus was delayed. The resulting inhibition began at approximately 25 msec after the cortical stimulus and lasted approximately 240 msec.

The results of a similar experiment on another Purkinje cell are shown in Fig. 5*C, D,* and *E.* Each pair of stimuli consisted of a click and a shock to the primary auditory cortex. In Fig. 5*C* and *D,* the clicks were presented at a fixed time and the cortical stimuli were progressively delayed. Responses to the cortical stimuli were inhibited for a period beginning at approximately 30 msec after the click and lasting approximately 250 msec. In Fig. 5*E* the cortical stimuli were presented at a fixed time and the clicks were progressively delays. Again, the responses to the clicks were inhibited for a period beginning at approximately 30 msec after the cortical stimuli and lasting approximately 200 msec. The inhibitory interaction between different pairs of stimuli in 31 Purkinje cells thus studied began between 24–32 msec after the conditioning stimulus and lasted for 200–250 msec.

It is apparent that a more subtle kind of interaction might occur between concurrent inputs to the cerebellar cortex: do they summate and, if so, do they summate linearly or do different combinations of inputs vary in their probability of influencing the activity of the Purkinje cell? A series of experiments in which different pairs of stimuli were timed to arrive at the Purkinje cell layer concurrently was performed. The LINC-8 and a specially constructed programmable digital stimulator were used to control precisely the intensity and timing of stimuli. The threshold of the Purkinje cell was determined for each of the two stimuli. The probability of response of the Purkinje cell for a given stimulus intensity was defined as the percentage of times the cell responded, with the characteristic burst of spikes followed by a prolonged period of silence (as shown in Fig. 1), in 100 trial stimuli.

This kind of experiment was performed

on nine cats, on a total of 43 cells. The results of one of these experiments are shown in Fig. 6. In this figure three peripheral stimuli (cutaneous, auditory, and visual) were paired with stimuli to three parts of the cerebral cortex. The top records of Fig. 6 show, as a function of relative stimulus intensity, the increase in probability of response of a Purkinje cell in lobule VI to: single-shock stimulation of the ipsilateral fore toepad (Fig. 6*A*, F); a click (Fig. 6*B*, C); and a flash of light of 2 msec duration (Fig. 6*C*, L). A horizontal reference line has been drawn at the 30% probability level in each record for comparison. (It is apparent that this cell had a very sharp threshold for the click stimulus and a less sharp threshold for the skin and light stimuli.) Each of these stimuli, given at incrementally increasing intensities as just described, were then paired in turn with stimulation of each of the following three areas of the cerebral cortex: that part of the contralateral primary sensorimotor cortex (SI) from which the maximum surface-evoked response to the skin stimulus was recorded (Fig. 6, SMC); that part of the contralateral primary auditory cortex (AI) from which the maximum surface-evoked response to the click was recorded (Fig. 6,

