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Paths of Information Flow Through Visual Cortex

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The main route of information flow in the cerebral cortex is from the middle layers of cortex to upper and lower layers. However, upper layers of the cat primary visual cortex can be directly driven by inputs from secondary visual cortex when activity in middle layers is disrupted. Upper-layer activity can be driven either by middle layers or by direct corticocortical inputs. One consequence of this result is that areas of cortex thought to be carrying out low-order analysis may be able to extract considerable information from higher order areas.

THE CEREBRAL CORTEX CONSISTS OF six layers, knitted by interlaminar connections into narrow, relatively independent vertical columns (*1*). The input-output transformations of the column are thought to be the key to understanding cortical function. Afferents from specific thalamic nuclei supplying sensory cortex terminate predominately in middle layers (primarily layer 4), suggesting that layer 4 is the main input stage of the column and that information flows from layer 4 to upper (1, 2, and 3) and lower (5 and 6) layers. This idea receives support from the anatomical projections of layer 4 cells to upper and lower layers (*2*), from current-source density analysis (*3*), and from the concentration of cells with "simple" receptive fields in layer 4 of primary visual cortex (V1, area 17) (*4*).

Although layer 4 is undoubtedly critical for full columnar function, our earlier studies showed that when normal interlaminar interactions with layer 4 are disrupted, other layers can generate organized outputs (*5*). The lateral geniculate nucleus (LGN), a laminated thalamic structure, is the major relay of retinal information to cortex. In the cat, the dorsal LGN layers (A and A1) provide the main geniculate input to V1, projecting primarily to layer 4 and secondarily to layer 6 (*6*). When layer A, which receives inputs from the contralateral eye, is

