Visual Projections Routed to the Auditory Pathway in Ferrets: Receptive Fields of Visual Neurons in Primary Auditory Cortex

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How does cortex that normally processes inputs from one sensory modality respond when provided with input from a different modality? We have addressed such a question with an experimental preparation in which retinal input is routed to the auditory pathway in ferrets. Following neonatal surgical manipulations, a specific population of retinal ganglion cells is induced to innervate the auditory thalamus and provides visual input to cells in auditory cortex (Sur et al., 1988). We have now examined in detail the visual response properties of single cells in primary auditory cortex (A1) of these rewired animals and compared the responses to those in primary visual cortex (V1) of normal animals. Cells in A1 of rewired animals differed from cells in normal V1: they exhibited larger receptive field sizes and poorer visual responsivity, and responded with longer latencies to electrical stimulation of their inputs. However, striking similarities were also found. Like cells in normal V1, A1 cells in rewired animals exhibited orientation and direction selectivity and had simple and complex receptive field organizations. Furthermore, the degree of orientation and directional selectivity as well as the proportions of simple, complex, and nonoriented cells found in A1 and V1 were very similar. These results have significant implications for possible commonalities in intracortical processing circuits between sensory cortices, and for the role of inputs in specifying intracortical circuitry.

Is cortex of a given sensory modality uniquely specified to process inputs of that modality, or can it, under certain conditions, process input of another modality? The question is important for understanding intrinsic and extrinsic determinants of cortical development, and for understanding plasticity and recovery of function following early brain trauma. In this article, we have addressed the issue by routing visual inputs into the auditory pathway during development and subsequently studying the resulting visual responses of cells in auditory cortex in the adult. We have previously demonstrated that, following specific neonatal lesions, retinal afferents in the ferret can be induced to innervate the auditory thalamus (specifically, the medial genic-

ulate nucleus, or MGN). Retinal afferents subsequently provide visual input to cells in primary auditory cortex (A1) of the "rewired" ferret (Sur et al., 1988) and establish a topographic visual map there (Roe et al., 1990a). We have now examined both qualitatively and quantitatively the physiological response properties of single visual units in A1 of rewired ferrets and compared them to the properties of cells in primary visual cortex (V1) of normal ferrets.

A preliminary report of these data has been published previously (Roe et al., 1990b).

Materials and Methods

Neonatal surgery to route retinal projections to the MGN

To induce retinal innervation of nonvisual thalamic structures, it is necessary to remove the normal retinal targets [primarily the lateral geniculate nucleus (LGN) and the superior colliculus (SC)] and to make alternative target space available [in this case, the medial geniculate nucleus (MGN); see Schneider, 1973].

Procedures were similar to those described previously (Pallas et al., 1990). Briefly, timed pregnant pigmented ferret jills were bred in our colony or purchased from a commercial supplier (Marshall Farms). Within 24 hr of parturition, ferret kits were removed and anesthetized by deep hypothermia. All surgery was performed under sterile conditions. A 1 cm midline incision was made in the scalp and the skull was exposed. After removing a small piece of overlying skull, the SC was ablated by cautery. To induce massive retrograde degeneration of the LGN, large regions of visual cortex (including areas 17, 18, and often 19) were lesioned by cauterizing through the skull. Fibers running in the brachium of the inferior colliculus were transected at the mid-SC level, thereby denervating the MGN. All lesions were made unilaterally (bilateral lesions significantly reduced survival rates). On completion of surgery, the skin was sutured and the kit revived under a heat lamp. A single dose of antibiotic (0.01 cc amoxycillin, 100 mg/ml) was given subcutaneously, and antibacterial ointment was applied to the wound. The kit was then returned to the mother for rearing.

These lesions result in induction of developing retinal afferents into the MGN (Sur et al., 1988). Since the normal thalamocortical connectivity from the MGN to primary auditory cortex (A1) is retained (Pallas et al., 1990), an aberrant visual pathway from the retina to MGN to A1 is established (Sur et al., 1988).

Visual physiology in adult ferrets

Surgical preparation. Normal and rewired adult ferrets were prepared for visual physiology using procedures similar to those described previously (Roe et al., 1989). Animals were anesthetized, paralyzed, and respirated. Following induction of anesthesia with ketamine hydrochloride (30 mg/kg) and xylazine (2 mg/kg), a cannula (24 gauge) for anesthetic and paralytic delivery was implanted in either the femoral or the jugular vein, and an endotracheotomy was performed. Animals were then placed in a stereotaxic apparatus, paralyzed, and artificially respired (rate, 30–40/min; vol, 25–30 cc) with a 70:30 mixture of nitrous oxide and oxygen. Ferrets received a constant intravenous infusion of a 5% dextrose solution containing ketamine hydrochloride (10 mg/kg/hr) for anesthesia and gallamine hydrochloride (3.6 mg/hr/kg) for muscular paralysis. End-tidal CO_2 was maintained at 4.0%, heart rate was monitored, and body temperature was maintained at 38°C with a heating

Table 1. Number of units recorded in V1 and A1

	V1	A1
Total	153	495
Electrically driven	124 (95)[a]	485 (98)
Visually driven	105 (69)	194 (39)
Visually and electrically driven	77 (59)[a]	184 (37)
Receptive field size determined	101 (66)	100 (20)
Ocular dominance determined	76 (50)	110 (22)
Cell class determined	101 (66)	52 (11)
Quantitatively characterized	38 (25)	24 (5)
Driven by auditory stimuli	0 (0)	0 (0)

Percentage of total is shown in parentheses.

[a] Percentage calculated from a total of 131 cells for which chiasm latencies were assessed. In one experiment, chiasm latencies were not assessed (22 cells).

Figure 1. Distribution of responsivities (1 indicates poor responsiveness and 4 good responsiveness) of cells in A1 (dark bars) and V1 (light bars). These distributions are significantly different ($p < 0.0001$, Mann–Whitney U test). Out of a total of 194 cells, 38 recorded from early experiments in rewired animals were not rated for responsivity.

pad. Supplemental halothane (1%) was supplied during all surgical procedures. The skull and dura overlying visual cortex in normal animals and auditory cortex in rewired animals were removed. Stimulating electrodes were lowered into the optic chiasm and cemented in place. Drops of atropine sulfate and phenylephrine hydrochloride were applied to the eyes to dilate the pupils. Eyes were fitted with zero-power contact lens and focused on a tangent screen 114 cm in front of the animal. Optic disks were plotted by reflection onto the tangent screen.

Recording and data collection. In 18 rewired and 13 normal adult ferrets, we used parylene-insulated tungsten microelectrodes (2–3 MΩ impedances) to record extracellularly from isolated cells in A1 of rewired and V1 of normal animals. Recording penetrations were made in A1 (located between the anterior and posterior limbs of the ectosylvian sulcus; Kelly et al., 1986) and V1 (located in the caudal half of the lateral sulcus; Law et al., 1988) on the basis of sulcal patterns. Penetrations were usually spaced 250–500 μm apart. Unit activity was assessed every 50–100 μm in each penetration (1) for response to electrical stimulation of the optic chiasm (1–15 V) and (2) for response to visual stimulation. In two rewired animals and one normal animal, pure tone bursts (ranging from 8 to 20 kHz) or broad-band auditory stimuli (100 ms square-wave clicks or white noise) were delivered binaurally through earphones. Visually responsive units were plotted and characterized on the tangent screen with a hand-held projection lamp. In addition to receptive field location (as determined by reflection of the optic disk, located at 33° azimuth and −3° elevation; Zahs and Stryker, 1985) and receptive field size (measured as 1° per 2 cm on a tangent screen located 114 cm from the eye), a number of other response characteristics were also examined. These included ocular dominance; orientation, direction, and velocity selectivities; spatial organization of on- and off-responses within the receptive field; presence or absence of summation and end-stopping; and strength of response. When possible, oriented cells were classified as simple or complex (Hubel and Wiesel, 1962). Electrolytic lesions (5 μA for 5 sec) were made in selected penetrations.

