Modification of the visual response properties of cerebellar neurons by norepinephrine

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Extracellular recordings were conducted in the paraflocculus of anesthetized Long–Evans pigmented rats to determine how iontophoresis of norepinephrine (NE) affects the responsiveness of individual Purkinje cells and interneurons to presentations of visual stimuli within their visual receptive fields. Presentations of moving or stationary visual stimuli during the control (pre-NE) period elicited simple spike excitations or inhibitory responses in slightly more than one-half (55%, $n = 32$) of the cells tested (20 of 38 Purkinje cells, 12 of 20 interneurons). The predominant effect of NE iontophoresis was to improve visually evoked responses in those neurons which showed modulations in their simple spike discharge to control presentations of visual stimuli. A clear enhancement of visual responses by NE (i.e., absolute increase over control) was observed in 18 of the units, and in 12 of the 14 remaining cells, reductions in stimulus-bound discharge during catecholamine iontophoresis were accompanied by much larger depressions in background activity, resulting in a net enhancement in the ratio of signal-to-noise. NE differentially affected responses to stimulus movement in the preferred and non-preferred direction in one-third of these neurons, such that directional selectivity was increased. However, the orientation bias of individual units was unchanged by NE. Iontophoretic application of the β-adrenergic antagonist sotalol but not the α-adrenergic antagonist phentolamine blocked these facilitating noradrenergic effects. An additional feature of noradrenergic action was revealed in tests conducted in 26 cells which did not respond to control presentations of visual stimuli. Iontophoresis of NE resulted in the elicitation of visual responses in 11 of these units, suggesting the possibility that NE might act in some cases to gate the efficacy of subliminal synaptic input conveyed by classical afferent channels. It is proposed that an important aspect of noradrenergic action within local cerebellar circuits might be to refine the receptive field properties of individual neuronal elements and thereby improve information flow through the cerebellum.

INTRODUCTION

Purkinje cells in the cerebellar cortex of the rat are known to receive a direct projection of norepinephrine (NE)-containing afferents from the nucleus locus coeruleus (LC)[5,17,20]. Previous work from a number of laboratories has yielded considerable information about the anatomy, physiology and pharmacology of this LC-to-Purkinje cell noradrenergic pathway (see Bloom[4]; Foote et al.[3]; Woodward et al.[37], for reviews). Despite such information, questions remain concerning the functional role that noradrenergic input may play in the regulation of information processing by the cerebellum. Early studies showed that NE released either synaptically or iontophoretically onto Purkinje cells suppressed spontaneous firing[16,17,30], which led initially to the suggestion that NE may function primarily as an inhibitory neurotransmitter. However, more recent studies have shown that NE iontophoresis or stimulation of the LC can augment synaptically driven responses of Purkinje cells to input from classical mossy and climbing fiber pathways and from local inhibitory interneurons[15,25,26]. These facilitating noradrenergic effects routinely occurred independent of any change in the spontaneous background discharge of the cell. Moreover, neuronal responses to direct postsynaptic application of the putative cerebellar neurotransmitters glutamate and γ-aminobutyric acid (GABA), but not glycine or β-alanine, were similarly shown to be enhanced during iontophoresis of NE[23,24,37]. On the basis of these and related findings the hypothesis was put forth that a normal function of noradrenergic input in cerebellar operation might be to facilitate the action of conventional afferent systems and thereby improve information transfer within local neuronal circuits[25,36].

An important prediction derived from this concept is that the modulatory effects of NE on neuronal activity evoked by electrical or chemical stimulation ought to be similarly expressed on specific patterns of cellular activity elicited by presentation of appropriate physiological

sensory stimuli. In the present study we describe the effects of iontophoretically applied NE on specific patterns of cerebellar Purkinje cell and interneuron responses to presentations of visual stimuli within their receptive fields. The results show that NE selectively augments both excitatory and inhibitory patterns of discharge evoked by visual stimulus presentations, independent of its effects on background discharge. The finding that some Purkinje cells only responded to visual stimulation during iontophoresis of NE suggests, in addition, that NE might act to increase the gain of subliminal or otherwise latent synaptic inputs and thereby gate information flow within local cerebellar circuits.

MATERIALS AND METHODS

Eighteen Long–Evans pigmented rats weighing 180–250 g were used in this study. Animals were anesthetized with a 2.5% halothane (Fluothane, Ayerst) oxygen mixture during surgical preparation and maintained at 0.1–0.2% halothane during the recording session. End-tidal CO_2 was monitored continuously throughout the experiment and maintained at 4–6% with a respirator. Body temperature was monitored with a rectal probe and maintained at 37 °C by means of a feedback-controlled heating unit.

Upon induction of anesthesia, the animal was placed in a specially modified stereotaxic frame in which the head was held by a Plexiglas block attached to the bone overlying the frontal cortex. The surface of the left parafloccular lobule of the cerebellum was then surgically exposed and covered with 3% agar in balanced salt solution. All wound margins were infiltrated with 2% xylocaine jelly, with additional applications administered at hourly intervals. The left eye was maintained open with an adjustable metal ring and protected with clear silicone fluid. Eye movements were minimized by i.p. administration of tubocurarine chloride, 1.0 mg/kg, every hour. The pupil was left undilated and the natural refractive power of the eye was unchanged since the rat's eye is normally emmetropic[18]. Following completion of all surgical procedures, the preparation was transferred to a sound-proof environmental isolation room in which all stimulation and recording was performed.

Extracellular spike responses were recorded from single parafloccular neurons during the presentation of visual stimuli. Recordings of extracellular activity were obtained using glass microelectrode assemblies consisting of a 5-barreled iontophoretic micropipet (tip diameter, 3–8 μm) to which a fine single-barrel glass recording electrode was cemented. The tip of the recording electrode (diameter less than 1 μm) extended 10–30 μm beyond the 5-barreled array in direct alignment with its longitudinal axis. The recording barrel was filled with a solution of Fast green dye in 2 M NaCl. Microiontophoresis was carried out using 4 of the barrels of the multibarreled micropipet, filled with freshly prepared solutions of 0.25 M L-NE hydrochloride, pH 4.5 (Sigma); 0.25 M sotalol hydrochloride, pH 4.5 (Bristol-Myers); 0.25 M phentolamine mesylate, pH 4.8 (Ciba-Geigy); or 0.25 M γ-aminobutyric acid, pH 4.0 (Sigma). Drug solutions were ejected as cations or retained by application of 15 nA holding currents of opposite polarity. Automatic current balancing was maintained through a fifth iontophoretic barrel filled with 3 M NaCl. Positive and negative currents were independently passed through this barrel at various times during an experiment to check for possible current artifacts. In some experiments the pH of the 3 M NaCl solution was adjusted with 0.1 N HCl to levels between 4.0–5.0 to control also for any contribution of drug pH to the effects produced by administration of NE. Cells ($n = 2$) were excluded from the analysis if the effects produced by NE administration were mimicked by passage of equivalent iontophoretic currents through to the NaCl-containing barrel.

Spike discharges were amplified with conventional electrophysiological instrumentation and displayed on an oscilloscope for visual inspection. The recording signal was filtered (high pass, 50 Hz with 3 dB cutoff) and passed to a window discriminator which generated a Schmitt triggered voltage pulse for each action potential. The voltage pulses were then led to a NOVA-3 digital computer (Data General Corp.) that was programmed to generate two separate peristimulus time histograms (PSTHs); one consisting exclusively of simple spike discharges and the second composed entirely of complex spike activations of Purkinje cells. The burst detection routine used by the computer discriminated between simple and complex spike discharges of a neuron based on the time interval between spikes and encoded all components of the burst discharge associated with complex spike activation as a single event. If an interspike interval was less than 4 ms, the computer declared the time of the first discharge (T_1) as the onset of a complex spike. Successive discharges were considered as potentials of the complex spike burst if the interspike interval between T_1 and the discharge was less than 7 ms and were used to terminate the detection routine for discriminating a burst when they occurred at intervals of 7 ms or longer.

At the end of the recording session, Fast green dye was deposited (30 μA, 5 min duration) into two electrophysiologically identified Purkinje cell layers to facilitate reconstruction of electrode tracts. Purkinje neurons were identified by the occurrence of complex spike potentials among a background of spontaneous (10–45 Hz) simple spike activity and verification of the recording site in a Purkinje cell layer. Neurons which showed no evidence of complex spike activation were included in the analysis and classified as local interneurons provided that their recording site was localized to the cerebellar molecular layer and a soma-dendritic notch was observed in their action potential as the electrode was advanced toward the cell body following data collection. The use of these criteria to identify Purkinje cells and interneurons in the rat paraflocculus is described in greater detail in several earlier reports[9,10].

Visual stimuli consisting of light spots, textured patterns or bars of various widths and lengths were projected onto a translucent, tangent screen using a computer-driven optical system (described in Burne et al., 1984). Stimulus intensities ranged from 4 to 10 cd/m^2 with background illumination set at the mesopic level (approximately 1 cd/m^2). Stimuli were moved across the screen at different velocities and orientations, with movement of light bars always being orthogonal to the long axis of the stimulus. A moving (50°/s), half-field, random dot pattern or a multigrey textured image was used first as a search stimulus to locate and determine visual responsiveness of individual parafloccular neurons. Once a cell was encountered and sufficiently isolated, moving presentations of bar or spot stimuli were used to collect responses for quantitative analyses. The approximate location and size of the responsive zone within a cell's receptive field were determined either manually with stationary flashing stimuli or reconstructed from PSTHs and plotted on orthogonal coordinates. The vertical axis of the plots shown in the figures indicates the retinal vertical meridian of the ipsilateral eye.