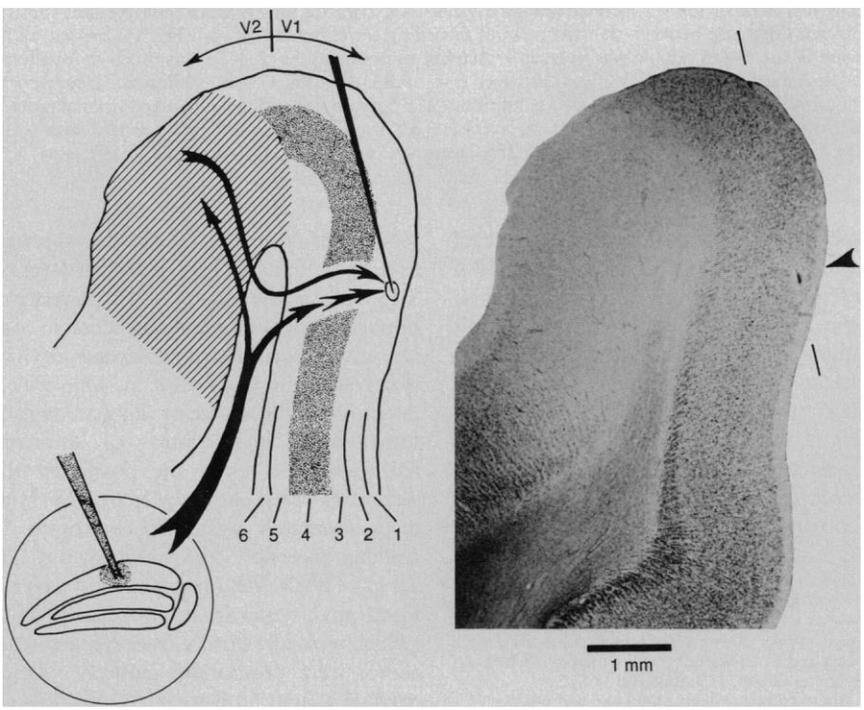

Fig. 1. Main pathways from LGN to upper layers of V1 (left) superimposed on tracing of photomicrograph from actual experiment (right). **Inset:** main LGN subdivisions (layers A, A1, and C, dorsal to ventral; small satellite on right edge is the medial interlaminar nucleus). The lesion in V2 (hatching) was made by injecting 16 mM cobaltous chloride (*18*) through a glass pipette after electrophysiologically mapping the region (460 nl at each of 18 sites in a 3 by 6 grid with 1-mm intersite spacing). The lesion spanned most of the width of V2, extending slightly across the V1-V2 border and 8 mm from anterior to posterior. It corresponded to visual directions from −4° to 16° azimuth and −4° to −17° elevation. Lesions of similar extent were also made with 0.5% ibotenic acid (115 nl at each site in the same grid pattern) (*19*). Entry and exit points of V1 microelectrode (glass-coated tungsten) are indicated by line segments near photomicrograph; arrow, electrolytic marking lesion (*20*).

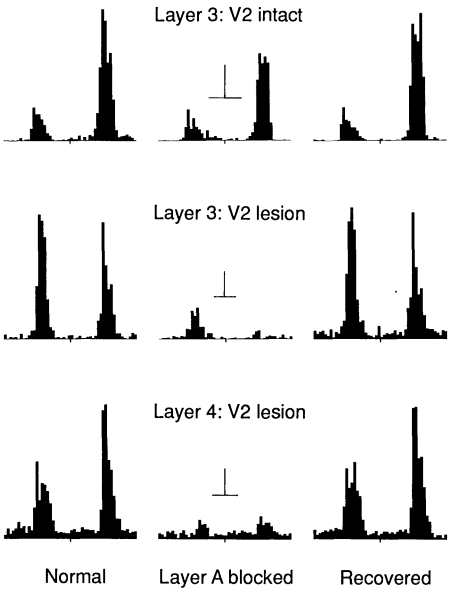

Fig. 2. Representative examples of the effects of reversibly inactivating LGN layer A on multiple-unit activity recorded in V1. Histograms show summed responses to 30 presentations of a rectangular stimulus to the contralateral eye, moving at constant speed back and forth through receptive field. Center marks indicate reversal of stimulus direction. Vertical scale markers represent 50 action potentials, horizontal markers represent 5°. Each horizontal series shows cortical activity before (left), during (middle), and after (right) blockade of a portion of geniculate layer A in retinotopic correspondence with cortical site. The blockades were achieved by pressure injection of 115 nl of 4 mM cobaltous chloride through metal-plated pipettes designed to facilitate extracellular recording at injection site (*21*). At this concentration, cobalt inactivates synaptic activity by blocking Ca^{2+} channels at presynaptic terminals, but spares axonal conduction of action potentials (*5*). Inactivations were effective for 1.5 to 2 min; recovery data were taken 6 min after injection (*5*). Multiple injections eventually kill cells, so no more than six inactivations were made at a given geniculate site. These examples were chosen because the fractions of activity surviving blockade of layer A are representative (upper series, 0.76; middle series, 0.25; and lower series; 0.15).