The tuning characteristics of a subset of isolated single units were studied quantitatively. For quantitative determination of orientation, direction, and velocity tuning preferences, moving bar stimuli, either projected with an optic bench or generated on a Tektronix monitor driven by a PICASSO (Innisfree) stimulus generator, were continuously swept (without interleaving) at each orientation (usually at 30° intervals) and velocity (from 5°/sec to 100°/sec) over the receptive field; each successive orientation and velocity was presented in a pseudorandom fashion. Spike responses of the cell under study were isolated with a pulse-shape discriminator (Ealing). For each category of stimulus, 15 cycles of response were collected and summed by the UNKELSCOPE program run on an IBM PC286 computer, and poststimulus time (PST) histograms were generated on line. Spike responses were also stored on tape, and PST histograms were analyzed off line. Background activity was collected in the absence of visual stimulation.

Histology. Following the completion of data collection, the animal was killed with an intravenous or intraperitoneal overdose of pentobarbital (65 mg/kg) and perfused through the heart with saline followed by fixative (1% paraformaldehyde, 2% glutaraldehyde) and 10% and 20% sucrose solutions. The brain was then removed from the cranium and stored in 30% sucrose overnight. After brain sulcal patterns (Kelly et al., 1986) were recorded photographically, frozen sections were cut
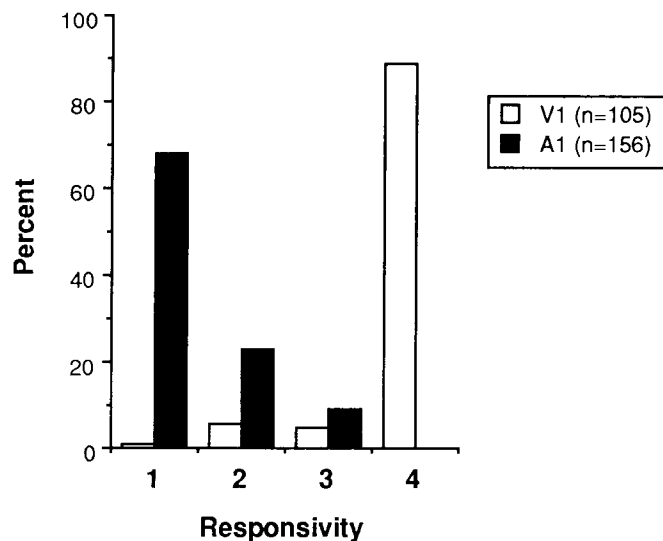
at 50 μm and stained with cresyl violet. Lesions and recording tracks were identified and located with respect to the borders of A1.

Data analysis. For each cell that was studied quantitatively, peak response (maximum spikes/sec summed over at least 10 trials) minus background (average spikes/sec of spontaneous activity summed over identical number of trials) was calculated for every stimulus condition. From these, orientation, velocity, and bar size tuning curves were plotted and selectivity indices calculated. The orientation index was defined as 1 − (orthogonal response/best response), and the direction selectivity index was defined as 1 − (response to direction opposite of preferred direction/response to preferred direction). These are normalized indices, with 1.0 indicating a highly selective and 0 a nonselective cell. In addition, orientation widths were determined at $1/\sqrt{2}$ height (cf. Schiller et al., 1976b). Unless otherwise specified, statistical tests between two parameters employed at the Mann–Whitney U test. Comparison of groups was done using the χ^2 test.

Results

Four-hundred and ninety-five visual units were recorded from A1 of rewired ferrets and 153 visual units from V1 of normal ferrets (see Table 1). Nearly all cells responded to electrical stimulation of the optic chiasm. Of these, 194 (39%) of the cells in A1 and 105 (69%) of the cells in V1 were visually responsive under our recording conditions. The smaller overall proportion (pooled over all animals studied) of visual cells recorded in A1 may be due to poorer responsiveness of A1 units (see below) as well as to interanimal variability in lesion size. [In some rewired animals with large visual cortical lesions, almost all units responsive to chiasm stimulation were visually driven, while in animals with small cortical lesions a much lower percentage of visual units was encountered. This variability probably relates to the size of the extant LGN, and hence to the size of the rerouted retinal projection to the MGN (Roe, 1991).] A subset of the visual cells in rewired A1 and normal V1 were characterized in further detail and their responses studied quantitatively (Table 1). Of the units that were tested for auditory responsiveness ($n = 35$ in A1 of two rewired ferrets; $n = 22$ in V1 of one normal ferret), none responded either to clicks or to
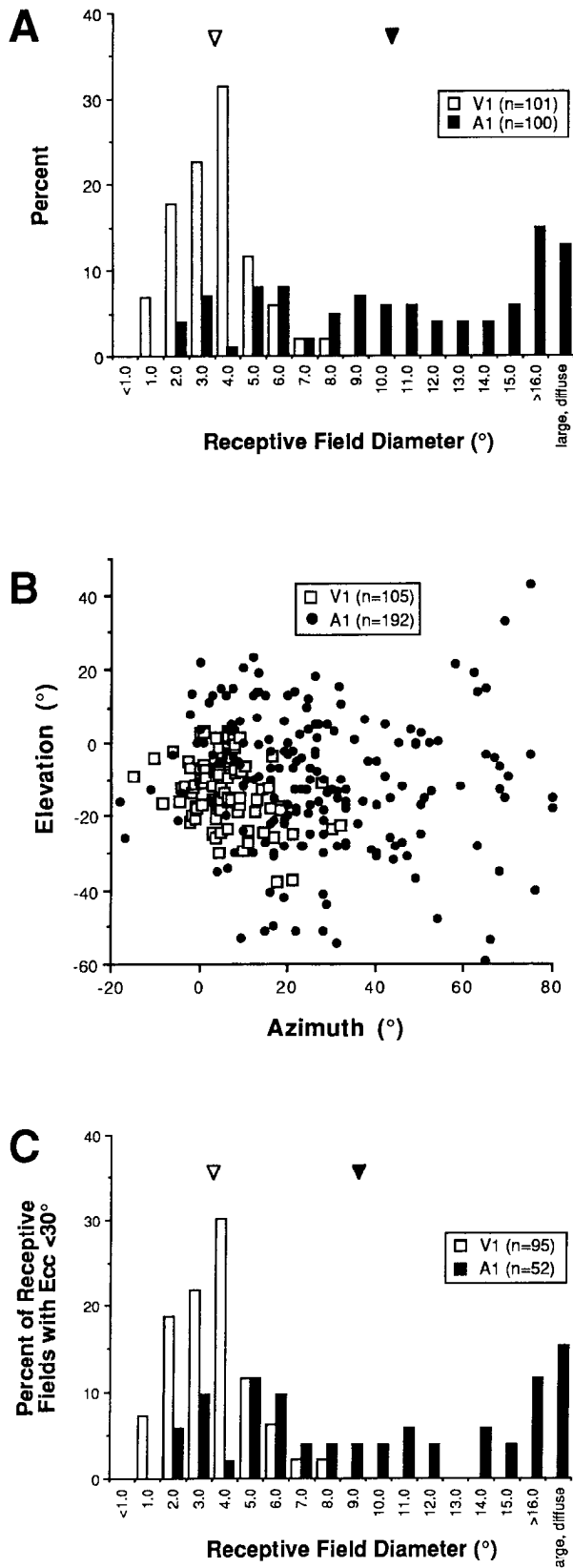
white noise. These same auditory stimuli produced robust responses in normal A1 ($n = 37$ in one normal ferret).

We have not attempted to conduct a laminar analysis of our data. However, visual units were recorded throughout cortical layers in both A1 and V1: cells were recorded throughout the ≈ 1 mm thickness of ferret A1 (Roe, 1991).

Differences between response features of cells in A1 and V1

There were three major differences between the characteristics of visual units in A1 and V1: responsivity, receptive field size, and latency to optic chiasm stimulation. As will be discussed later, these differences appear to arise primarily from the properties of retinal and thalamic input to A1 and V1.

Responsivity

One salient difference between visual units in A1 and V1 was their responsiveness to visual stimulation. Most cells in V1 responded in robust and consistent fashion to visual stimuli. In contrast, cells in A1 were much more difficult to drive, exhibited labile responses, and responded with fewer spikes. Cells were qualitatively rated, during recording, on a four-point scale, where 1 indicates poor responsiveness and 4 good responsiveness. This index reflects both robustness (qualitative determination of response strength, i.e., number of spikes) as well as reliability of response. (Units that were responsive only to electrical stimulation were not rated; 38 A1 cells recorded in early experiments also were not rated.) Of 105 V1 cells and 156 A1 cells that were rated, 93% of units in V1 were rated 4 and 68% of units in A1 were rated 1 (Fig. 1). The poorer responsivity of A1 cells often made receptive field characterization of A1 cells difficult and time consuming; proportionally fewer cells in A1 were fully characterized as a result (see Table 1).