The response of a cell to a particular visual stimulus was determined by presenting that stimulus 15–20 times and computing a raster display 'on line' and a PSTH with a bin width of 10 or 20 ms. Once the control response to stimulus presentation had been determined, iontophoresis of NE was begun. When a new steady state level of spontaneous discharge was established, usually 1–2 min later the stimulus presentation and data collection procedure was repeated. Experimental trials were typically conducted at several levels of iontophoretic NE application. After cessation of NE iontophoresis, successive PSTH records were constructed to monitor the decay of NE effects and recovery of the control response to visual stimulus presentation. Unless recovery was observed, a change in responsiveness during drug iontophoresis was not considered as related to NE application. Occasionally, this entire sequence was repeated several times for a given neuron to minimize the contribution of uncontrolled fluctuations in respon-

siveness in certain trials. Cells were typically held for at least 30 min to generate a series of control, NE and recovery records.

The effects of NE on the visual responsiveness of a neuron were assessed by comparing the discharge in identical portions of the 'response epoch' from histograms computer before, during and after periods of NE iontophoresis. For each cell, periods of stimulus-related and spontaneous activity were identified in the PSTHs. In the control record of Fig. 1A, for example, the spontaneous activity was defined to include all counts during the 500 ms interval prior to stimulus onset, and the visually evoked activity, shown by the solid bar below the simple spike histogram, consisted of all counts during a 1500 ms interval commencing with movement of the stimulus (upslope of trapezoidal waveform). In all cases, the period of spontaneous activity was selected to be at least 500 ms in duration and free of obvious stimulus-related activity. With the aid of the computer, the discharge rates in each epoch of spontaneous and stimulus-evoked activity were calculated and the response(s) to visual stimulation expressed as a percentage of the baseline rate of spontaneous firing (excitations and inhibitions) and in spikes elicited per stimulus presentation (excitations only). In this way the effects of NE on visual responsiveness could be assessed both in terms of changes in the absolute number of impulses and in the ratio of signal to noise. Application of NE was considered to have changed the visual responsiveness of a cell under study when the response to stimulus presentation during drug iontophoresis was increased or decreased by 20% or more relative to control.

RESULTS

The paraflocculus of the cerebellum in the rat has recently been identified by way of both anatomical and electrophysiological techniques as an important target lobule for visual input from the visual cortices and midbrain tegmentum[7,9,10]. We have demonstrated in electrical stimulation experiments[9,10] that the response properties of parafloccular neurons to input from the visual cortex and superior colliculus are comparable to those of neurons in the vermis of lobules VI and VII, the classical cerebellar visual area[31]. However, because little is known about how individual neurons in the parafloc-culus respond when their receptive fields are stimulated with an appropriate visual stimulus, it was necessary here to first describe the basic patterns of visually evoked simple and complex spike activity and receptive field properties of Purkinje cells and interneurons in this region of the cerebellum. The present analyses were not intended to provide a detailed account of the receptive field properties of visually responsive parafloccular neu-rons, but designed instead to yield the necessary baseline data for assessing the influence of local NE iontophoresis on the processing of physiologic visual input by these cerebellar neurons.

Visual response properties of parafloccular neurons

Responses to presentations of visual stimuli, consisting primarily of large textural patterns or rectangular bars of light, were examined in 83 parafloccular neurons. Sixty-four percent of these neurons ($n = 53$; 32 of 53 Purkinje cells, 21 of 30 presumptive interneurons) responded to visual stimulation with changes in their simple spike discharge pattern. The present analysis is confined to 58 of the 83 recorded parafloccular neurons which were positively identified as either Purkinje cells ($n = 38$) or molecular layer interneurons ($n = 20$) on the basis of electrophysiological characterization (see Materials and Methods) and subsequent verification of their site of recording.

Simple spike responses

Presentations of visual stimuli during the control period elicited simple spike responses in 55% (32 of 58; 20 of 38 Purkinje cells, 12 of 20 interneurons) of these parafloccular cells. The changes in simple spike activity evoked by presentations of visual stimuli within the receptive fields of the responsive neurons consisted of either pure excitations (69%, 22 of 32 units), sequences of excitation followed by inhibition (19%, 6 of 32 units) or pure inhibitions (12%, 4 of 32 units) (Table I). Complex spike potentials, mediated by input from climbing fibers, were observed in all recordings from Purkinje cells and were readily discriminated from simple spike activity of the neuron. However, only three cells demonstrated complex spike discharges in response to control presentations of visual stimuli. The same three Purkinje cells also displayed stimulus evoked increases in simple spike discharge (see Fig. 1).

Receptive field size

All of the visually responsive neurons had relatively large receptive fields which ranged in size from approx-imately 4° × 5° to somewhat more than half of the visual field. The responsive zones of most of the visual neurons were centered within the ipsilateral hemifield and usually extended somewhat into the visual field on the contra-lateral side (see Fig. 1F). Although the responsive areas of these parafloccular cells were relatively large, stimuli presented outside of the receptive field of a given neuron failed to elicit responses.

Movement sensitivity

The majority of the visual cells (21 of the 32; 16 Purkinje cells, 5 interneurons) were responsive only to stimuli moving through their receptive fields and did not respond to stationary stimuli flashed on and off. These neurons preferred relatively large (greater than 5° × 40°) light bars or spot stimuli and maintained their respon-siveness to stimulus movement over a wide range (20–500°/s) of target velocities. Although large light bars or spots were the most effective, exact stimulus config-urations were not critical. Most individual cells (86%, 18 of 21) demonstrated a preferred direction of movement over a wide range (90°) of stimulus orientation. However,

no overall orientation or directional preference was seen in the population. It should be noted that the response profiles of these parafloccular neurons (see Fig. 1) were remarkably similar to those described for visual ponto-cerebellar cells[2].

For the neuron illustrated in Fig. 1, both mossy and climbing fiber excitations were evoked by movement of a vertical bar of light (9° × 45°) from the left to right and in the reverse direction through the excitatory region of its receptive field (shading, Fig. 1F). The approximate boundaries of the excitatory region were reconstructed from the simple spike responses elicited by left-to-right movement of the stimulus at 118°/s (upslope of trapezoidal waveform, Fig. 1A). These responses were not simple excitatory bursts, but rather were characterized by gradual and sustained increases in activity during movement, which was typical of the simple spike excitatory responses of such cells. Movement of the stimulus from left-to-right across the receptive field of this Purkinje cell elicited the largest increase in simple spike discharge (Fig. 1A, upper PSTH). Note, in comparison, that complex spike responses of roughly equal magnitude were obtained with movement of the bar of light in either direction (Fig. 1A, lower PSTH).

Stationary responsiveness

The remaining 34% of the visually responsive units (n = 11; 4 Purkinje cells, 7 interneurons) were distinguished by their ability to respond to stationary flashing lights. All of the cells in this category also responded to moving stimuli presented at various orientations and over a wide range of velocities (20–500°/s) (see Fig. 2). However, most of these neurons (7 of 11 cases) showed no directional preference for moving stimuli.

The visual response properties of such a neuron are shown in Fig. 2. This interneuron responded with increases in simple spike discharge to moving bars of light

(Fig. 2A–D) as well as to stationary flashing stimuli (Fig. 2E). The optimal stimulus for excitation was a horizontally oriented bar moving in the upward or downward direction (Fig. 2C,D); however, this neuron exhibited very little orientation selectivity overall, and all visually evoked responses were essentially bidirectional. Note that the excitations did not diminish with increasing stimulus speeds, but rather became more phasic with sharply defined onsets and decays (cf. Fig. 2C,D), as was characteristic of the cells that were responsive to stationary light flashes.

Effects of NE on visually evoked responses

The effects of microiontophoresis of NE on the responses of parafloccular neurons to visual stimulation were examined in all 58 cells. In each case, the effects of NE on neuronal responsiveness to visual stimulation were assessed during presentations of moving stimuli.

Table I summarizes the changes in visual responsiveness produced by NE iontophoresis in the 38 Purkinje cells and 20 molecular layer interneurons that were studied. The predominant effect of NE was to improve visually evoked responses in those neurons (n = 32) which demonstrated visual stimulus induced changes in simple spike discharge under control conditions. A clear enhancement of the visual response by NE, manifested as an absolute increase above control, was observed in 18 of the units. In 12 of the remaining cells, reductions in stimulus-bound discharge during NE iontophoresis were accompanied by much larger depressions in background activity, resulting in a net improvement of the ratio of signal-to-noise. A third distinctive feature of NE action was revealed in tests that were conducted in 26 additional neurons which appeared unresponsive to presentations of visual stimuli in the control (predrug) period. Iontophoresis of NE resulted in the elicitation of visually evoked responses in 11 of these units, suggesting the possibility

TABLE I

Effects of norepinephrine on visually evoked responses of cerebellar neurons

Control response to visual stimulation	Purkinje cells (n = 38)				Interneurons (n = 20)			
	Total cells	Enhance*	S/N increase	No change	Total cells	Enhance*	S/N increase	No change
Excitation	13	7	4	2	9	5	4	0
Excitation-inhibition	3	2	1	0	3	1	2	0
Inhibition	4	3	1	0	0	0	0	0
	Response during NE application:				Response during NE application:			
	Total cells	Excitation	Inhibition	No response	Total cells	Excitation	Inhibition	No response
Unresponsive	18	4	6	8	8	0	1	7

* Enhancement of the response by NE was defined as an absolute increase in visually evoked spiking or a potentiation of the inhibitory response with little or no depression in background discharge.

that NE might act in some cases to gate the efficacy of subliminal synaptic input conveyed by classical afferent channels. Each of these facets of noradrenergic action is described separately in detail in the results given below.