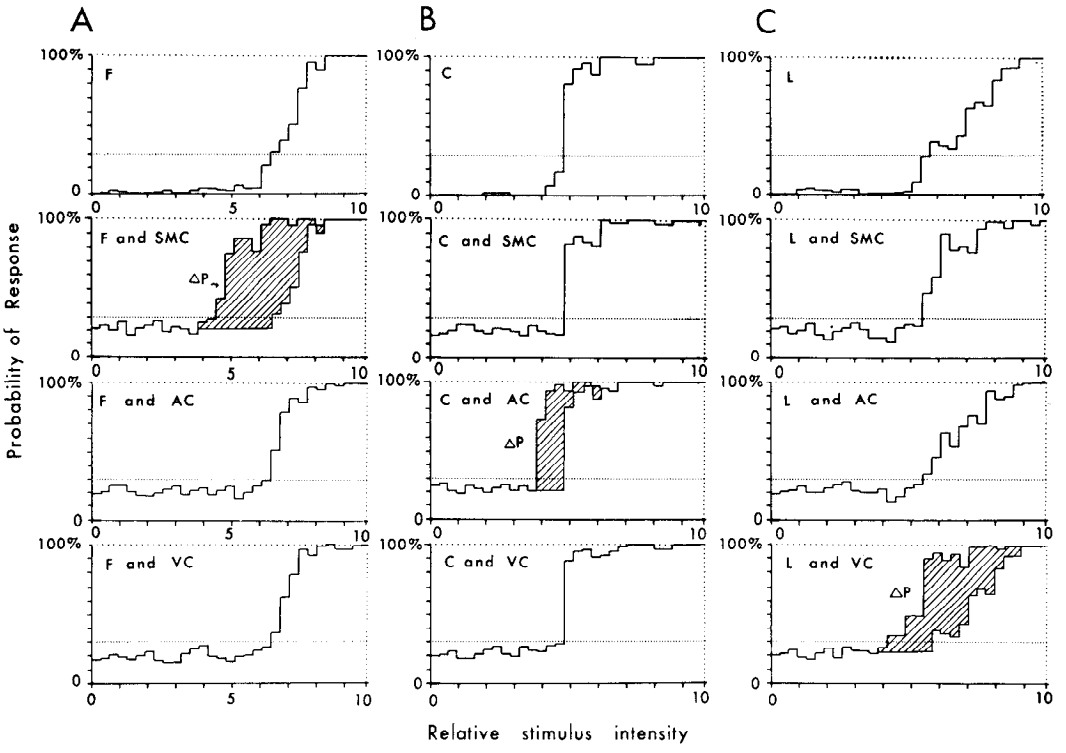

FIG. 6. Facilitatory convergence between inputs from cerebral cortex and from the periphery. The probability of response of a Purkinje cell was determined as a function of stimulus intensity for two concurrent inputs, one from the periphery and one from the cerebral cortex. The top records of *A*, *B*, and *C* show the probability of response as the relative intensity of each of three different stimuli (electrical stimuli of the ipsilateral fore-toepad, F; a click, C; and a flash of light, L) were incrementally increased. In the bottom three records in each column, the peripheral stimuli were delivered concurrently with stimuli to the ipsilateral primary sensory receiving areas of the cerebral cortex (sensorimotor cortex, SMC; auditory cortex, AC; visual cortex, VC). The intensity of each of the cortical stimuli was held constant at a level which produced on the average a 20% probability of response. (Horizontal dotted lines are drawn at the 30% probability response level.) A LINC-8 computer and a digital programmable stimulator were employed to control stimulus intensities at precise increments and to compute probabilities of response (defined as number of responses out of 100 trial stimuli). The pairing of peripheral stimuli and the stimuli to the primary sensory areas of the cerebral cortex receiving inputs from the same peripheral source produced a selective increase in probability of response of the Purkinje cell, shown by the shaded areas. No increase in probability of response was produced by pairing of inputs subserving different sensory modalities.

AC); and that part of the contralateral primary visual cortex (area 18) from which the maximum surface-evoked response to the light flash was recorded (Fig. 6, VC). The cortical stimuli were delivered at a rate of 1 stimulus/2 sec, and at a constant intensity which was adjusted to produce, on the average, a 20% probability of response.

Pairing of a given peripheral stimulus with stimulation of the noncorresponding regions of the cerebral cortex produced no significant alteration in the probability of response of the Purkinje cell to the peripheral stimulus. On the other hand, pairing of the peripheral stimulus with stimulation of the corresponding areas of representation in the primary receiving areas of the cerebral cortex significantly and selectively increased the probability of response of the Purkinje cell over the values obtained when just the peripheral stimuli were given alone. This can be readily seen in the shaded areas of Fig. 6, which represent the difference between the probabilities of response when the two stimuli were given together and when the corresponding peripheral stimuli were given alone.