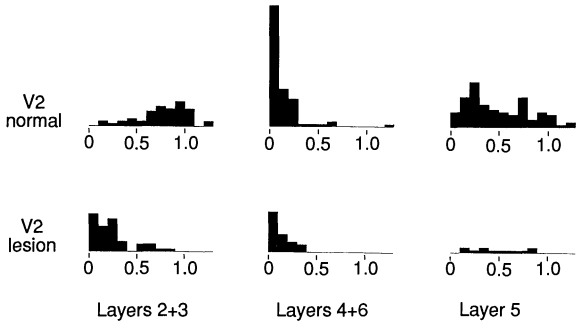

Fig. 3. Summary data for reversible inactivation of layer A for normal V1 (above) and V1 with the retinotopically corresponding part of V2 destroyed (below). For each inactivation, a "blocked/normal" index was calculated by dividing the response magnitude during inactivation by the normal response magnitude (*5*). A ratio near 1 indicates little effect; a ratio near zero indicates a large reduction in response. Frequency histograms of blocked/normal ratios grouped by layer (layer 1 is acellular). Effects were uniform within the pairs 2 + 3 and 4 + 6. Data for normal V1 are mostly from (*5*), with the addition of 15 control sites in layers 2 and 3 located several millimeters posterior to the region affected by the V2 lesion. There was no significant difference between new data for normal V1 and our previously reported results. For normal V1, single-cell and multiple unit sites are about equally represented; for V1 corresponding to V2 lesions, data are mostly from multiple unit sites (no significant difference between the two types of recording for either condition). For V2 lesions, all but one site in the 4 + 6 sample was in layer 4. Activity in upper layers (2 + 3) was much more affected by layer A inactivation when V2 was destroyed ($t = 10.88$, df = 98, $P \approx 0$). Otherwise there were no significant differences between the two conditions (*22*). Sample size and mean blocked/normal ratio for each group were as follows: for V2 intact, layers 2 + 3 (50, 0.74), layers 4 + 6 (80, 0.14), layer 5 (92, 0.50); for V2 lesion, layers 2 + 3 (50, 0.25), layers 4 + 6 (30, 0.13), layer 5 (11, 0.49).

temporarily inactivated with injections of synaptic blocking agents, cells in layers 4 and 6 are no longer driven by visual stimuli (to the contralateral eye) (*5*). However, cells in other layers (2, 3, and, to a lesser extent, 5) are still well driven, and orientation selectivity, a major columnar property of visual cortex, is unaffected (*5*).

There are several possible sources of this upper layer activity: inputs from other areas of cortex (many of which receive direct projections from the LGN); direct projections from the LGN to the upper layers of V1; and, on the assumption that relatively minor inputs can sustain considerable cortical activity, weak activity in layer 4 surviving inactivation of LGN layer A. One way of determining the source of this activity is the identification and control of alternative pathways. We tested the possibility that secondary visual cortex (V2, area 18) is the main alternative source by destroying V2 and then reversibly inactivating layer A (Fig. 1) (*7*). With V2 destroyed and layer A inactivated, responses in upper layers of V1 (which normally survive layer A inactivation alone) were profoundly reduced, whereas residual activity in layer 4 escaping layer A inactivation was not further reduced (Figs. 2 and 3). Thus the upper layer activity is supported neither by residual activity in layer 4 nor by direct thalamic inputs: it comes from V2.

The V2 projection originates mainly in upper layers of V2 (*8*), terminates most heavily in upper layers of V1 (*9*), and is excitatory (*10, 11*). Therefore, the most likely source of the V2 influence revealed in this study is a direct projection from upper layers of V2 to upper layers of V1. At least two distinct pathways sustain responses in upper layers of V1: the classical intracolumnar pathway through layer 4, and the corticocortical pathway from V2. Either can be shut off without major loss of activity (*11*), and both must be manipulated for the actual dependencies to be revealed (*12*). The effectiveness of V2's input is all the more remarkable when one considers that geniculate inactivations blocked layer A inputs to V2 as well as those to V1 (*13*).

The many distinct areas of cerebral cortex that are devoted to vision have been arranged into hierarchical schemes according to the following rule: pathways from lower order to higher order areas ("feedforward") originate in upper layers and terminate in layer 4, whereas pathways from higher order to lower order areas ("feedback") originate and terminate outside of layer 4 (*14*). Areas higher on the hierarchy are thought to be driven by those lower on the hierarchy, by means of the feedforward inputs to layer 4. Because the feedback pathways avoid layer 4, the main input stage of cortex, it was reasonable to suppose that they do not actively drive cortex but provide more subtle, modulatory influences (*15, 16*). However, our results do not support this view of feedback circuits: corticocortical inputs that bypass layer 4 can drive cells vigorously (*17*). Therefore, one cannot assume that each cortical area receives driving inputs only from lower order areas. The cortex can actively extract information from pathways other than feedforward pathways, as currently defined.

Although the column is a fundamental unit of organization of cerebral cortex, so too is the cortical layer. Individual layers or subsets of layers are capable of considerable organization of response properties and are able to process corticocortical inputs in the absence of the normal interlaminar interactions of the column.