Enhancement of visual responses by NE

Presentation of visual stimuli evoked increases in simple spike discharge in 28 of 32 cerebellar units (including 6 cases that responded with sequences of excitation followed by inhibition). In 15 of these cells, NE caused an absolute increase in stimulus-evoked simple spike activity (Table I). This noradrenergic enhancement of visually evoked discharges was observed in the absence of appreciable changes in background firing
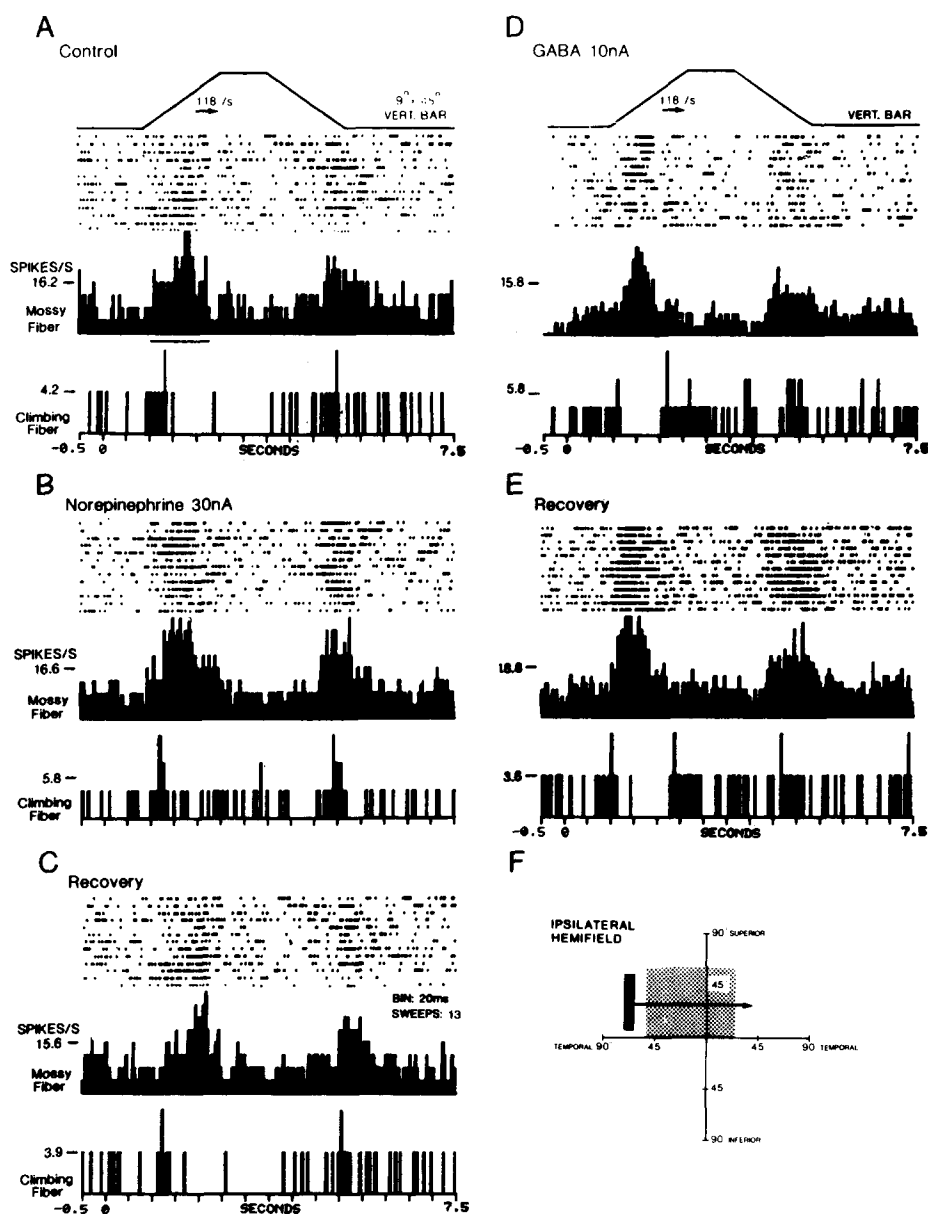
Fig. 1. Comparison of the effects of iontophoresis of NE and GABA on visually evoked simple and complex spike responses of a parafloccular Purkinje cell. A–E: raster and PSTH records illustrate increases in simple and complex spike discharge in response to movement of a vertical bar of light ($9° \times 45°$) from left to right (forward, upslope of trapezoidal waveform) and in the opposite direction (backward, downslope of trapezoidal waveform) through the cell's receptive field. Small arrows indicate the direction of stimulus movement during the upslope of the trapezoid. Numbers adjacent to the arrows indicate stimulus velocity. Zero time indicates the beginning of a stimulus presentation in all trials. This cell only responded to light stimuli moving through its visual receptive field and did not respond to stationary flashing lights. B: during iontophoresis of NE 30 nA both simple and complex spike responses to visual stimulation were enhanced, whereas spontaneous activity was unchanged from the control level. D: iontophoresis of GABA 10 nA depressed both visually evoked and spontaneous simple spike activity and appeared to randomize the occurrence of complex spike discharges in relation to stimulus presentation. However, during GABA application visually evoked simple spike activity was reduced to a lesser extent than spontaneous firing, resulting in an increase in the ratio of signal to noise. F: the receptive field location of the excitatory zone (shading) and forward movement trajectory (arrow) of the light stimulus. Complex spike potentials in the histogram records were coded as single events. Note the change in ordinate scales for the PSTH records. The same number of stimulus presentations ($n = 13$) was used to generate the records shown in (A–E).

rate (Fig. 1), as well as under conditions in which NE iontophoresis produced suppressions in spontaneous discharge (see Fig. 3). In the Purkinje cells shown in Fig. 1, for example, iontophoresis of NE augmented the excitatory response to stimulus movement in both the preferred and reverse directions, but did not alter the rate or pattern of spontaneous firing.

Among the 28 neurons were 3 Purkinje cells which also exhibited complex spike responses to visual stimulation during the control period. Administration of NE resulted in an increased frequency of occurrence of spontaneous climbing fiber discharges in all 3 cells; however, in only one cell was there clear evidence of an enhancement in

visually evoked complex spike activity (Fig. 1).

Four of 32 visually responsive cells (all Purkinje neurons) showed decreases in simple spike activity in response to visual stimulus presentations. The inhibitory responses in three of these were increased during application of NE at iontophoretic levels which had no appreciable effect on the background discharge (Table I). In the fourth cell, NE reduced spike discharge within the period of stimulus-bound inhibition to a much greater extent than spontaneous activity, increasing the size of the inhibitory response relative to the background level of firing (reported as an increase in signal-to-noise, Table I). Iontophoresis of NE also enhanced stimulus-bound
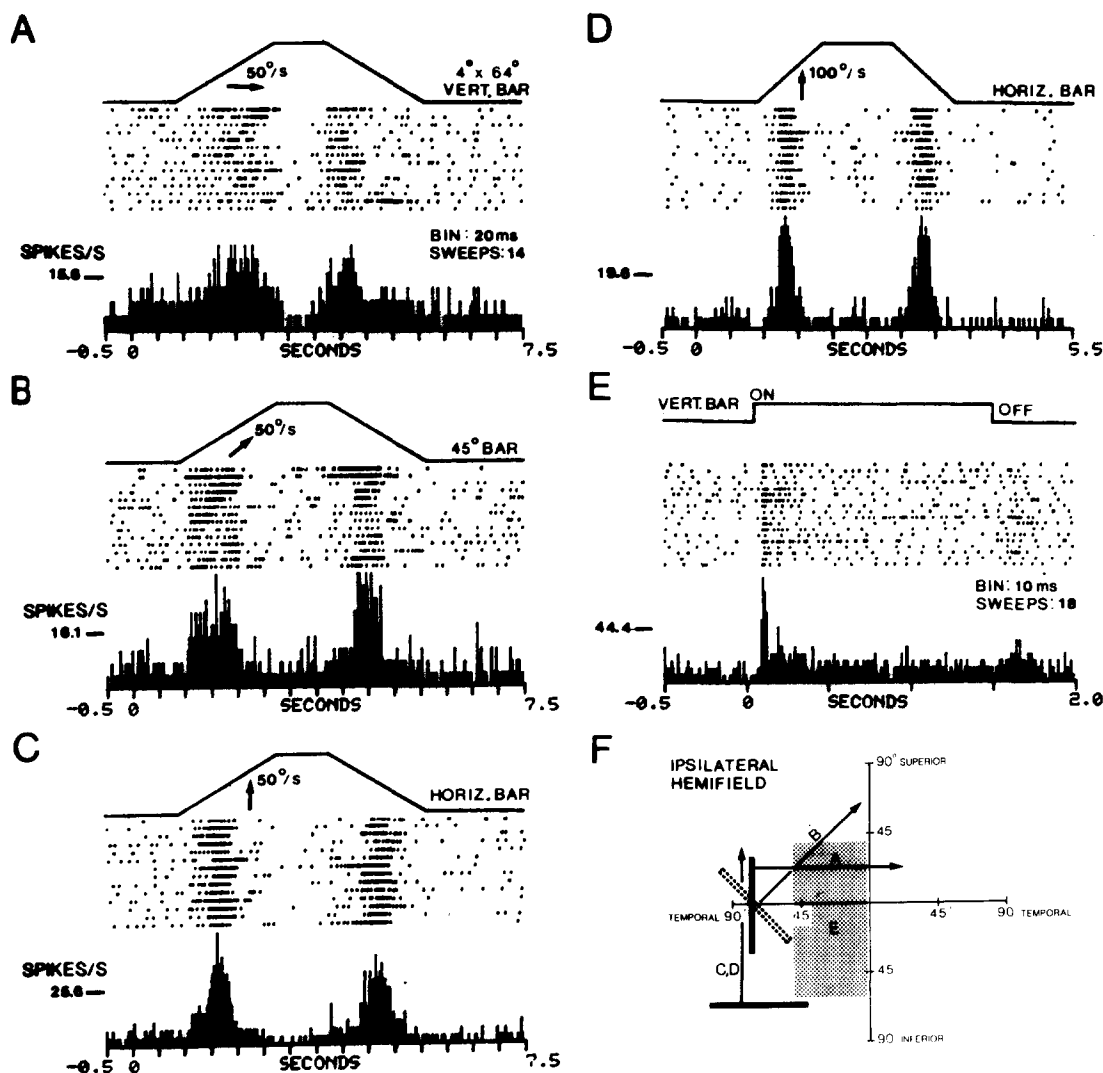