Receptive field size

A second prominent difference between A1 and V1 cells was the size of their receptive fields. Receptive field sizes (calculated as the average of the length and width of the receptive field) of visual cells in A1 were significantly larger than those of V1 cells, their mean diameter (mean = 10.9°, $n = 87$) reaching almost three times that of V1 cells (mean = 3.9°, $n = 101$) (Fig. 2A). Of the cells in A1, 64% had receptive fields larger than the largest receptive fields recorded in V1. In addition, 13% of cells in A1 had receptive fields that were large (15–30° in diameter) and whose borders were difficult to determine precisely (Fig. 2A, large, diffuse; not included in calculation of mean).

The difference in the receptive field sizes were not eccentricity related. The receptive field eccentricities of cells recorded in A1 were significantly different from those of cells recorded in V1 ($p < 0.0001$, Mann–Whitney U test) (Fig. 2B), consistent with the much flatter distribution of visual field magnification in A1 compared to V1 (Roe et al., 1990a). However, receptive field sizes in A1 were still larger ($p < 0.0001$) when eccentricity-matched ($<30°$) populations were compared (Fig. 2C). This was also true for eccentricity-matched samples below 15° (A1, $n =$

Figure 2. *A*, Receptive field diameters (defined as average of width and height of receptive field) of cells in A1 (*dark bars*) and V1 (*light bars*). Receptive field sizes in A1 (mean = 10.9°, *solid arrowhead*) are significantly larger ($p < 0.0001$) than those in V1 (mean = 3.9°, *open arrowhead*). *B*, Distribution of receptive field locations recorded in A1 (*solid circles*) and V1 (*open squares*). In A1, significantly many more fields were recorded representing peripheral regions of the visual field

than in V1 ($p < 0.0001$). *C*, Taking into consideration only receptive fields whose eccentricities are less than 30° reveals that A1 cells still have much larger receptive fields (A1 mean = 9.7°, V1 mean = 3.9°, $p < 0.0001$).
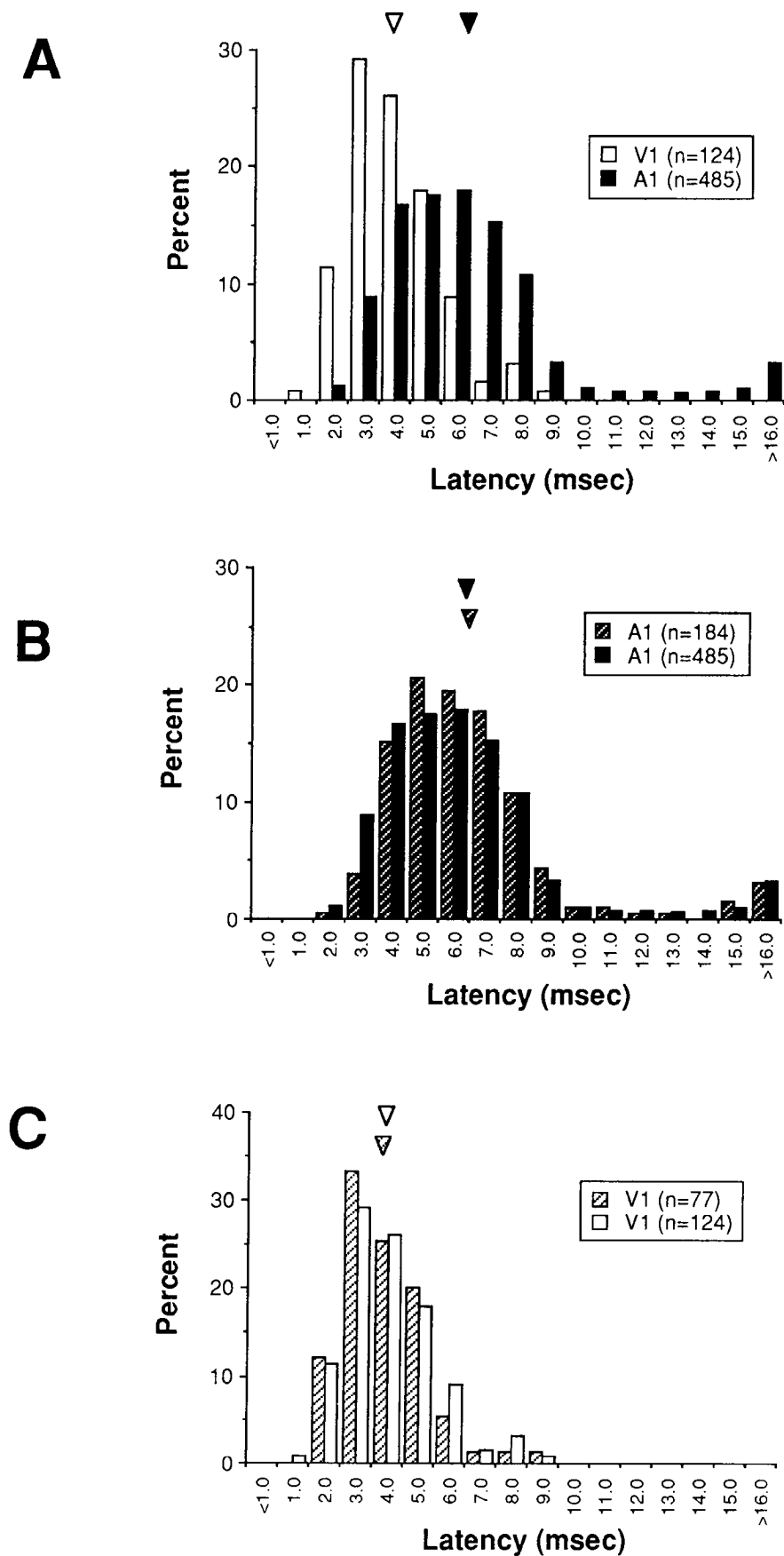
Figure 3. Latencies of cells in A1 and V1 to electrical stimulation of the optic chiasm. *A,* Cells in A1 (*dark bars, n* = 485, mean = 6.8 msec) have significantly longer latencies to chiasm stimulation than those in V1 (*light bars, n* = 124, mean = 4.4 msec) (p < 0.0001). *B,* Latencies of visually responsive cells in A1 (*shaded bars, n* = 184, mean = 6.9 msec) are similar to those of all cells recorded in A1 (p > 0.13). *C,* Similarly, visually responsive cells in V1 (*shaded bars, n* = 77, mean = 4.3 msec) have latencies similar to all cells recorded in V1 (p > 0.7).

18; V1, n = 53; p < 0.0001) and below 45° (A1, n = 78; V1, n = 101; p < 0.0001).

Conduction latency of afferents

Cells in A1 and V1 also differed in their latencies to optic chiasm stimulation. When the latencies of all cells in A1 and V1 were compared (Fig. 3*A*), those recorded in A1 (mean = 6.8 msec) were significantly longer than those in V1 (mean = 4.4 msec; p < 0.0001). In both A1 (Fig. 3*B*) and V1 (Fig. 3*C*), the latencies recorded for the subpopulation of visually responsive cells (A1, n = 194; V1, n = 77) were representative of all units recorded. There was no correlation between the latency to optic chiasm stimulation and cortical depth, receptive field size, or responsivity.

Similarities between cells in A1 and V1: integrative features of receptive fields

Of the visual cells recorded in A1 of rewired ferrets, a portion were sufficiently responsive to allow further characterization, including determination of cell class, ocular dominance, and orientation, direction, and velocity selectivities. As mentioned previously, reliably responding visual cells were much more frequently encountered in V1 than in A1; this difference is reflected in the higher percentage of cells in V1 (25%, n = 38) than in A1 (5%, n = 24) whose responses were quantified.