Interaction studies of the type just described required stable recording from the same cell for prolonged periods of time and were difficult to perform. Of the 43 Purkinje cells studied in this fashion, 31 were held long enough to test for facilitatory convergence between six or more different pairs of inputs. A modality-specific facilitatory convergence was demonstrated in 29 of these units in one or more sensory modality. Of these 29 units, 21 units demonstrated a modality-specific convergence in two sensory modalities. Of these 21 units, 14 were held long enough to perform a complete test in three sensory modalities. Modality-specific facilitation was found in 12 of these 14 units.

The experiments illustrated in Fig. 6 show the probability of response of a Purkinje cell to different pairs of stimuli delivered at a fixed interstimulus interval. A set of experiments was performed to measure the probability of response for different interstimulus intervals. First, that value of stimulus intensity for which a particular Purkinje cell responded an average of 25 times out of 100 stimulus presentations (25% probability of response) was determined for several different peripheral and cerebrocortical stimuli. Next, two different stimuli were presented in pairs, each at the intensity just determined and at an interstimulus interval which was systematically varied in small increments so that stimulus A first preceded, then followed, stimulus B. The number of Purkinje cell responses to the second stimulus in each paired presentation was counted, out of 50 presentations at each interstimulus interval.

The results of one such experiment are shown in Fig. 7. They were obtained from

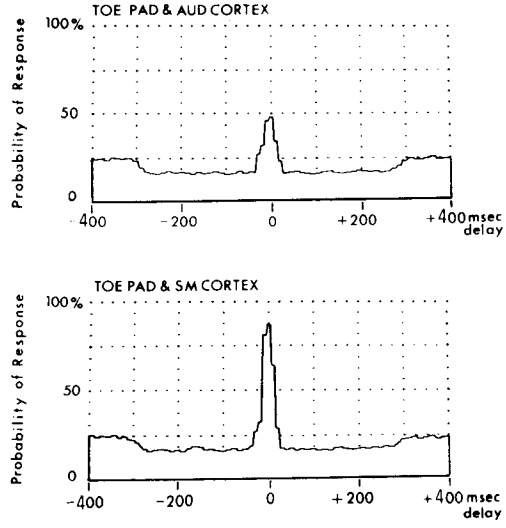

FIG. 7. Probability of response of a Purkinje cell to paired inputs, as a function of their relative time delay. Experimental arrangement described in text. Top record: pairing of toepad stimulus with stimulation of primary auditory cortex. For long (> 300 msec) interstimulus delays, the probability of response was the same (25%) as that for either stimulus given alone. Inhibitory interaction between stimuli occurred for intermediate interstimulus delays (± 20–280 msec), during which the probability of response decreased from 25% to approximately 19%. For short delays (± 20 msec) the probability of response increased to a value (47%) nearly equal to the sum of the probability of response for each stimulus given alone. Bottom record: pairing of toepad stimulus with stimulation of that region of the primary sensorimotor cortex from which was recorded the maximum surface-evoked response to the same toepad stimulus. Probability of response was similar to top record, except that for short interstimulus delays (± 20 msec) the probability of response increased to a value (88%) approximately 1.8 times the sum of the probability of response for either stimulus alone.

the same Purkinje cell described in Fig. 6, in response to the toepad and cerebrocortical stimuli described for that figure. Several features of the response probability records of Fig. 7 are of interest. In the top record, toepad and primary auditory cortical stimuli were paired. When the cortical stimuli preceded (left-hand side of record) or followed (right-hand side of record) the toepad stimulus by greater than approximately 280 msec, the same probability of response (25%) was obtained as when either stimulus was given above. That is, there was no effect of one stimulus on the probability of response to the other stimulus for interstimulus intervals greater than 280 msec. For interstimulus intervals between approximately 20 msec and 280 msec, however, there was a reduction in the probability of response from 25% to approximately 19%. Finally, for interstimulus intervals between ± 20 msec, there was an increase in probability of response from 25% to approximately 48%. That is, for small interstimulus intervals the probability of response was approximately the same as the sum of the probability of response to each stimulus given alone.

