

THE TRANSFER OF ABNORMAL VISUAL FIELD REPRESENTATIONS FROM THE DORSAL LATERAL GENICULATE NUCLEUS TO THE VISUAL CORTEX IN SIAMESE CATS

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SUMMARY

It has previously been shown that Siamese cats have abnormal retino-geniculate pathways. In the lateral geniculate nucleus of the Siamese cat two layers (A and C) represent the nasal retina of the contralateral eye in a normal manner. Two other layers (A1 and C1) have some segments that carry a normal retinotopically organized representation of the visual field, and other segments in which the representation of the visual field is abnormal and reversed²⁶. In order to determine the pattern of input that the visual cortex receives from these normal and abnormal geniculate segments, the visual field representations in the visual cortex of Siamese cats have been studied. Recordings have been obtained from cortical neurons or neuron groups with micro-electrodes, and the retrograde cell changes that occur in the lateral geniculate nucleus following lesions of the visual cortex have been studied.

The geniculo-cortical pathway is modified in one of two quite distinct ways. Each modification produces a complete and orderly sequential representation of the visual field upon the cortex. One involves the suppression of geniculo-cortical input from layers A1 and C1, without any modification of the pathway from the normal layers, and the other involves a rearrangement of the whole geniculo-cortical projection, with a reversal of the input from the abnormal segments of layers A1 and C1 (see ref. 36).

In Siamese cats that suppress input from layers A1 and C1 the suppression can be reduced but not abolished by lid suture. That is, after a unilateral lid suture in Siamese cats, input relayed through the normal geniculate layers still dominates over that coming through the abnormal layers, even on the side on which the normal layers were deprived by the suture. However, the suppression of the input from the abnormal layers is less on this side than it is in a normal Siamese cat.

INTRODUCTION

The retino-geniculate pathways of albino mammals are abnormal. The number of fibers passing from the eye to the ipsilateral cerebral hemisphere is reduced in albino individuals of all 8 mammalian species that have been studied^{7-9,19,21,23,27-29,39,43,51}. The details of this abnormality are known best in the Siamese cat, which is homozygous for an allele of the albino series⁵⁴ and, in view of the great deal of information that is already available about the visual pathways of normal cats, the Siamese cat forms an excellent model for detailed studies of the albino abnormality.

In the Siamese cat each cerebral hemisphere receives information from the contralateral visual hemifield, as is normal, but there is an additional input via the contralateral eye from a strip of the ipsilateral hemifield^{3,26,36}. The general arrangement of the abnormal retino-geniculate projections in Siamese cats is shown in Fig. 1. Layer A1 of the lateral geniculate nucleus, which normally receives afferents only from the temporal retina of the ipsilateral eye, is divided into segments. Some of the segments receive a normal input while other segments receive an abnormal input from the temporal retina of the contralateral eye, and thus from the ipsilateral hemifield. Layer C1 (see ref. 22) is similarly divided into normal and abnormal segments.

The abnormality affects the chiasmatic course of some retino-geniculate axons, which cross instead of remaining uncrossed, but it does not alter the laminar distribu-

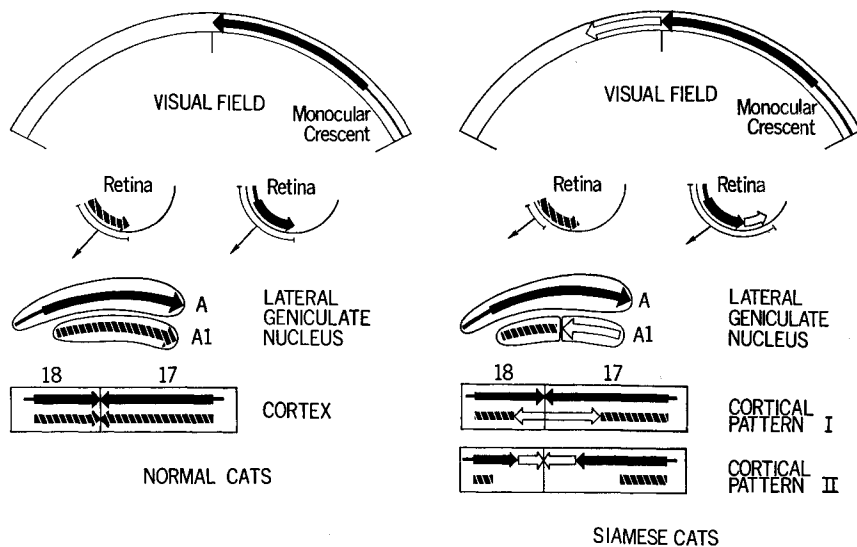


Fig. 1. Simplified schema of the visual pathways in normal (left) and Siamese cats (right) showing two possible geniculo-cortical projection patterns (I and II) for Siamese cats. Cortical pattern I shows the cortical organization that would be produced if the geniculo-cortical projection were not modified. Cortical pattern II shows the main pattern of cortical organization described by Hubel and Wiesel³⁶, in which the reversal that occurs in the abnormal segment of lamina A1 (white arrow) has been corrected, so that a sequential representation of the visual field is recreated at the cortical level. For simplicity layers C and C1 are not included in this schema and only two segments of layer A1, one normal and the other abnormal, are shown.