Fig. 2. Raster and peristimulus time histogram (PSTH) records of simple spike activity recorded from a single parafloccular Purkinje cell during presentations of a bar of light (4° × 64°) in the ipsilateral visual field. This cell was stimulated by moving stimuli and stationary flashing lights presented within the excitatory region of its receptive field. A–D: raster and PSTH records illustrate excitatory responses of the neuron elicited by movement of the light stimulus at different orientations, different velocities and in opposite directions (upslope and downslope of trapezoidal waveform). This cell showed the largest responses to upward and downward movement of a bar of light oriented horizontally, but exhibited little or no directional selectivity. E: raster and PSTH displays of spike activity following stationary presentations of a vertically oriented light bar flashed on and off within the excitatory zone. F: the receptive field location (shading) of the excitatory zone and the corresponding movement trajectories (long arrows) of the light bar stimuli. Letters correspond to the PSTHs in A–E. Note the change in abscissa and ordinate scales of PSTHs. The same number of stimulus presentations (n = 14) was used to generate the records shown in A–D.

inhibition without changes in background firing in 3 of the 6 neurons in which inhibition of cell firing flanked a primary simple spike excitatory response.

Overall, NE enhanced visually evoked responses above control levels in 12 of the 20 Purkinje cells and 6 of the 12 interneurons which altered their simple spike pattern of discharge in response to control presentations of visual stimuli (Table I).
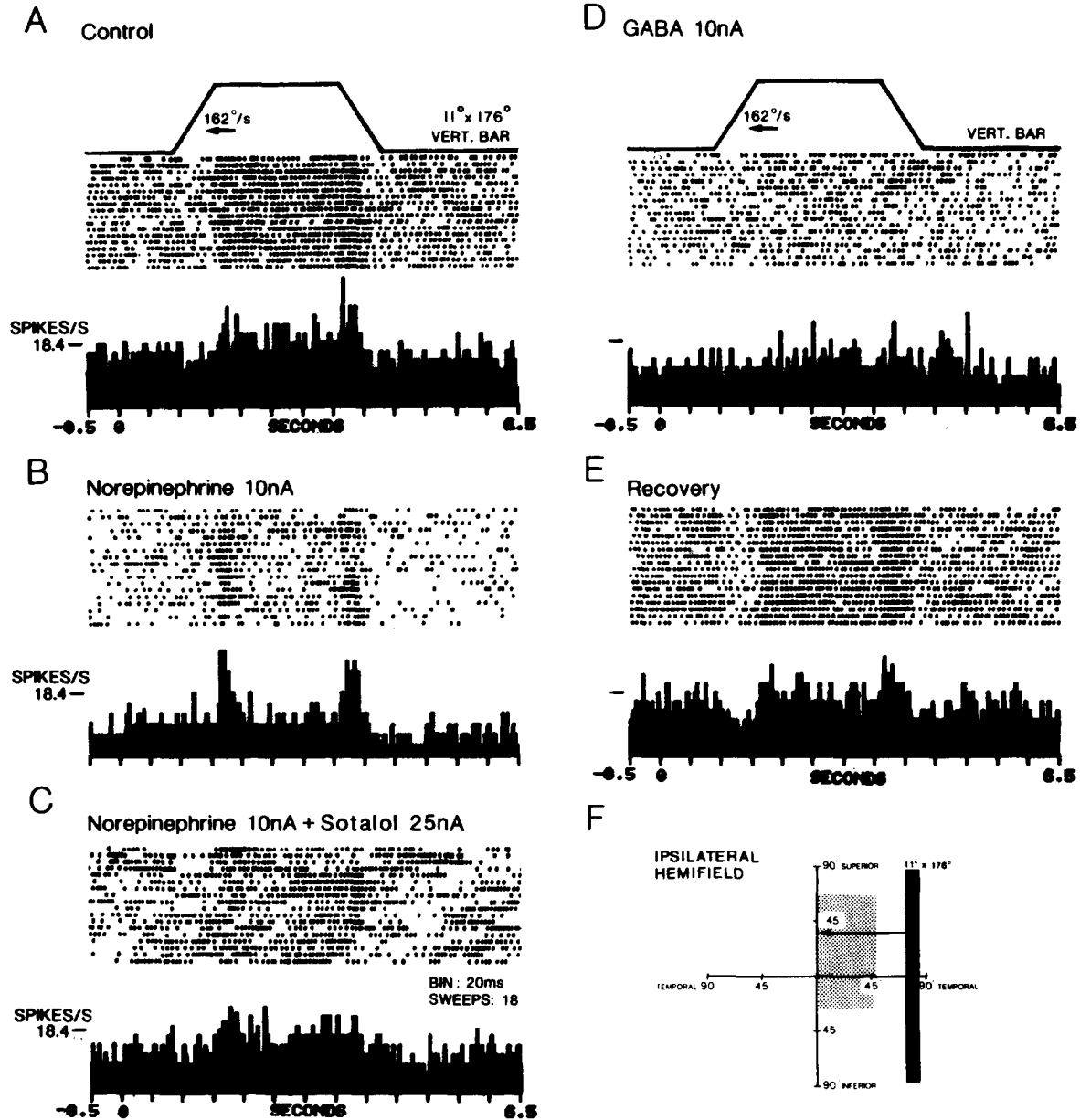

Fig. 3. Comparison of the effects of iontophoresis of NE and GABA on visually evoked and spontaneous simple spike discharge of a Purkinje cell. A: this neuron was stimulated by movement of a vertical bar of light ($11° \times 176°$) from right to left (upslope and trapezoidal waveform) and in the reverse (preferred) direction through its receptive field. B: during iontophoresis of NE 10 nA, spontaneous discharge was markedly reduced, whereas activity evoked by stimulus movement in the preferred direction (left to right) was only slightly decreased, resulting in the enhancement of the ratio of signal to noise. Note that NE had the additional effect of enhancing the cell's excitatory response to movement of the stimulus in the non-preferred direction (from right to left). C: this enhancement of the visual responses by NE was blocked when the specific β-adrenergic antagonist sotalol 25 nA was applied concurrently to the cell by iontophoresis. Note that sotalol antagonized both the depression in spontaneous activity by NE and the enhancement of the response to right-to-left movement of the visual stimulus. Drug iontophoresis was suspended for 20 min following the generation of this histogram record to allow for complete recovery to the control levels of visually evoked and spontaneous activity before further testing with GABA was initiated. D: in contrast to the effects observed during NE, iontophoresis of GABA 10 nA produced a smaller suppression in background firing and yet virtually eliminated the responses to visual stimulation. Recovery of the visually evoked responses to near control levels was observed following the cessation of NE and GABA iontophoresis E. F: the receptive field location of the excitatory zone (shading) and forward movement trajectory (arrow) of the light bar stimulus.