Pairing of toepad stimulation with stimulation of the primary somatosensory cortex (bottom record of Fig. 7) produced a probability of response record similar to that just described: i.e., for long interstimulus intervals there was no effect of one stimulus on the probability of response to the other stimulus, whereas for intermediate interstimulus intervals there was a symmetrical reduction in probability of response. For short (between ± 20 msec) interstimulus intervals, however, the probability of response increased to almost 88%, which is approximately 1.8 times greater than the sum of the probability of response to either stimulus alone. Similar experiments involving the pairing of different combinations of peripheral and cerebrocortical stimuli were performed on a total of 16 Purkinje cells. For each cell it was found that: *1)* for interstimulus intervals greater than 300 msec, there was no effect of one stimulus on the probability of response to the other stimulus; *2)* for intermediate interstimulus intervals (between approximately 20 msec and 300 msec) there was a symmetrical reduction of response probability; *3)* for short interstimulus intervals (between ± 20 msec) there was an increase in probability of response, *a)* from 25 to 75 ± 14% for particular pairs of inputs, i.e., for a peripheral input paired with an input from the area of representation of that same input in the corresponding primary sensory receiving area of the cerebral cortex; and *b)* from 25 to 37 ± 12% for other combinations of inputs.

DISCUSSION

Convergence of polysensory information on Purkinje cells in posterior vermis

The convergence of polysensory information in the posterior vermis has been demonstrated, on a gross level, by extensive work done by previous investigators (see reviews by Fadiga and Pupilli (27), Bell and Dow (6), and Evarts and Thatch (26)).

Because the response properties of any neuron are anesthesia dependent, the actual extent of convergence of afferent activity onto Purkinje cells in the posterior vermis determined experimentally in anesthetized preparations is uncertain. Maps published by Eccles et al. (21, 24) of extracellular field potentials recorded in the anterior cerebellar cortex of barbiturate-anesthetized cats reveal rather circumscribed, systematically spaced mossy and climbing fiber responses to stimulation of different peripheral nerves. Similarly, Oscarsson (47) contends that there is a highly ordered distribution of mossy and climbing fibers from the different ascending spinal pathways. Provini, Redman, and Strata (49) found areas in the anterior cerebellar cortex from which mossy fiber field potentials could be evoked by convergent inputs from several different limb nerves and from the sensorimotor cortex. Responses of Purkinje cells to stimuli subserving different sensory modalities have also been reported by other investigators (4, 5, 41), but receptive fields have not been analyzed in detail.

Results of the present study show that this extensive convergence of polysensory information is preserved at the level of individual Purkinje cells. Determination of the site of convergence, or of the neuronal pathways involved, has not been the pur-

pose of this study; in addition to the convergence and mixing of mossy fiber afferents which occur in the granule cell layer (21), and the further convergence of afferent activity onto the extensive Purkinje cell dendritic tree, it is likely that considerable convergence and preanalysis of afferent activity occurs outside the cerebellum (for example, in the lateral reticular nucleus (14, 16, 18, 39)). The present work suggests that this great wealth of afferent information is distributed nonselectively to individual Purkinje cells, rather than being "sorted out" and distributed to particular sets of Purkinje cells.

Coding of afferent information

A fundamental question regarding the analysis of afferent information by the cerebellum is whether particular events occurring in the external world are reflected by specific patterns of activity in Purkinje cells; that is, whether afferent information is translated, by some sort of coding paradigm, to specific sequences of spikes. The great majority of Purkinje cells encountered in this study generated remarkably similar responses to different types of natural and electrical stimulation (as shown in Figs. 1, 2, and 3). Of the 126 cells activated at short latency by inferior olivary stimulation, 14 failed to respond in this fashion. Instead, they generated complex, irregular patterns of spikes following different test stimuli. These cells may have been injured or they may represent Purkinje cells which respond differently to those described in detail in this study.