Ocular dominance

To determine a cell's ocular dominance, we compared (with an audio monitor) the ipsilateral and the contralateral monocular responses to visual stimulation of its receptive field. We subsequently rated the cell on a scale from 1 to 7, with 1 indicating complete contralateral dominance, 7 complete ipsilateral dominance, and 4 equal dominance by the two eyes (Hubel and Wiesel, 1962). In V1, we recorded predominantly contralaterally dominated cells (Fig. 4): 65% of all units tested exhibited complete contralateral ocular dominance (OD group 1) and only 10% exhibited an ipsilateral dominance (OD group 5, 6, or 7). [A few cells (n = 3) to which we did not give an ocular dominance rating were not responsive to monocular stimulation but exhibited clear responses to binocular stimulation.] This contralaterally biased visual representation in the mustelid visual cortex has been previously reported and is due to both an extensive monocular segment as well as a true contralateral bias in the binocular segment (LeVay et al., 1987; Law et al., 1988; Zahs and Stryker, 1988; Redies et al., 1990).

In A1, a similar ocular dominance distribution was seen: 66% of the visual cells rated were completely contralaterally dominated (OD group 1) and 7% exhibited ipsilateral preference (OD group 5, 6, or 7). Approximately 30% of units recorded in both A1 and V1 are binocular (OD groups 2–6). These two ocular dominance distributions are not significantly different [$\chi^2(0.95)$ = 4.6, df = 6].

Cells recorded in A1 and V1 with any ipsilateral contribution had receptive fields in the binocular segment. The receptive fields of five cells in V1 (one contralaterally, two ipsilaterally, two binocularly driven) and five cells in A1 (all contralaterally driven) fell in the ipsilateral hemifield. This may be a reflection of inappropriate location of some retinal ganglion cells with respect to the nasotemporal division in the ferret retina (Vitek et al., 1985).
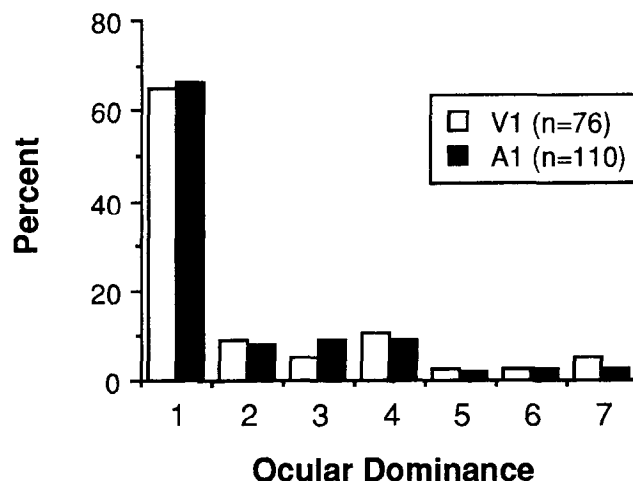

Figure 4. Ocular dominance distributions of visual cells recorded in A1 (*dark bars*) and in V1 (*light bars*). These two distributions are not significantly different [$\chi^2(0.95)$ = 4.6, df = 6].

Receptive field types

V1 cells. Receptive fields of cells in V1 of normal ferrets were classified as simple or complex, if oriented, or as nonoriented, and in general resembled those described previously in cats (Hubel and Wiesel, 1962), minks (LeVay et al., 1987), and ferrets (Law et al., 1988). Most simple cells (n = 20) exhibited two or three spatially segregated contrast-specific subfields, responding to either onset or offset of optimally oriented flashing bars and/ or to moving light or dark contrast edges of optimal orientation. Responses within a single subfield exhibited spatial summation to flashing bars of increasing size. Some cells that we classified as simple (n = 4) exhibited spatial summation but had only a single on or off region (see Zahs and Stryker, 1988; cf. Palmer and Davis, 1981; Schiller et al., 1976a). Complex cells (n = 50) had only a single oriented response field to flashing bars or moving contrast edges of the appropriate orientation and typically responded to both the onset and offset of light and/or to edges of either light or dark contrast. Complex cells typically were equally responsive to small as well as large bars within their receptive fields. Two cells that we classified as complex responded only to very small moving or flashing oriented bars within their receptive fields and were silenced by bars illuminating the entire receptive field. These cells may correspond to "special complex" cells described in previous studies (Palmer and Rosenquist, 1974; Gilbert, 1977). End-inhibition was seen in both simple (n = 8) and complex cells (n = 10). Nonoriented cells (n = 27) had either circular or elongated receptive fields with weak or absent inhibitory surrounds.

A1 cells. In A1, as mentioned above, receptive fields were larger. In general, receptive field organization was somewhat more difficult to determine due to weakness and lability of response. Despite this, similar receptive field structures were observed. We were able to classify approximately one-half (52 of 100) of the cells in A1 as simple, complex, or nonoriented. Similar to cells in V1, simple cells in A1 (n = 16) displayed orientation selectivity and had one (n = 4), two (n = 6), or three (n = 4) spatially segregated subfields. Borders between subfields were not as sharp as those in V1, but were nonetheless clearly present. Complex cells (n = 24) were oriented, exhibited either on-, off-, or on/off-responses throughout their receptive fields,
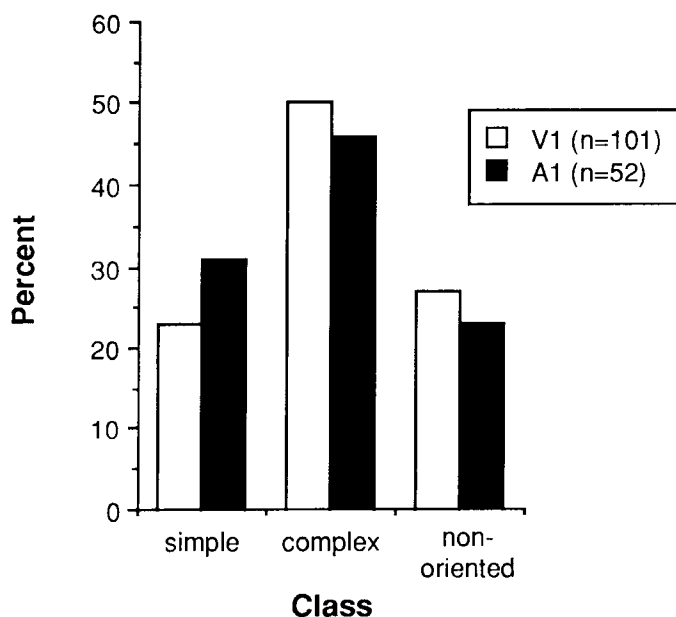
Figure 5. Percentage of simple, complex, and nonoriented cells in A1 (*dark bars*) and V1 (*light bars*). These distributions are not significantly different [$\chi^2(0.95) = 3.7$, df = 2].

and responded equally well to small and large bars. End-stopping was seen in one simple and five complex cells. In one case (a simple cell), the degree of end-inhibition was quite dramatic: extending a light bar by 10% beyond the receptive field border reduced the cell's response by 50%. Nonoriented receptive fields ($n = 12$) were either circular or elongated with weak or absent inhibitory surrounds.

Relative proportions. Not only do simple, complex, and nonoriented cell types occur in A1, they also occur in proportions similar to that found in V1. In both the A1 and the V1 populations recorded, approximately 50% of the cells were complex, 25% simple, and 25% nonoriented (Fig. 5). While we do not claim that these figures reflect actual cell class composition in A1 and V1, at no time did we attempt to "find" cells of any particular class. Our sampling was based solely on units with appropriate strength and consistency of response. We found no statistically significant correlations, in either A1 or V1, between receptive field type and receptive field size, latency to optic chiasm stimulation, or depth. Neither were there any correlations between cell type and orientation, direction, or velocity selectivities (see also below).

Tuning characteristics of single units in A1 and V1

To determine orientation tuning, we first examined responses to flashing bars at various orientations. For cells not responsive to standing flashes, we made a qualitative assessment of orientation selectivity with moving or "jiggling" bars or moving edges. We also tested the response to moving spots; however, moving spots were generally not an effective stimulus. For quantitative determination of orientation selectivities, moving bars were used as stimuli and polar plots made of the responses. In almost all cases, quantitative characterization of the optimal orientation agreed with our qualitative assessment. For some cells in A1, quantitative collection of spikes in response to multiple stimulus sweeps revealed orientation tuning not obvious from responses to single sweeps assessed by ear.