Increase in signal-to-noise ratio by NE

Simple spike responses to visual stimulation were decreased during iontophoresis of NE in the 13 remaining cells (7 Purkinje neurons, 6 interneurons) that were excited by control presentations of stimuli. In these cases, NE did not alter visually evoked responses except when administered at iontophoretic levels which produced a suppression in spontaneous discharge. Moreover, in 11 of these neurons, background discharge was suppressed to a much greater extent by NE than was stimulus-related activity, such that the net effect of catecholamine application was an increase in the ratio of signal to noise
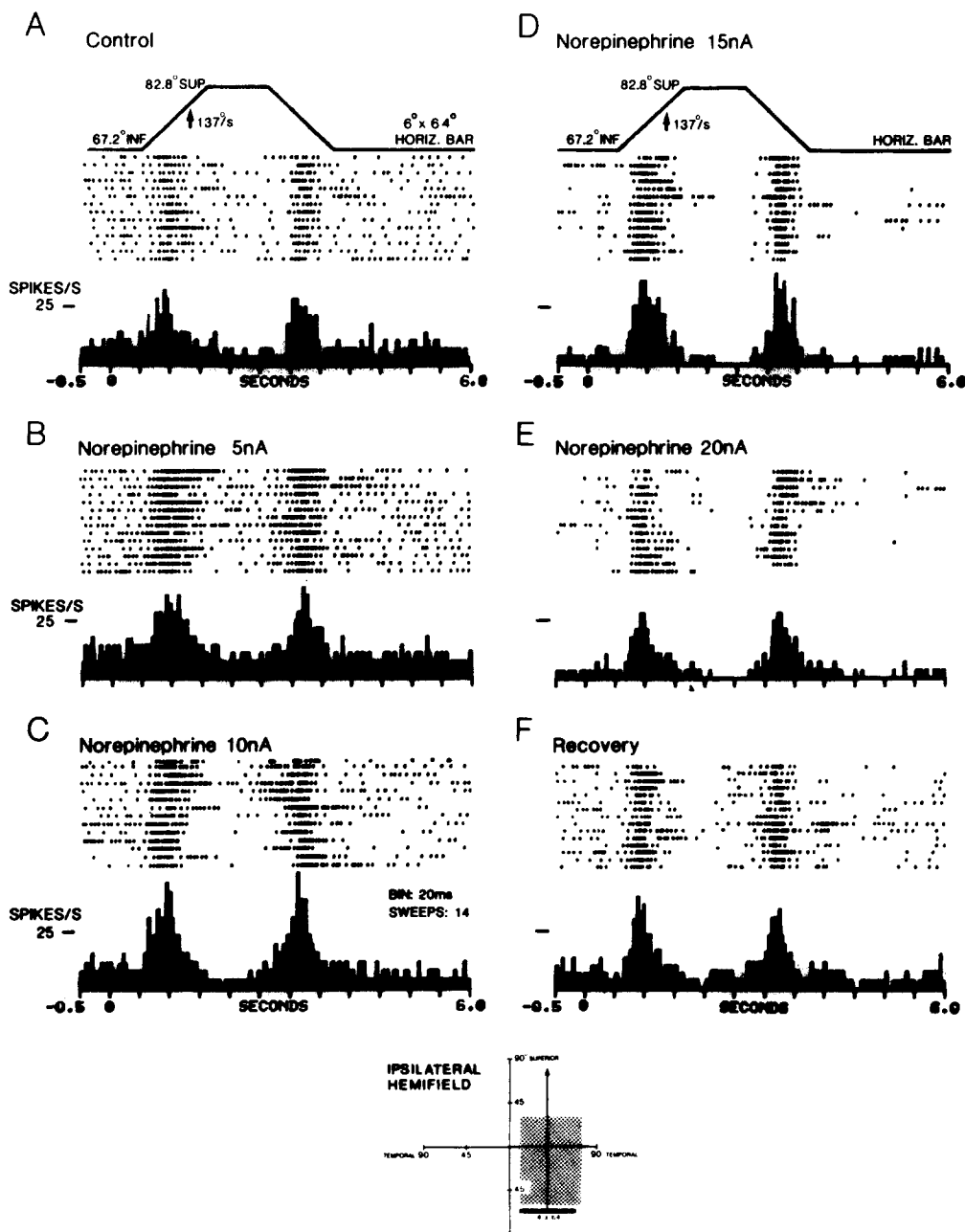

Fig. 4. Examination of the dose–response profile of noradrenergic facilitation of visually evoked responses of a parafloccular neuron. A–F: raster and PSTH records of spike activity recorded from an interneuron during upward and downward (upslope and downslope of trapezoidal waveform) movement of a horizontally oriented bar of light (6° × 64°) through the excitatory zone of its receptive field. This neuron was excited to a similar extent by movement of the stimulus in both upward and downward directions and also responded to stationary light flashes. B–C: increasing the level of NE iontophoresis from 5 to 10 nA resulted in a progressive enhancement of visually evoked activity, whereas spontaneous discharge of the neuron decreased. D–E: at higher levels of NE iontophoresis, evoked spiking began to diminish back toward control levels, whereas background discharge was nearly totally abolished such that the ratio of signal to noise was markedly increased (see Table II). Plot below the PSTH and raster records indicates the movement trajectory of the light bar stimulus (arrow) through the receptive field (shading) of the neuron. The same number of stimulus presentations (*n* = 14) wa used to generate the records shown in A–F. Other details as in legend to Fig. 1.

(Table I). An example of this is shown in Fig. 3. In this Purkinje cell, a marked reduction in spontaneous discharge during NE iontophoresis was accompanied by only a small decrease in the excitatory response to stimulus movement in the preferred direction (from left to right). Interestingly, the response of the cell to movement of the visual stimulus in the opposite direction (from right to left) became more phasic and increased somewhat during the same period. This latter result suggests that the effects of NE are not likely to be resolved in terms of simple enhancement or suppression of visually evoked firing, but might instead reflect more complicated interactions involving the spatio-temporal patterning of visual input to the neuron (see below). In two neurons, NE produced roughly proportional reductions in background and stimulus-evoked discharge and thus had no significant effect on the ratios of signal to noise (Table I).

Iontophoretic dose dependency of NE effects

Fig. 4 illustrates the results from an experiment in which administration of NE produced dose-dependent increases in visually evoked excitatory responses in a molecular layer interneuron. This cell was somewhat unusual in that iontophoresis of the lowest dosage of NE (5 nA) resulted in a slight elevation in spontaneous discharge in addition to marked increases in stimulus-evoked activity (Fig. 4B). The enhancement of visually evoked activity, however, could be clearly dissociated from the effects of NE on spontaneous firing since increases in the visual responses of the cell were also obtained during iontophoresis of NE at levels causing near complete suppression of background discharge (Fig. 4C,D). The effects of increasing levels of iontophoretically applied NE on the visual responses are quantified in Table II both in terms of percentage changes in background activity and as changes in the number of spikes evoked per stimulus. Although administration of NE at

the highest iontophoretic dose (20 nA) examined resulted in some attenuation of the activity evoked by upward movement of the stimulus, relative to control (from 9.1 spikes/stimlus, Fig. 4A, to 8.2 spikes/stimulus, Fig. 4E), this was associated with a further and proportionately greater reduction in the level of baseline firing. Thus, the net effect of increasing the level of NE was to enhance the ratio of stimulus-related vs spontaneous discharge, i.e., signal to noise. The dose dependency of NE's facilitating action on visually evoked excitatory responses was examined in this manner in 4 additional interneurons and 7 Purkinje cells. In all but two of these cases, continual improvement in the magnitude of the response and/or in the signal-to-noise ratio was observed with increasing levels of NE iontophoresis over the range of ejection currents tested.

Receptor mediation of NE-induced facilitation

We have reported previously that NE acts via a β-adrenergic receptor to augment simple spike excitations of Purkinje cells elicited by direct stimulation of cerebellar parallel fibers[26]. In the present study selective α- or β-adrenergic antagonists were applied concurrently during iontophoresis of NE to characterize the nature of the adrenergic receptor mediating the facilitating noradrenergic effects on visually evoked responses in these neurons. In 3 of 4 Purkinje cells tested, iontophoretic application of sotalol, a highly specific β-adrenergic blocker, reversibly antagonized the enhancement of visually evoked simple spike excitation produced by NE (Fig. 3, see responses to stimulus movement from right to left). In each of these cases a complete reversal of the enhancement in visually evoked spiking back to the control (pre-NE) of the response was obtained. Administration of sotalol also reversed the increases in signal-to-noise ratio produced by NE in those cases (3 of 3 Purkinje cells) where the overall effect of catecholamine application yielded a preservation of stimulus related

TABLE II

Effects of increasing levels of iontophoretically applied NE on visually evoked responses

Data are from the experiment shown in Fig. 4. All rates of firing are given in Hz. Initial responses were to upward movement and return responses to downward movement of the stimulus through the cell's receptive field.

Condition	Background firing rate	Initial response			Return response		
		Rate	% Change of background	Spikes/stimulus	Rate	% Change of background	Spikes/stimulus
Control	4.8	14.3	198	9.1	13.1	173	7.6
NE 5 nA	5.4	21.8	289	14.0	19.6	250	11.4
NE 10 nA	3.6	22.7	531	14.6	20.8	478	12.3
NE 15 nA	1.0	17.4	1640	11.0	15.8	1480	10.8
NE 20 nA	0.6	11.4	1800	8.2	13.6	2167	7.9
Recovery	3.0	15.9	430	10.9	14.4	380	8.4

increases in firing despite substantial reductions in the spontaneous background activity of the cell (Fig. 3). This latter effect of β-antagonist administration appeared to result in part from a blockade of NE-induced depressions in background firing, rather than changes in the visual responses per se, as shown, for example in Fig. 3. It should be noted that application of sotalol in the same iontophoretic current range that was used here to block the actions of NE had negligible effects on visual responses that were recorded in the absence of exogenously applied catecholamine. In contrast to these re-

sults, iontophoretic application of the specific α-adrenergic antagonist phentolamine failed to block the NE-induced facilitation of visually evoked responses in three additional Purkinje cells tested (data not shown). Phentolamine was also without effect on NE-induced depressions in spontaneous firing, except when administered at relatively high iontophoretic levels which alone produced a non-specific slowing of action potential discharge.