Of the 183 Purkinje cells which had similar response characteristics (an initial burst of spikes followed by a prolonged period of silence), there were significant differences in the latencies of the onset of the burst. These can be seen in Figs. 2 and 3. These responses resemble the "long-latency response" of presumed Purkinje cells described by Jansen and Fangel (41) and the long-latency responses, to stimulation of the sensorimotor cortex, of Purkinje cells in the anterior lobe described by Armstrong and Harvey (4). No other evidence for a specific sequence of spikes in response to a particular input was found; i.e., these cells demonstrated *1)* little or no variability of the pattern of response; *2)* very little variation of the total number of spikes per burst (second column of Figs. 2 and 3), of the duration of the initial burst, or of the distribution of first-order interspike intervals during the burst (third column of Figs. 2 and 3); *3)* little variation in the duration of spike suppression following the initial burst; *4)* no specific inhibition, either of a particular input or of particular sequences of inputs, as shown in Fig. 5. It is conceivable, on the other hand, that the temporal activity of these cells embodies a type of coding of afferent information too subtle to be revealed by the methods used in this study. Given the great amount of afferent information received by these cells and the apparent uniformity of response, it is unlikely that such a code exists.

Facilitatory convergence of cerebrocortical and peripheral inputs

An overlap of the auditory, visual, and somesthetic areas of the cerebellar cortex with the projections from the primary sensorimotor, auditory, and visual receiving areas of the cerebral cortex has been described by other investigators (2, 12, 19, 27, 52). Experiments illustrated in Fig. 6 demonstrate that there is a facilitatory convergence between a peripheral input subserving a given sensory modality and an input from the primary sensory receiving area of the cerebral cortex serving the same sensory modality. The mechanism by which an input from the cerebral cortex can selectively increase the probability of response to a particular peripheral input is unknown; however, evidence suggesting that neurons in the inferior olive are involved in this mechanism will be presented in a subsequent paper.

What conclusions can be drawn from these findings concerning the mechanisms by which integration of afferent activity is performed in the posterior vermis of the cerebellar cortex? First, it is clear that any such conclusions are necessarily speculative because the exact function which the cerebellum has evolved to perform, the logical principles by which this function is performed, and the detailed patterns of input and output activity, are unknown. (It

should also be stressed that the experimental findings described here apply to the posterior vermis (principally lobules VI and VII) and may not be generalizable to other areas of the cerebellar cortex.) It is clear, however, that an extensive intermixing of inputs from multiple sources occurs, with the result that the Purkinje cells over a wide area of the cortical sheet of the posterior vermis share similar functional inputs and have similar response properties. This stands in sharp contrast to the neuronal response specificity and topographical organization described for visual cortex (40) and sensorimotor cortex (45), and is more similar to the apparent nontonotopic organization of cat primary auditory cortex described by Evans et al. (25).

One of the most impressive histological features of the cerebellar cortex is its regularity. Eccles, Ito, and Szentagothai (21) have pointed out that the dendrites of Purkinje cells are spatially segregated one from another by virtue of their parallel planar orientation, as well as by intervening glial elements. The present findings suggest a physiological corrolate of this unique structural arrangement, namely, that each Purkinje cell functions in the manner of an independent general-purpose information processer; that is, a large number of Purkinje cells can be operated on by similar, if not the same, peripheral and cerebrocortical inputs, but the probability of response to a given input differs from cell to cell, depending on *a)* the time delay between inputs; and *b)* concurrent inputs from particular parts of the sensory receiving areas of the cerebral cortex and, possibly, from other parts of the central nervous system.

The facilitatory interaction between particular peripheral and cortical inputs is analogous to a tunable filter in which the probability of response of a Purkinje cell is selectively tuned by inputs from the cerebral cortex. The experiments illustrated in Fig. 7 show quantitatively the magnitude of this facilitatory interaction, as well as the constraints on the timing of inputs which govern it. The enhancement of probability of response which occurs for a particular pair of properly timed inputs is apparent.