An example of an orientation selective cell in V1 is shown in Fig. 6*A*. This cell is a simple cell and responds optimally to a bar oriented at $-45°$ from vertical, sweeping in either direction. A second example is shown in Fig. 6*B*. This complex cell prefers bars oriented at $+45°$ from vertical and is slightly directional for upward movement.

Cells in A1 were also characterized similarly. Fig. 7*A* illustrates the orientation selectivity of a nondirectional simple cell in A1 that preferred horizontally oriented bars. A directionally selective simple cell is shown in Fig. 7*B*. This cell responds best to downward-sweeping bars oriented 30° from vertical. As can be seen from these plots, cells in A1 respond with fewer spikes overall than those in V1 and their responses appear to be modulated less strongly with respect to background levels.

Orientation tuning. The orientation tuning of 38 cells in V1 and 24 cells in A1 was studied quantitatively. For each of these cells, two measures of orientation tuning were calculated: orientation selectivity and orientation tuning width. The orientation selectivity index is defined as: 1 − (orthogonal response/best response) (cf. Felleman and Van Essen, 1987). A cell whose response in the best orientation is twice the level of that to the orthogonal orientation would have an orientation selectivity of 0.5; one whose best response is 1.5 times that in the orthogonal orientation would have a selectivity of 0.33. We have considered those units with selectivities below 0.3 to be unoriented, those with selectivities from 0.3 to 0.5 to be weakly oriented, and those with selectivities above 0.5 to be strongly oriented. Both A1 and V1 contained cells exhibiting a range of orientation tuning selectivities, ranging from unoriented to strongly oriented. In fact, no significant difference was seen in the distribution of orientation strengths of cells in A1 and V1 (Fig. 8*A*). Of oriented cells, approximately 40% of units in A1 (three simple, six complex) and V1 (six simple, eight complex) were sharply oriented (selectivity > 0.5), while 33% of units in A1 (five simple, three complex) and 26% in V1 (three simple, seven complex) were broadly oriented (selectivity 0.3–0.5).

Orientation tuning widths (defined as the width of the orientation tuning curve at $1/\sqrt{2}$ peak height) were also determined. For both A1 and V1 cells, orientation tuning widths ranged from narrow tuning (<30°) to very broad tuning (>90°) (Fig. 8*B*). While a greater percentage of cells in V1 than in A1 had tuning widths of 30°–59°, these distributions were not significantly different. Thus, neither measure of orientation tuning revealed any quantitative difference between A1 and V1 with respect to orientation tuning.

Direction selectivity. A directionality index was calculated from the responses obtained at the preferred orientation of each cell; this index was defined as 1 − (nonpreferred/preferred response). The frequency distribution of these values in A1 and V1 also proved to be similar (Fig. 9). Interestingly, V1 contained a higher proportion (40%) of nondirectional (directional selectivity < 0.3) cells than A1 (21%). A1 also contained a greater proportion (25%) of highly directional cells (selectivity > 0.6) than V1 (15%). Overall, however, the two distributions were not significantly different ($0.1 < p < 0.5$). No relationship was seen between cell class and directionality in either A1 or V1: directionality strengths for each of the simple, complex, and nonoriented cells classes ranged from nondirectional to highly directional.

Velocity selectivity. One of the more unexpected findings of this study was that the velocity tuning of cells in A1 were similar to those of cells in V1. The velocity selectivity of each cell was
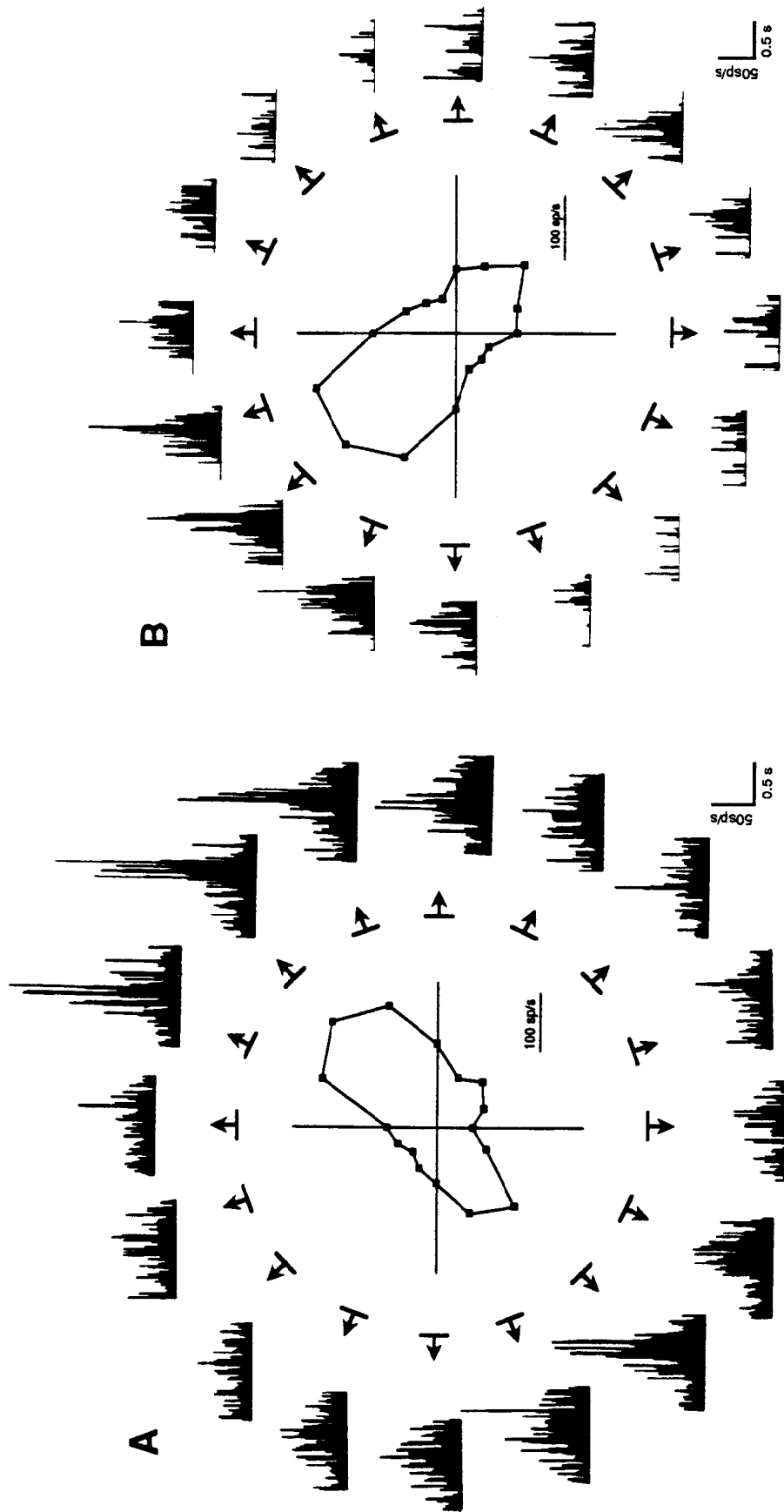
Figure 6. Orientation tuning of two cells in V1: polar plots of each cell's response (peak minus background) to sweeping bars at different orientations and directions (indicated by *bars with arrows*). PST histograms for each bar orientation and direction are shown. *A,* A simple cell with an orientation tuning selectivity of 0.57, an orientation tuning width of 63°, and a directionality selectivity of 0.25. Stimulus bar, 2.4° × 4.4° (L × W), sweeping at 19°/sec. *B,* An end-stopped complex cell with an orientation tuning selectivity of 0.73, an orientation tuning width of 65°, and a directionality selectivity of 0.38. Stimulus bar, 6.1° × 3.0° (L × W), sweeping at 12°/sec.