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13. The thalamic origin of the sustaining activity is probably LGN subdivisions other than the A layers, all of which project to both V1 and V2, and possibly the pulvinar (*5*). We have determined that many cells in upper layers of V2 remain active during blockade of layer A (C. Lee, T. G. Weyand, J. G. Malpeli, unpublished data).
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20. Recording sites were assigned to cortical layers from histological reconstructions of electrode tracks and electrolytic marking lesions, by the cytological criteria of R. Otsuka and R. Hassler [*Arch. Psychiatr. Nervenkr.* **203**, 212 (1962)].
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23. We thank S. Adler, K. Akins, E. Dzhafarov, R. LaClair, D. Lee, T. Weyand, and two anonymous reviewers for advice and comments. Supported by NIH grant EY02695.

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The Role of the Primate Extrastriate Area V4 in Vision

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Area V4 is a part of the primate visual cortex. Its role in vision has been extensively debated. Inferences about the functions of this area have now been made by examination of a broad range of visual capacities after ablation of V4 in rhesus monkeys. The results obtained suggest that this area is involved in more complex aspects of visual information processing than had previously been suggested. Monkeys had particularly severe deficits in situations where the task was to select target stimuli that had a lower contrast, smaller size, or slower rate of motion than the array of comparison stimuli from which they had to be discriminated. Extensive training on each specific task resulted in improved performance. However, after V4 ablation, the monkeys could not generalize the specific task to new stimulus configurations and to new spatial locations.

TO UNDERSTAND HOW VISUAL INformation is analyzed by the brain, philosophers and psychologists have classified perception into such categories as color, brightness, form, motion, and depth (*1*). After the discovery of the numerous visual areas of the occipital, parietal, and temporal lobes (*2*), it was assumed that each area is involved in the analysis of one of these categories. This idea received strong impetus from work on the extrastriate area V4 of the monkey, which Zeki had proposed to be specialized for color vision (*3*). This inference was based on the claim that most single cells in V4 respond selectively to various colors. Subsequently it was demonstrated, however, that pattern and motion selectivities are also common among area V4 neurons (*4*) and, furthermore, that the responses of many of these neurons are affected by such factors as attention and stimulus relevance (*5*). Lesions of area V4 have resulted in a range of perceptual deficits, from virtually none to significant losses in color and in pattern perception (*6*).

To attempt to resolve the controversy about the function of area V4, we have examined the effects of its ablation on a broad range of visual capacities. Five monkeys were trained to do both visual detection and discrimination tasks that allowed us to confine stimuli to selected portions of the visual field and to test concurrently in regions that were intact and those that were affected by the V4 lesions (*7*). Each trial was initiated by the appearance of a small spot on a color monitor screen. After the animal had fixated this spot, as determined by eye-movement recordings (*8*), either a single stimulus or an array of stimuli appeared, and the animal had to shift his gaze to the appropriate visual stimulus by making a saccadic eye movement directly to it, to be rewarded with a drop of apple juice. Eye movements made to other locations were not rewarded and were recorded as errors. In the detection task a single target stimulus appeared somewhere on the monitor screen, whereas in the discrimination task several stimuli appeared simultaneously (4 to 64, but most commonly 8), one of which, the target, was different from the other identical stimuli (*7, 9*).

We examined brightness, size, shape, color, pattern, motion, and stereoscopic depth perception. Brightness discrimination was tested by the appearance of an array of identically shaped stimuli, one of which was of a different contrast from the other stimuli. The contrast difference between the target and comparison stimuli, as well as the location of the target within the array, was varied randomly by trial. To be rewarded the animal had to saccade to the odd stimulus (the target). There are two principal ways brightness discrimination can be tested with this task. In the first (Fig. 1A), the contrast of the target is higher than the comparison stimuli; in the second (Fig. 1B), the contrast of the target is lower. These two forms of testing revealed one of the new deficits we report here after V4 lesions. For size discrimination the targets and comparisons were similar to those shown (Fig. 1, C_1 and

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