tion or the retinotopic sequence of the terminals. Thus, layers A1 and C1 receive some afferents from each eye, and each set of afferents is arranged in a retinotopic sequence appropriate for its eye. The abnormal sequences come from the wrong hemifield and are therefore a mirror reversal of the normal sequences (see white arrow in Fig. 1). In contrast to this, geniculate layers A and C, which receive afferents from the contralateral eye in a normal cat, receive the same input in Siamese cats.

The organization of the abnormal pathways is known in less detail in other albino mammals. However, in albino rabbits⁵¹, mink⁵¹, rats²⁹ and ferrets²³ the ipsilateral projection is disrupted by one or more patches of contralateral input, as in the Siamese cat, and it is probable that in all albino mammals, including man, some geniculate layers will show the double input and partial mirror reversal of the visual field that we have found in Siamese cats.

Thus, the albino abnormality represents a situation in which the orderly representation of a sensory field within the brain is disturbed, and it offers an opportunity for studying the way in which the mammalian brain can adjust to abnormal sensory inputs. We undertook to study the visual cortex of Siamese cats in order to determine if the abnormal organization seen in the lateral geniculate nucleus is preserved or altered in the geniculo-cortical projection. Fig. 1 shows that if the geniculo-cortical projections of a Siamese cat are organized as are those of a normal cat (cortical pattern I in Fig. 1) then there will be areas of cortex that receive their inputs from two quite different parts of the visual field. Further, a stimulus that moves from left to right in the one part of the visual field and a stimulus that moves from right to left in the other could produce the same pattern of cortical activation. If the cortex is to perform useful visual functions, then the cortical representations of the two visual hemifields must be kept distinct, and the mirror image effect must be dealt with in some manner.

Our first electrophysiological observations of the visual cortex in Siamese cats led us to conclude that some secondary modification of the geniculo-cortical system does occur. Most cortical neurons are activated from the nasal retina of the contralateral eye, which is normally connected; the abnormal input to the cortex tends to be suppressed³⁷.

Hubel and Wiesel³⁶ have also analyzed the organization of the visual cortex in Siamese cats. They reported a quite different mechanism for correcting the retinogeniculate defect. In their animals the abnormal parts of layers A1 and C1 are represented in a separate portion of cortex (cortical pattern II in Fig. 1). A new retinotopic sequence for the abnormal segment is established next to the border between cortical areas 17 and 18, and the normal sequence is moved away from the border. Thus, the zero vertical meridian is represented once within each of these two cortical areas, instead of having a single representation at the border. Further, within the representation of the abnormal segment, the orderly sequence of the geniculo-cortical projection system appears to be reversed, so that the mirror reversal that occurs at geniculate levels is corrected at cortical levels.

The results reported by Hubel and Wiesel were so strikingly different from ours that we studied several more Siamese cats. We have looked at the patterns of geniculate

degeneration that can be produced by localized lesions of the visual cortex in order to determine whether the cortical changes that can be recorded electrophysiologically reflect a modification of cortico-cortical circuits or whether they are produced by a primary alteration of the geniculo-cortical pathway. We have also studied the visual field representations in the cortex of Siamese cats that had been raised with the lids of one eye sutured. These animals were prepared in order to study how the lid suture modifies geniculate cell growth in Siamese cats (Guillery and Kaas, in preparation). Electrophysiological study of the cats showed the cortical distribution of the abnormal inputs particularly clearly, and so these results of visual deprivation are also included here.

The several experimental results show that there are at least two distinct ways in which the visual cortex of Siamese cats can deal with the disordered visual representation in the lateral geniculate nucleus. In some cats there is one, in some the other pattern.

MATERIALS AND METHODS

Most of the cats used in these experiments were obtained from local dealers. Three were born in the laboratory and had the lids of one eye sutured when they were 8 or 19 days old. All except one of the cats had the characteristic Siamese fur coloring and blue eyes. The one exception had streaks of 'tabby' fur and appeared not to be a purebred Siamese cat. However, it did have such Siamese features as blue eyes and some indication of 'points' and, since it had the interrupted lamina A1 that is characteristic of Siamese cats^{26,39}, this animal (no. 315) was included in the series of cortical lesion experiments.