Figure 7. Orientation tuning of two cells in A1 (conventions as in Fig. 6). *A,* An end-stopped complex cell with orientation tuning selectivity 0.73, orientation tuning width 65°, and directionality selectivity 0.38. Stimulus bar, 5.7× × 6.5° (L × W), sweeping at 72°/sec. *B,* A simple cell with orientation tuning selectivity 0.63, orientation tuning width 47°, and directionality selectivity 0.71. Stimulus bar, 12.5° × 13.2° (L × W), sweeping at 78°/sec.
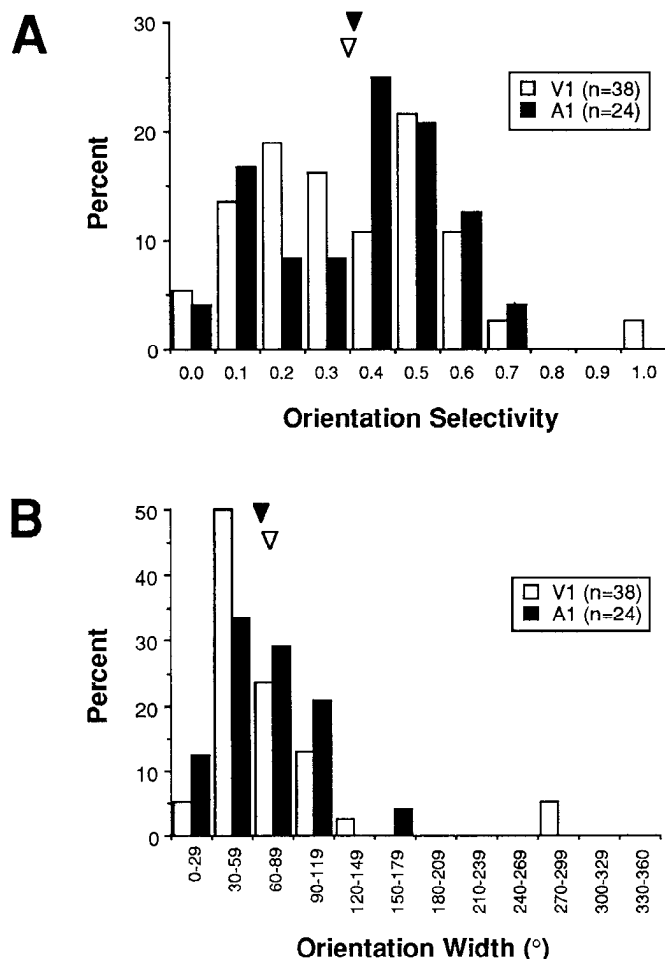
A

B

Figure 8. Orientation tuning of cells in A1 (*dark bars*) and in V1 (*light bars*). *A,* Distributions of orientation tuning selectivities in A1 (mean = 0.41) and V1 (mean = 0.39) are similar ($p > 0.65$). *B,* Distributions of orientation tuning widths (defined as width at $1/\sqrt{2}$ height) in A1 (mean = 65.3°) and V1 (mean = 72.5°) are not different ($p > 0.90$).

studied by collecting responses to optimally oriented light stimuli swept at several velocities, generally between 5°/sec and 100°/sec, over its receptive field; 29 V1 cells (9 simple, 11 complex, and 9 nonoriented) and 18 A1 cells (6 simple, 9 complex, and 3 nonoriented) were studied in this fashion. The stimulus orientation chosen for nonoriented cells was arbitrary.

Examples of velocity tuning preferences are shown in Fig. 10*A* (A1, right column; V1, left column) and are similar to those previously described in cat visual cortex (e.g., Orban et al., 1981). Most cells were tuned to either slow (<15°/sec, curves 1 and 2), medium (15–50°/sec, curves 3), or fast (>50°/sec, curves 4) velocities. Some cells exhibited velocity high-pass or low-pass characteristics (curves 5; see also curves 1). We recorded a few cells that responded equally well to slow and to fast, but not to medium, stimulus velocities (curves 6). Cells exhibiting broad tuning were also encountered (curves 7). Thus, cells in both A1 and V1 exhibited a range of velocity tuning. Furthermore, the velocity tuning distributions were found to be similar in these two areas: approximately 45% of the cells recorded in A1 and V1 were best tuned to slow, 35% to medium, and less than 10% to fast velocities (Fig. 10*B*). No consistent relationship was seen between velocity tuning and cell type.
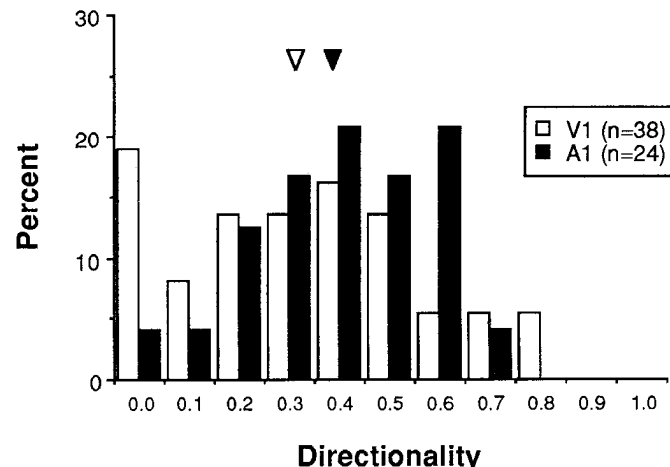

Figure 9. Directionality of cells in A1 (*dark bars*) and in V1 (*light bars*). A1, mean = 0.45; V1, mean = 0.36. The two distributions are not significantly different ($0.1 < p < 0.5$).

Discussion

Our goal in this study has been to explore the developmental and functional specificity of mammalian cerebral cortex. Toward this goal, we have challenged A1 in ferrets with visual input and studied the resulting visual processing in A1. Previously, we reported that retinal projections can be induced to innervate auditory thalamus in ferrets following specific neonatal lesions (Sur et al., 1988; cf. Schneider, 1973). These projections, which appear to arise primarily from retinal ganglion cells of the W cell class, provide visual input to cells in A1 (Sur et al., 1988; Pallas et al., 1990; Roe et al., 1990a; Roe, 1991). In this article we have characterized in detail the receptive field properties of visually responsive cells in A1 of rewired ferrets and have compared them both qualitatively and quantitatively to visual cortical cells recorded in V1 of normal ferrets. We find that receptive field properties of visual cells in rewired A1 bear remarkable similarities to those in normal V1. We will first summarize and discuss the generation of these receptive field properties in A1 and then turn to two possible interpretations of these results.

Generation of visual receptive field properties in A1

Sources of visual input to A1

It is important to consider at the outset what the sources of visual input to A1 are in rewired ferrets. It is possible, for example, that there are novel corticocortical projections to A1 in rewired animals that arise from remaining unlesioned visual cortical areas, and that certain features of visual integration (such as orientation selectivity, direction selectivity, and binocularity) are already present in these cortical inputs. The issue has been addressed by making injections of retrograde tracers into A1 in rewired ferrets, and comparing the cortical and thalamic inputs with those to A1 in normal ferrets (Pallas et al., 1988, 1990). In brief, the cortical areas that project to A1 in rewired animals are the same areas that project to A1 in normal animals, and do not include any visual cortical areas.

The overwhelming proportion of thalamic input to A1 in rewired animals arises from the MGN (Pallas et al., 1990). In addition, a sparse input arises from the lateral posterior (LP)/pulvinar complex to A1 in rewired ferrets (Pallas et al., 1990). It is unlikely that these LP/pulvinar projections contribute to