Gating of subliminal visual input by NE

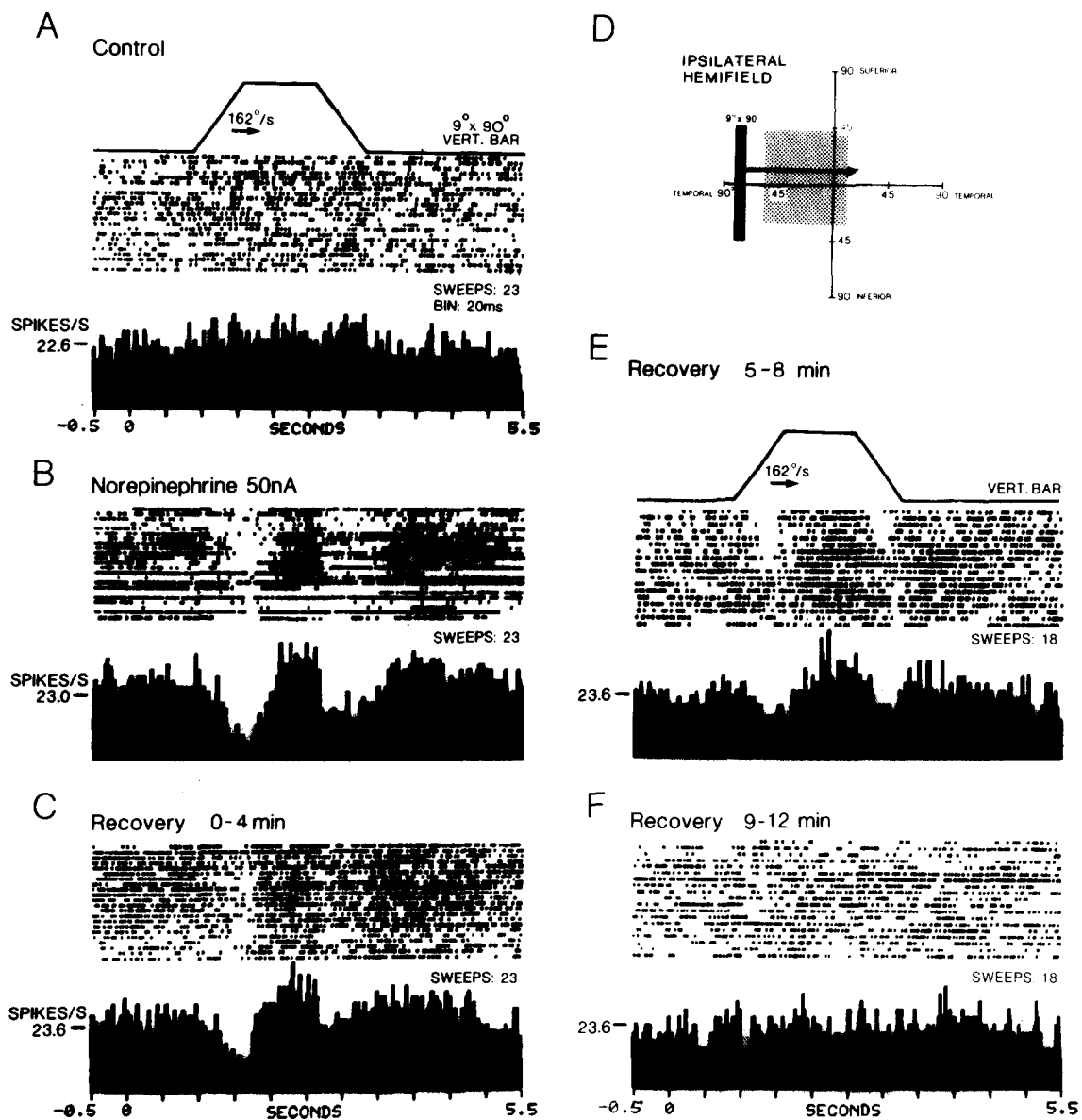An unexpected finding of the present study was the

Fig. 5. Expression of an inhibitory response of a neuron to visual stimulation by NE iontophoresis. Prior to administration of NE, this Purkinje cell showed no appreciable response to presentations of a vertically oriented light bar stimulus (9° × 90°) moving from left to right (upslope of trapezoidal waveform) and back through its receptive field. B: during iontophoresis of NE 50 nA, the cell responded in an inhibitory manner to presentations of the visual stimulus with a preference for movement in the forward (left to right, indicated by small arrow) direction. Note that the expression of the inhibitory response by NE was accompanied by an elevation in background discharge of the neuron. C,E: note also that the cell continued to show inhibitory responses to visual stimulation for upwards of 8 min following the termination of NE administration. D: the movement trajectory of the light bar stimulus (long arrow) through the inhibitory zone of the cell's receptive field (shading).

ability of NE to express responsiveness to visual stimulation in many of the Purkinje cells which failed to respond to control presentations of visual stimuli. Eighteen of the 38 Purkinje cells (47%) and 8 of the 20 interneurons (40%) that were studied did not respond to visual stimulation during the control period. These 26 cells are treated in Table I as a distinct category of 'unresponsive' neurons, and for the purposes of discussion are described similarly in the text. When NE was administered, 10 of the 18 unresponsive Purkinje cells began to respond to visual stimulation, showing either excitations (4 cells) or inhibitions (6 cells) in simple spike discharge (Table I). The responsiveness of these 10 neurons to visual stimulation was maintained throughout the period of NE iontophoresis and gradually diminished with increasing time after cessation of NE administration (Fig. 5). Fig. 5 illustrates a case where an inhibitory response to visual stimulation was expressed during NE administration in an unresponsive Purkinje cell. Note the prolonged time course of decay of this noradrenergic effect on visual responsiveness which is still apparent in both the PSTH and raster displays generated 5–8 min after the termination of the NE ejection current (Fig. 5E).

The outcome of interactions of NE iontophoresis with Purkinje cells and interneurons that were classified as unresponsive was notably different, in that administration of the monoamine resulted in the expression of responses to visual stimulation in only 1 of the 8 interneurons (Table I). A further observation was that the 18 Purkinje cells which did not respond to visual stimulation during the control period fired at significantly ($P < 0.01$) higher mean rates of spontaneous discharge (30.5 ± 1.36 Hz, group mean ± S.E.M.) than corresponding responsive Purkinje cells (22.8 ± 1.65 Hz) (Fig. 6A). On the other hand, differences in mean rates of baseline firing were not observed between visually responsive and unresponsive interneurons (Fig. 6).

Effects of GABA iontophoresis on visual responsiveness

In order to examine the possibility that the expression of visual responsiveness produced by NE might involve a simple hyperpolarization of the neuronal membrane, we compared the effects of iontophoretic GABA with those of NE on responsiveness to visual stimulation in the same 18 cerebellar neurons. The outcome of GABA interactions with the visual responses of these 13 Purkinje cells and 5 interneurons is summarized in Table III. Administration of GABA did result in the expression of responses to visual stimulation in 1 of 6 Purkinje cells and 1 of 3 interneurons which did not respond to control presentations of visual stimuli. In comparison, 3 additional neurons from this group (4 Purkinje cells and 1 interneuron in all) exhibited responses to the same stimulation during iontophoresis of NE. This difference in action between NE and GABA was for the most part observed during iontophoretic application of these agents at levels producing similar depressions in background discharge. Moreover, the ability of NE to express responses to visual stimulation was also found in three of these cases in the absence of any changes in spontaneous activity.

The effects of GABA on visually responsive parafloccular neurons were also found to differ from those of NE. Simple spike excitatory (6 Purkinje cells, 2 interneurons) and inhibitory responses (1 Purkinje cell) to visual stimulation were examined before, during, and after iontophoresis of GABA and NE in 9 cells (Table III). An increase in visually evoked excitatory responses was never observed during GABA administration, whereas in three of the Purkinje cells iontophoresis of NE resulted in increases in simple spike excitation above the control level of response. In 5 of the other neurons (3 Purkinje cells, 2 interneurons), NE improved excitatory responses relative to background levels of firing, in that activity evoked by visual stimulation was unchanged or only slightly reduced from control despite appreciable reduc-

TABLE III

Effects of GABA on visually evoked responses of cerebellar neurons

Control response to visual stimulation	Purkinje cells (n = 13)				Interneurons (n = 5)			
	Total cells	Enhance*	S/N increase	S/N decrease	Total cells	Enhance*	S/N increase	S/N decrease
Excitation	3	0	3	0	1	0	0	1
Excitation-inhibition	3	0	2	1	1	0	0	1
Inhibition	1	0	1	0	0	0	0	0
	Response during GABA application:				Response during GABA application:			
	Total cells	Excitation	Inhibition	No response	Total cells	Excitation	Inhibition	No response
Unresponsive	6	1	0	5	3	0	1	2

* Enhancement of the response by NE was defined as an absolute increase in visually evoked spiking or a potentiation of the inhibitory response with little or no depression in background discharge.

tions in the rate of spontaneous discharge by the catecholamine. In comparison, the effect of GABA iontophoresis was to reduce visually evoked firing and inhibit spontaneous activity in all 8 cells which showed simple spike excitatory responses to control presentations of visual stimuli. In 5 of these cells, GABA reduced spontaneous discharge to a much greater extent than visually evoked activity, thereby producing a net increase in the ratio of signal to noise (Table III). An example of this effect is shown in the Purkinje cell in Fig. 1. Note, however, that in this same cell (and in two other cases showing simple spike excitation) iontophoresis of NE resulted in an absolute increase in the simple and complex spike responses of the neuron to the same visual stimulus.

In the other 3 neurons, the suppression of stimulus-evoked discharge produced by GABA was greater than the depression in background firing, such that the net effect of drug application was to abolish visually evoked excitation reported as a decrease in signal-to-noise, Table

III. A suppression of responses to visual stimulation by GABA is shown in Fig. 4. A similar depressant action of NE on visually evoked activity was never encountered, even during administration of iontophoretic doses of NE which produced complete suppression in spontaneous neuronal discharge. Overall, the suppressions in firing rate induced by GABA were found to produce a profile of changes in the pattern of visually evoked firing quite different from that produced by noradrenergic action. Tests in a final Purkinje cell revealed, in addition, that whereas NE increased inhibitory responses to visual stimulation without affecting spontaneous activity, increases in stimulus-bound inhibition by GABA could not be completely associated from the depressant action of the amino acid (Table III).