By selectively tuning the probability of response of each member of an ensemble of Purkinje cells, considerable sharpening in discriminability between different inputs might be achieved. Although it is impossible to tell from the present experiments whether this type of tunable-filter mechanism might operate in the awake, unrestrained animal, it is reasonable to suppose that input activity from the cerebral cortex is continuously received by the cerebellar cortex, both in response to peripheral inputs and to intrinsic cortical activity.

Because the Purkinje cells provide the only output from the cerebellar cortex, the parameters which control their firing patterns are of particular interest in understanding its function. Braitenberg (8) has postulated that the intrinsic cellular geometry of the cerebellar cortex is an important parameter in determining the relative times of firing of different Purkinje cells. This postulate is intriguing because it attributes a function to the unique arrangement of Purkinje cells at regular intervals along different beams of parallel fibers. Freeman (32), and Freeman and Nicholson (36) have shown that in response to several different kinds of natural and electrical stimuli, parallel fibers in the frog cerebellar cortex can function as a tapped delay line, causing a row of Purkinje cells to fire in sequence.

There is no corresponding experimental evidence in the cat to support this hypothesis and, indeed, one would expect that the extensive branching of the mossy fibers in the cat cerebellar cortex would result in a spatial as well as temporal randomization of parallel fiber inputs to the Purkinje cells unless, as previously emphasized (32, 36), *a)* some topographical specificity is maintained in the branching patterns of mossy fibers, and *b)* clusters of granule cells whose axons form a beam of parallel fibers are synchronously activated (44). The present results point out that other factors in addition to the intrinsic cellular geometry of the cerebellar cortex might play an important role in the analysis of afferent information, in particular, the convergence and relative timing of inputs from different sources in the periphery and the central nervous system.

SUMMARY

The activity of individual Purkinje cells in the posterior vermis of the cat was studied in response to different inputs from the periphery and from the cerebral cortex. The experimental objectives were to determine *a)* the distribution of afferent activity at the single-unit level in order to characterize the functional inputs to different Purkinje cells; and *b)* what type, if any, of stimulus coding is represented in the temporal activity of Purkinje cells in response to specific afferent inputs.

It was found that Purkinje cells in lobules VI and VII received many inputs subserving different sensory modalities (somesthetic, auditory, and visual) from the periphery and from the cerebral cortex. Responses were very similar and consisted of a short burst of spikes followed by a long period of spike suppression. There was no discernable mapping within a given folium or between adjacent folia of Purkinje cells having different response characteristics.

Quantitative analysis of the responses to different peripheral and cerebral cortical inputs did not reveal any evidence of stimulus coding. Other than variations in latency of the burst response produced by different stimuli, there was little or no variability of the pattern of response, of the total number of spikes per burst, of the duration of the initial burst, of the distribution of first-order interspike intervals during the burst, or of the duration of spike suppression following the initial burst.

An inhibitory interaction between inputs occurred such that responses to the second of a pair of inputs were inhibited beginning approximately 30 msec after response to the first input and lasting approximately 250 msec. This inhibition was not input specific.

A facilitatory convergence between peripheral and cortical inputs in the same sensory modality was discovered: the probability of response of the Purkinje cell to a particular peripheral input was selectively increased by a concurrent input from that part of the primary sensory receiving area of the cerebral cortex which received inputs from the same peripheral source. This kind of probabilistic interaction between inputs is analogous to a type of tunable filter. These results suggest that the posterior cerebellar vermis processes afferent information according to a probabilistic rather than a spatial or temporal coding mechanism.

ACKNOWLEDGMENTS

I express my gratitude to Professors P. D. Wall, J. Y. Lettvin, J. E. Brown, W. A. Rosenblith, and S. K. Burns of the Massachusetts Institute of Technology, and to Dr. Rodolfo Llinas of the Institute for Biomedical Research, for their valuable help.

This work was supported in part by the United States Air Force, by The National Institutes of Health (Grant SR01 NB-04897-04), and by the American Medical Association, AMA/ERF.

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