Figure 10. *A,* Examples of velocity tuning curves in V1 (*left column*) and A1 (*right column*). In each column, *curves 1* and *2* are tuned for slow (<15°/sec), *curves 3* for medium (15–50°/sec), and *curves 4* for fast (>50°/sec) velocities. *Curves 5* display high-pass or low-pass, *curves 6* U-shaped, and *curves 7* broad-band velocity characteristics. *B* (*opposite page*), Distributions of cells in A1 (*dark bars*) and V1 (*light bars*) displaying peak velocity preferences near 6°/sec, 13°/sec, 25°/sec, 50°/sec, 100°/sec, as well as those displaying broad-band (*BB*) and U-shaped (*slow/fast*) tuning curves. These distributions are not significantly different ($p > 0.8$). A1, mean = 27.9°/sec; V1, mean = 24.6°/sec.
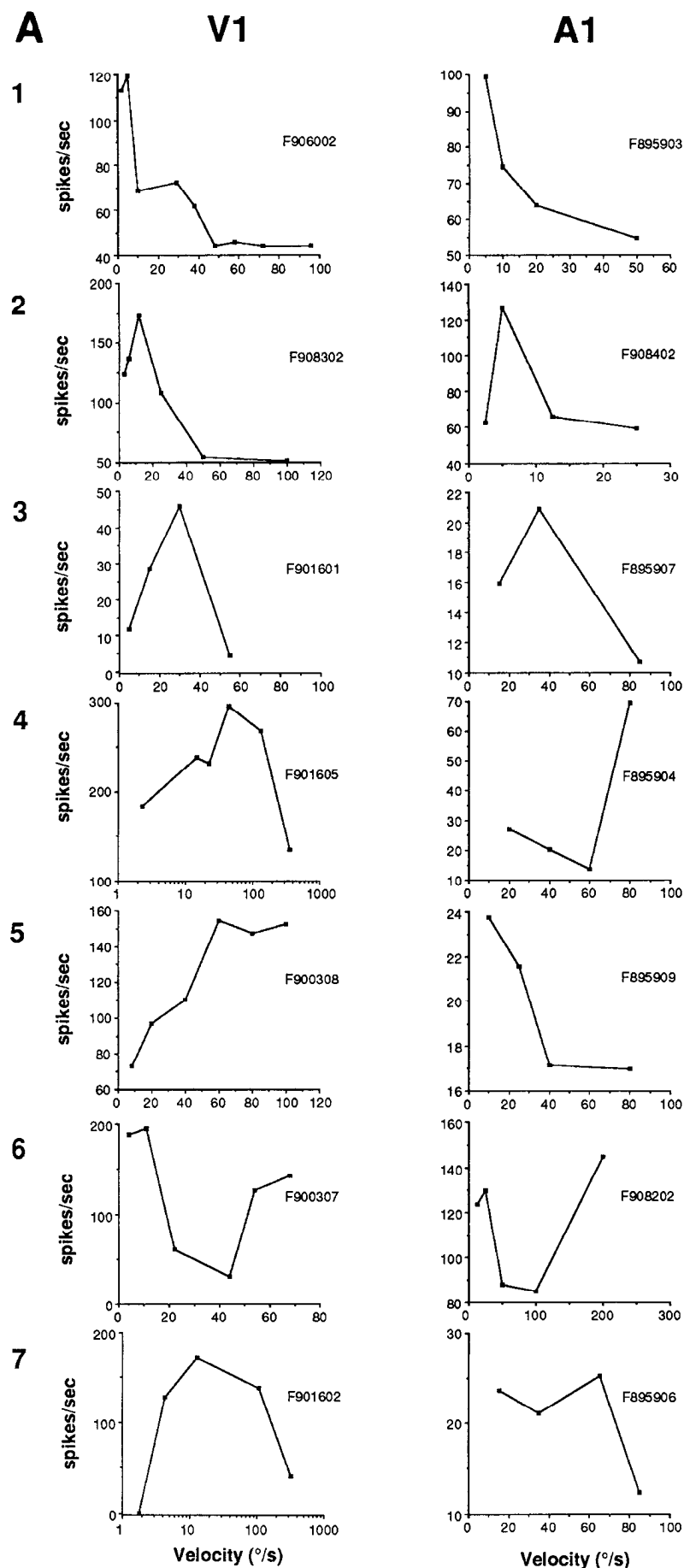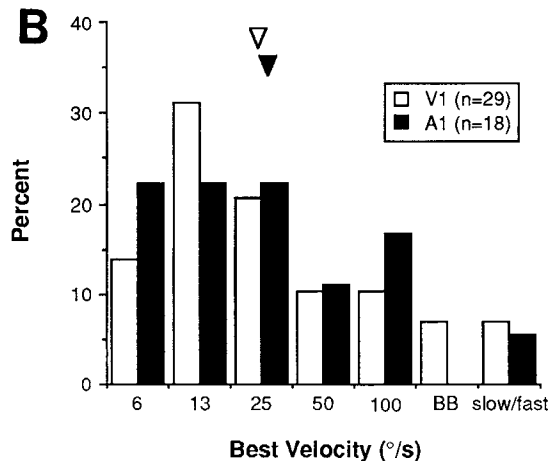
Figure 10. Continued.

the visual responses of A1 neurons since (1) these projections are much sparser than the projections from the MGN, (2) they arise from cells that lie deep within the LP/pulvinar region and that show almost no overlap with retinal projections in these animals, and (3) ibotenic acid lesions of the MGN abolish previously visually responsive recording sites in A1 and similar lesions of the LP/pulvinar complex do not (S. L. Pallas, L. Toth, and M. Sur, unpublished observations).

Contribution of retinal inputs

Our results show that visual cells in A1 are poorly responsive and have large receptive field sizes and long latencies to optic chiasm stimulation. These characteristics are already present in and can be predicted by the retinal and thalamic input to A1. We have suggested previously that the auditory thalamus in rewired ferrets receives retinal ganglion cell input of the W cell type (Roe et al., 1987; Sur et al., 1988; Pallas et al., 1989; Roe, 1991). Retinal W cells have "sluggish" responsiveness to visual stimuli and are characterized by large, often diffuse, receptive fields, some of which have center-surround organization but many of which do not (Wilson et al., 1976; Fukuda et al., 1984; Stanford, 1987). Similar receptive field properties are found in postsynaptic visual cells in the MGN in rewired ferrets (Sur et al., 1988; Roe, 1991). Large receptive field sizes of A1 cells may be due to both the W cells that form the retinal source of inputs and to the pattern of highly convergent and divergent thalamocortical connectivity typical of the auditory system and shown to be retained in these rewired ferrets (Pallas et al., 1990; cf. Andersen et al., 1980; Middlebrooks and Zook, 1983). The poor responsivity of cells in A1 is consistent with its W type input (Sur and Sherman, 1982). In addition, we cannot rule out abnormal synaptic configurations of retinal axons on MGN cells or additional inhibitory mechanisms within MGN or A1 that decrease the responsiveness of MGN and A1 cells in rewired animals. Retinal W cells also have slowly conducting, poorly myelinated axons (Cleland and Levick, 1974a,b) consistent with the relatively long latencies to optic chiasm stimulation found both in the MGN (Sur et al., 1988) and in A1.

Contribution of intracortical mechanisms: similarity of rewired A1 to normal V1

Single cells in A1 exhibit aspects of receptive field organization, orientation selectivity, and direction selectivity absent in visual

cells in the MGN. Visual cells in the MGN have circular or elongated receptive fields; these cells lack orientation selectivity and exhibit lower degrees of direction selectivity than visual cells in A1 (Sur et al., 1988; Roe, 1991). These findings parallel patterns of receptive field generation in the normal visual pathway through the LGN to area 17 in the ferret (Esguerra et al., 1986; Price and Morgan, 1987; Roe et al., 1989). While a limited degree of orientation bias may be present at the retinal or thalamic level (e.g., Leventhal et al., 1990), the generation of a marked degree of orientation and direction selectivity is believed to occur intracortically (e.g., Sillito, 1975). Direction selectivity is affected following selective lesions of superficial cortical layers (Eysel et al., 1987). These cortical receptive field properties of V1 and A1 cells are thus likely to arise from intracortical circuits common to both V1 and visually innervated A1. In our recordings from normal V1 as well as from rewired A1, we found a fairly large proportion ($\approx 25\%$) of nonoriented cells (Fig. 5). There appears to be a true species difference between ferret and cat visual cortex in terms of the prevalence of nonoriented cells. While visual cortex in cats (Hubel and Wiesel, 1962) and mink (LeVay et al., 1987) has few nonoriented cells, approximately one-quarter of cells recorded in ferret V1 are nonoriented. A previous study of receptive fields in ferret V1 reported only that "most single neurons . . . were orientation-selective" (Law et al., 1988). It is unlikely that our nonoriented cells represent recordings from geniculocortical afferents, since (1) afferents were recognized by their higher level of spike activity, (2) nonoriented units were clearly distinguished as cell spikes rather than axon spikes, and (3) nonoriented units were recorded at all depths in the cortex. While it is possible that some of the recording sites were influenced by multiunit activity, the presence of orientation selectivity would still be detected at such sites since visual cortical cells within a single columnar locale share similar orientation selectivities (LeVay et al., 1987; Law et al., 1988; Redies et al., 1990).