Effects of NE on directional selectivity and orientation bias

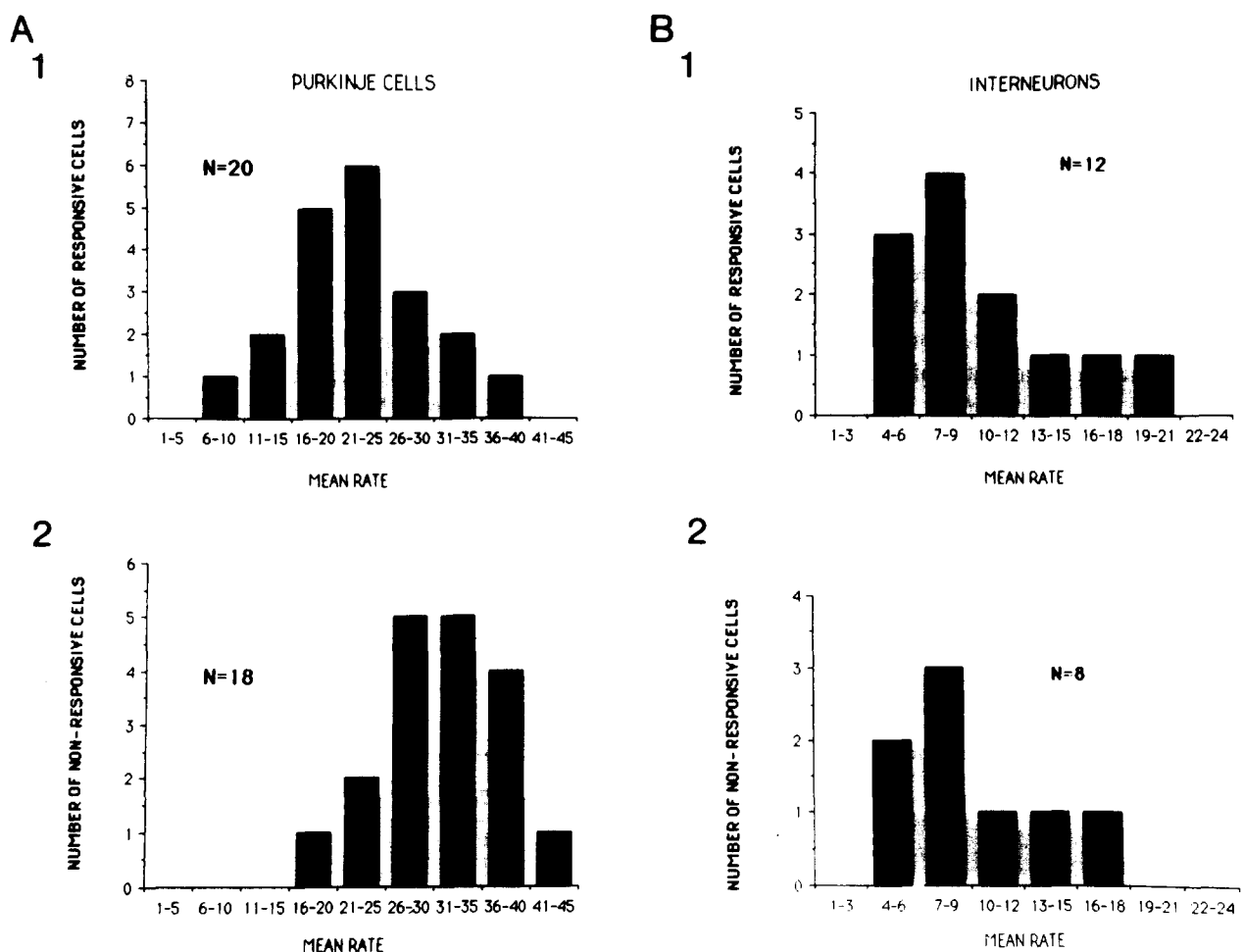A final issue addressed in this study was whether there

Fig. 6. Comparisons between the mean rates of spontaneous discharge of parafloccular neurons responding and those found unresponsive to control presentations of visual stimuli. Bar graphs in A show comparisons for Purkinje cells and those shown in B for interneurons. Purkinje cells which did not respond to visual stimulus presentations during the control period (A_2) tended as a group to discharge at a significantly higher mean rate of firing (30.5 ± 1.4 Hz, S.E.M.) than did visually responsive Purkinje cells (A_1 22.8 ± 1.7 S.E.M.), $P < 0.01$ as determined by rank sum test.

might be components of the visual response properties of parafloccular neurons which are insensitive to changes in local synaptic action. We compared the directional selectivity and orientation bias of visual cells before and during monoamine iontophoresis to determine whether NE might alter the spatial distribution of excitability in and around the receptive field. Of the visually responsive neurons, 69% (15 Purkinje cells, 7 interneurons) showed a preference for stimulus movement in a particular direction, whereas the remaining 10 cells (5 Purkinje cells, 5 interneurons) exhibited responses to visual stimulation that were essentially bidirectional. Typical examples of a directionally selective and a bidirectional

neuron are shown, respectively, in Figs. 1 and 2).

Overall, NE did not appear to qualitatively affect the directional selectivity of individual units, in that cells typically maintained their initial preference for a specific direction of movement (20 of 22 cells) or their bidirectionality of response (all 10 cells) during iontophoresis of the drug. In all 10 bidirectionally responsive neurons, the simple spike responses to forward and reverse movements of visual stimuli were altered, relative to control levels, (enhanced in 6 cases, decreased in 4 cases) to an equivalent extent during NE iontophoresis. This effect is clearly illustrated in Fig. 4. In this cell, the excitatory responses evoked by movement of the stimulus both
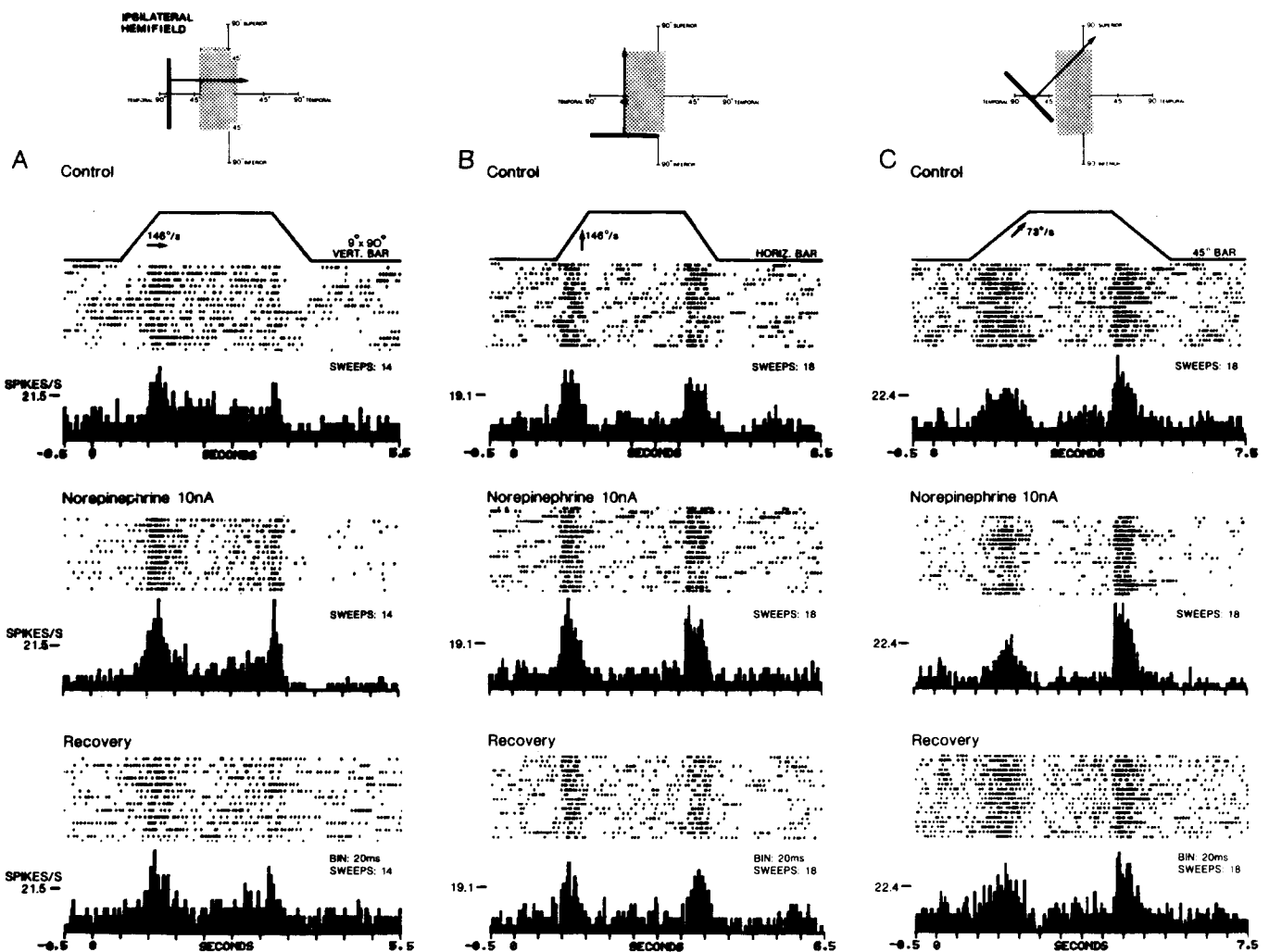

Fig. 7. Effects of NE iontophoresis on the orientation tuning and directional selectivity of a visual parafloccular cell. A–C: raster and PSTH records of spike activity recorded from an interneuron illustrate excitatory responses elicited by movement of a light bar stimulus (9° × 90°) at different orientations and in the forward and backward direction (upslope and downslope of trapezoidal waveform) through the excitatory region of the cell's receptive field. Small arrows indicate the forward direction of stimulus movement during the upslope of the trapezoidal waveform. This neuron showed bidirectional responses to presentations of light bar stimuli at various orientations. During iontophoresis of NE 10 nA (A–C, middle panels) visually evoked responses were enhanced, whereas spontaneous firing of the neuron was depressed. Enhancement of visually evoked activity by NE was observed for responses elicited by stimuli presented in both the forward or backward direction and at different orientations. Consequently, NE did not appear to significantly affect orientation tuning or directional selectivity of the neuron. Panels above the PSTH and raster displays in A–C indicate the respective movement trajectories (long arrows) of the light bar stimuli through the cell's receptive field (shading). Other details as in legend to Fig. 1.

upward and downward through the receptive field were enhanced by roughly the same amount (see responses expressed as a percentage change in background, Table II) as the level of NE iontophoresis was increased. A similar profile of NE action on the visual responses of a neuron to stimulus movement in the preferred and non-preferred direction was also found in 10 of the 22 directionally selective cells (Fig. 1).