The marked degree of similarity between A1 and V1 is apparent not only in the orientation, direction, and velocity selectivity of cells but also in the types of receptive field organizations found there. As in V1, A1 contains simple and complex (and nonoriented) receptive field types and in roughly similar proportions. These findings are somewhat surprising in view of the fact that A1 and V1 receive significantly different types of input from the retina. V1 in normal cats and ferrets is dominated by X and Y cell inputs from the retina relayed through the LGN. Previous studies devoted to examining the contribution of X and Y cell inputs to receptive field properties of simple and complex cells in primary visual cortex have shown that neither the simple nor the complex cell classes are exclusively X- or Y-cell driven (Malpeli et al., 1981; Tanaka, 1983; Mullikin et al., 1984; Ferster 1990a,b). Given that visual inputs to A1 arise from retinal W cells (Roe, 1991), the results of this study demonstrate that (1) X and Y cell inputs are not necessary, and (2) W cell input is sufficient, for the generation of simple and complex receptive field types. The finding that similar orientation tuning selectivities can be generated in A1 and V1 further increases the likelihood that such tuning properties are generated intracortically and are relatively independent of specific visual input characteristics. We argue, therefore, that the *generation of these cortical receptive field organizations and tuning properties is not dependent on input cell type (i.e., X, Y, or W) but arises via intracortical circuitries activated by a minimum of visual input.*

Do inputs specify intracortical circuitry?

A possible interpretation of these data is that visual input during development has actually instructed the establishment of specific cortical circuits in A1, which thereby exhibits the functional properties similar to those normally seen in V1. In this view, the temporal patterns of sensory activity unique to each sensory modality actively instruct the development of specific cortical circuits possibly from an initially naive cortical template. This is an attractive hypothesis in view of the significant literature on activity-dependent mechanisms during cortical development, and has been recently discussed in the context of this experimental preparation (Pallas, 1990; Sur et al., 1990).

It is clear that the development of functional properties of cells in primary visual cortex can be modified by changes in visual input. Studies using abnormal visual rearing conditions (for review, see Sherman and Spear, 1982), blockade of retinal activity (Chapman et al., 1986; Stryker and Harris, 1986), and perturbation of postsynaptic activity (Kasamatsu and Pettigrew, 1979; Reiter and Stryker, 1988; Bear et al., 1990) during development have shown that changing the quality and quantity of activity can greatly influence the establishment of ocular dominance in visual cortex. Other cortical receptive field properties (such as orientation selectivity, direction selectivity, and receptive field organization) can also be affected by altering the visual environment. For example, binocular lid suture and dark rearing produce dramatic reductions in the number of cells with normal activity levels and normal orientation and direction tuning properties (Wiesel and Hubel, 1965; Pettigrew, 1974; Imbert and Buisseret, 1975). Rearing in striped environments of a single orientation results in a proportionally higher incidence of cells with similar orientation (Blakemore and Cooper, 1970; see, however, Movshon and Van Sluyters, 1981).

In this context, the functional similarity of visually innervated auditory cortex or somatosensory cortex (Frost and Metin, 1985; Metin and Frost, 1989) to normal visual cortex may be interpreted as the first functional demonstration of cross-modal induction of modality-specific cortical circuitry by peripheral input. If significant differences exist in the intracortical circuitry of normal V1 and normal A1, these findings would suggest that inputs do not simply influence, but actually instruct the establishment of cortical circuits. At the time that the lesions are made in the ferret, cerebral cortex is still quite immature. In primary visual cortex, only the deeper cortical layers (layers 4, 5, and 6) have migrated into place and geniculocortical afferents are still waiting in the subplate (McConnell, 1988; Peduzzi, 1988; Jackson et al., 1989; cf. Shatz and Luskin, 1986). Primary auditory cortex is likely to be at a similar stage of development (see, e.g., Feng and Brugge, 1983; Myslivecek, 1983). Thus, in the rewired ferrets, we have replaced auditory input with visual input at a time when cortical circuits have not yet been fully established. It is likely that, at this stage in development, the microcircuitry of A1 can be regulated significantly by afferent input, regardless of modality (see also Schlaggar and O'Leary, 1991). It is possible that similar lesions made at an earlier stage of development would produce an even more dramatic change in organization of the auditory pathway, such as changing the divergent nature of auditory thalamocortical connectivity to a point-to-point connectivity (cf. Pallas, 1990; Sur et al., 1990).

Do sensory cortices share common processing circuits?

An alternative interpretation of our data is that A1 and V1 normally share at least certain similar processing circuits, and that visual inputs to A1 simply activate circuits normally present in A1. A1 thus comes to exhibit visual receptive field properties similar to those in normal V1. In this view, the common functional transformations that sensory cortices perform would include tuning for orientation and direction as well as generation of specific receptive field organization.

Anatomically, cortical laminae in A1 and V1 are characterized by similar patterns of inputs, outputs, as well as laminar cell type composition (e.g., Jones, 1984; Winer, 1984a,b, 1985; Mitani and Shimokouchi, 1985); similar intralaminar projection patterns (e.g., Gilbert and Wiesel, 1979; Mitani et al., 1985); and the presence of patchy local horizontal connectivity patterns (Matsubara and Phillips, 1988; e.g., Gilbert and Wiesel, 1989b). Physiologically, perhaps akin to direction selectivity in V1, many neurons in A1 respond selectively to the direction and rate of frequency modulation (Whitfield and Evans, 1965; Mendelson and Cynader, 1985). In addition, similar to cells in normal V1, the tuning of A1 cells is shaped importantly by intracortical inhibition. Analogous to findings in both the adult and developing visual cortex (Sillito, 1975; Fregnac et al., 1988; Greuel et al., 1988; Hata et al., 1988), local application of GABA antagonists such as bicuculline and excitatory agents such as ACh, norepinephrine, NMDA, and glutamate results in dramatic changes in receptive field tuning properties of cells in A1 (Müller and Scheich, 1988; Ashe et al., 1989; McKenna et al., 1989a; Metherate and Weinberger, 1989). In addition, the study of context-dependent responses in both visual (Gilbert and Wiesel, 1989a; Fox et al., 1990) and auditory cortices (Espinosa and Gerstein, 1988; McKenna et al., 1989b; Shamma et al., in press) supports the role of lateral inhibitory/modulatory mechanisms in shaping receptive field characteristics. These anatomical and functional parallels suggest that sensory cortices may indeed utilize some common processing mechanisms. Thus, the presence of orientation-selective cells in A1 of rewired ferrets may suggest that similar "orientation tuning" transformations occur normally in A1.

If sensory cortices share some common processing circuits, these circuits can be established regardless of input modality during development. Consistent with this view, certain receptive field properties such as orientation tuning and simple/complex receptive field organization are already present in the young, visually inexperienced visual cortex (Hubel and Wiesel, 1963; Albus and Wolf, 1984; Braastad and Heggelund, 1985). The fact that "normal" visual receptive field properties are found in A1 of rewired ferrets suggests that the development of many cortical receptive field properties is not dependent on cell class–specific (X, Y, or W) patterns of sensory input, and develop, in fact, despite a relatively weak source of retinal input (of the W type) and despite the different pattern of thalamocortical connectivity that characterizes the auditory pathway (Pallas et al., 1990). That is not to say that normal cortical circuits develop in the total absence of sensory input; a minimal amount of sensory input may be required to trigger events that result in establishment of these cortical circuits.

Concluding remarks

In conclusion, our results demonstrate that sensory neocortex is not uniquely specified to process inputs of a single modality. Auditory cortex, following specific lesions during development, can accept and process visual input. The visual transformations performed by auditory cortex appear very similar to those in normal visual cortex. Whether these functional similarities are

due to input-induced changes in intracortical circuitry or to intrinsic commonalities across sensory cortices remains to be determined. A view consistent with that in other developing systems is that basic intracortical connections would be established independent of afferents, while input activity would play a role in the elaboration or fine-tuning of these connections. Such modulation by input activity would include alterations in the weights of preexisting synapses in the cortex (e.g., Merzenich et al., 1984; Donoghue and Sanes, 1988; Gilbert and Wiesel, 1989a; Mioche and Singer, 1989; Fox, 1990; Jenkins et al., 1990; Kaas et al., 1990). Indeed, our experiments on the mapping of the visual field in A1 of rewired animals (Roe et al., 1990a) indicate that one way for the map to form is by alterations in intracortical inhibition due to visual inputs (Sur et al., 1990).

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