Although the directional selectivity of individual neurons was essentially preserved during monoamine iontophoresis, NE was sometimes found to differentially affect responses to movement in the preferred vs non-preferred directions such that directional selectivity was measurably enhanced (in 5 Purkinje cells and 4 interneurons) or in some cases (3 Purkinje cells) reduced. Fig. 3 illustrates one such case where the unidirectional preference of the visual response was reduced in favor of the emergence of bidirectional sensitivity during NE iontophoresis.

The effect of NE on the orientation bias of visual parafloccular cells was examined in detail in 3 interneurons and 1 Purkinje cell. All 4 neurons showed increases in simple spike discharge to visual stimulation and maintained their responsiveness to visual presentations over a wide range of stimulus orientations. During iontophoresis of NE, the visually evoked excitatory discharges of each neuron were enhanced. The enhancement induced by NE occurred regardless of whether the response was elicited by stimuli presented in the optimal or non-optimal orientations. Fig. 7 illustrates the relative non-selectivity of NE action in modulating orientation bias in an interneuron. This neuron showed robust bidirectional excitatory responses to control presentations of light bar stimuli oriented vertically (Fig. 7A), horizontally (Fig. 7B), and at 45° counterclockwise from vertical (Fig. 7C). During NE iontophoresis, background discharge of the cell was depressed, whereas evoked activity related to 5 of 6 different presentations of visual stimuli was enhanced. No evidence of a change in orientation bias was observed during NE application in the other 3 cells studied.

DISCUSSION

The data reported here are discussed with respect to two general issues: (1) the visual responsiveness and receptive field properties of neurons in the rat parafloccculus, and (2) the effects of NE iontophoresis on visually evoked patterns of activity in these neurons.

Response properties

The present findings confirm our previous electrophysiologic and anatomic studies in the rat which indicated that the parafloccculus is a target area of the cerebellum for visual information[7,9,10]. Our results show that moving or stationary presentations of visual stimuli readily activated cells of the paraflocculus via mossy fiber afferents. On the other hand, visual stimuli did not routinely elicit complex spike potentials in parafloccular Purkinje cells.

The response characteristics of parafloccular cells to visual stimuli corresponded closely to those reported for cerebellar cortical neurons in the vermal region of lobules VI and VII (in cat)[3,6,12]. The majority of cells in the midvermis have large receptive fields, are preferentially responsive to moving stimuli over a wide range of speeds (10–1000°/s), respond to pattern and bar stimuli, demonstrate directional selectivity and are activated by stationary light flashes. These properties also characterized the visual responses reported here for parafloccular cells. Midvermal Purkinje cells also demonstrate complex spike activations in response to visual stimulation, and the majority of the visually responsive cells in lobules VI and VII respond to both moving and stationary on-off stimuli (cat)[12]. Aside from the activation of complex spike potentials, the response properties of midvermal and parafloccular cells are strikingly similar and suggest that the two cerebellar regions receive similar visual information.

Modification of cerebellar visual responses by NE

The results of the iontophoretic experiments showed that local application of NE had a predominantly facilitating effect on visually evoked simple spike responses in parafloccular neurons. The enhancement of visual responses by NE was expressed as relative or absolute increases in stimulus-evoked simple spike excitations and as augmentations of stimulus-bound suppression of activity without appreciable change in spontaneous firing rate. These findings are consistent with and extend previous results from this laboratory which indicated that iontophoretic or endogenous release of NE can augment synaptically evoked responses of Purkinje cells elicited by electrical stimulation of conventional excitatory and inhibitory afferent pathways[15,25,26]. The finding here that sotalol but not phentolamine antagonized the facilitation of visual responses by NE is also in keeping with the demonstration in our previous work that these noradrenergic potentiative effects on synaptically evoked activity in cerebellum are mediated via a β-adrenergic receptor[25,26]. A further outcome of the present study was the clear demonstration that NE can augment complex patterns of neuronal responses that are elicited by presentations of physiologic stimuli.

Reductions of visually evoked responses, below the level of control, were observed during the period of NE iontophoresis in 40% ($n = 13$ cells) of the visually

responsive parafloccular Purkinje cells and interneurons that were studied. In all but two of these cases, the reduction of visual evoked discharge was accompanied by much larger suppressions of spontaneous activity, such that the net effect produced by NE administration was an enhancement in the ratio of signal to noise. Similar 'modulatory-type' effects of NE, in which stimulus-bound activity of the neuron is preserved relative to suppression in its spontaneous discharge, have been reported in areas other than the cerebellum, including the somatosensory[35], visual[1,19,34] and auditory cortex[14].

It has been argued that increases in the signal-to-noise ratio might result from a general inhibition of the cell by NE. A 'selective' depressant action on background firing over evoked excitation might be expected in the particular case in which inhibition is caused by a simple membrane hyperpolarization and when spontaneous firing is initiated by weak depolarizing inputs compared to evoked discharges arising from larger postsynaptic potentials. However, several lines of evidence indicate that the improvement by NE in the ratio of visually evoked firing to background activity in parafloccular neurons cannot be resolved simply in terms of such differential effects on synaptically induced vs spontaneous firing. First, iontophoresis of NE resulted in the elicitation of simple spike excitations and inhibitory responses in a large number of the Purkinje cells tested which failed to respond to control presentations of visual stimuli. In some cells, this ability of NE to gate the effectiveness of subliminal visual input was clearly dissociated from its effects on background activity. Second, comparisons of NE effects with those of GABA in the same neurons revealed a profile of changes in the pattern of visually evoked firing during amino acid-induced suppressions in activity which were quite different from those produced by noradrenergic action. Moreover, whereas iontophoresis of GABA resulted in the complete suppression of visually evoked excitation in 3 neurons, a similar outcome was never encountered with NE, even when it was administered at iontophoretic doses which completely eliminated spontaneous firing.

An important issue to consider is whether the enhancement in visual responsiveness produced by NE was due to postsynaptic changes in the neuron under study or occurred indirectly via interactions of NE with presynaptic elements (for example, see ref. 11). We have shown previously that the ability of NE to enhance mossy and parallel fiber evoked excitations of Purkinje cells can be mimicked by interaction of the catecholamine with neuronal responses produced by direct postsynaptic application of the putative synaptic transmitter, glutamate[23,24,37]. The enhancement of glutamate responses by NE appeared to reflect changes in postsynaptic respon-

siveness to the excitatory transmitter, since increases in glutamate-evoked spiking could be produced under conditions where presynaptic input from the parallel fibers was eliminated (Yeh and Moises, unpublished results). Recent intracellular studies of NE actions in pyramidal neurons of rat hippocampus[22] have provided a cellular mechanism which could, in fact, account for such effects. In these neurons, NE has been shown to increase excitatory responses to intracellular depolarizing stimuli and to glutamate iontophoresis by blockade of a calcium-dependent potassium conductance which normally limits spiking following action potential generation. The calcium-dependent potassium conductance which is found in Purkinje cells[21] could provide a similar substrate for mediating the noradrenergic enhancement of visually evoked simple spike activity found here.

In other cases reported here visual stimulus-bound inhibition was enhanced during NE application. Recent work by Sessler et al.[29] has shown that, like NE and specific β-adrenergic receptor agonists, agents such as forskolin which also increase intracellular levels of cyclic AMP can augment cerebellar neuronal responses to iontophoretically applied GABA. These results coupled with other recent data suggesting a role for protein phosphorylation in maintaining GABA receptor function[28,32,33] provide a potential mechanism whereby NE could regulate neuronal responses to GABAergic inhibitory synaptic inputs.

Role of NE in visual information processing within the cerebellum

The present results are consistent with the hypothesis that a significant component of noradrenergic action in cerebellum (and other brain areas receiving LC-NE innervation) is to augment target neuron responsiveness to conventional afferent inputs which mediate detailed information transfer[36]. The finding that some parafloccular Purkinje neurons only responded to visual stimulation during local administration of NE suggests further that NE might act to bias the gain of subliminal or otherwise latent synaptic inputs to these neurons and thereby gate information flow within local cerebellar circuits. It is tempting to speculate that the combined effect of these actions would result in an enhancement of visual information processing by the cerebellum under conditions where local noradrenergic activity is increased. Still the question remains how the changes in visual responsiveness found in Purkinje cells and interneurons might be translated into improvements in the integration and transfer of visual information within the cerebellum.

Although the overall effect of NE was to augment the visually evoked responses of both kinds of parafloccular

neurons, NE did not appear to influence the orientation bias of individual units. One possibility is that this component of the receptive field properties of these cerebellar neurons is determined extrinsically, and therefore largely insensitive to changes in local synaptic actions. It should be noted in this regard that the visually-responsive parafloccular neurons closely resembled visual pontine cells in that exact stimulus orientations and configurations were not critical to elicit responses[2,27]. Although qualitatively the directional selectivity of visual parafloccular neurons was also unchanged during catecholamine iontophoresis, the visual responses to movement in the preferred and non-preferred direc-

tions were differentially affected by NE, such that in more than one-third of the cells directional selectivity was measurably enhanced ($n = 9$) or occasionally ($n = 3$) reduced. Thus, there is some basis to propose that the physiological expression of noradrenergic action in visually responsive parafloccular neurons might be reflected in a refinement of their visual receptive field properties.

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