The cats were not markedly cross-eyed but we did not check for mild degrees of strabismus⁵⁵. The 3 cats that were born in the laboratory had parents who both showed slight medial deviation of the eyes.

(A) Electrophysiological mapping of receptive field positions

Extensive explorations of the visual cortex were undertaken in 5 normal Siamese cats and limited cortical recordings were obtained from 8 other normal Siamese cats, which were used primarily to study the lateral geniculate nucleus or the superior colliculus. In addition, the 3 Siamese cats which had been raised with one eyelid sutured were used to explore the representation of the visual fields within the visual cortex.

The general methods of preparation and recording have been described previously^{1,26}. The cats were anesthetized with urethane, placed in a stereotaxic head holder, and the dorsal aspect of the visual cortex was exposed. A pool of mineral oil, which was retained within a plastic frame, protected the exposed cortical surface. The eyelids were removed and both eyes were firmly held by suturing the sclera to metal rings that were anchored to the head holder. One eye, usually the one contralateral to the cortex that was to be studied in detail, was centered within a translucent plastic hemisphere. This hemisphere served as a screen upon which the visual stimuli were

presented, and thus formed the visual field. One eye was always slightly off center in the hemisphere but, since the interocular distance was small in relation to the diameter of the hemisphere (60 cm), no correction was made for the small distortion that this produced in the apparent receptive field positions and sizes. The optic disc of each eye was projected on to the surface of the hemisphere by the method of Fernald and Chase¹⁴. In some cases the area centralis was similarly projected. Receptive field positions were recorded in terms of coordinates related to the position of the optic disc⁴⁶.

The activity of small clusters of neurons or, on occasion, of single neurons, was recorded with tungsten microelectrodes. The distance between the electrode tip and the cortical surface was noted at each recording point, and within each electrode penetration one or two small electrolytic lesions (10–20 A for 10–20 sec) were made so that the positions of critical recording points could be more readily identified in the frontal sections that were prepared after each experiment.

Receptive field positions were determined by moving small light or dark bars across the surface of the plastic hemisphere. The stimulus was always repeated with first one and then the other eye occluded. We recorded receptive field position and ocular input only, and generally did not determine other properties of the neurons. For each electrode penetration, receptive field positions were recorded when they showed a significant shift from a previously noted position, generally more than 2° or 3°, or when the ocular input changed. Thus, a great many neurons or neuron clusters were encountered, and were checked for receptive field position and ocular input, but were not recorded or included in the quantitative comparisons that have been made.

At the end of each experiment the brains were perfused with 10% formol-saline and were hardened in the fixative. The brains were frozen and cut as 50 μ m coronal serial sections in the plane of the electrode tracks. The sections, which were stained with cresyl violet, always included the dorsal lateral geniculate nucleus, and in each of the animals the appearance of the nucleus was checked to confirm that the cat did show the characteristic Siamese abnormality^{26,39}.

(B) Geniculo-cortical interconnections

In 12 Siamese cats the geniculo-cortical interrelationships have been studied by making lesions in the visual cortex and studying the degenerative changes in the dorsal lateral geniculate nucleus. Since there was no reason for expecting any crossed geniculo-cortical interconnections, lesions were made bilaterally in 10 of the animals.

The cats were anesthetized with sodium pentobarbital, the skull was opened under aseptic conditions and a small amount of visual cortex was removed by suction. The cats were given antibiotics postoperatively and were allowed to survive for periods varying from 10 days to 3 months. At that time they were anesthetized and were perfused through the heart with 10% formol-saline. Six of the cats survived for 30–90 days postoperatively. Three of these brains were cut as frozen sections in a frontal plane and stained with cresyl violet, while 3 were cut frontally in celloidin and stained with buffered thionine. These sections showed the cellular degeneration and the extent of the lesions. The other 6 cats survived 10–12 days postoperatively and in these

brains the fiber degeneration was studied as well as the retrograde cellular degeneration. The brains were cut as frozen sections ($45\ \mu\text{m}$ thick) and every tenth section was stained with cresyl violet to show the cellular degeneration and the cortical lesion. Other sections through the lateral geniculate nucleus, at least 1 in 10 but generally more, were stained by the Nauta-Gygax⁴⁴ or Fink-Heimer¹⁵ method. These hemispheres were also cut frontally, except for one which was cut in a parasagittal plane.

RESULTS

(Part I) Electrophysiological studies of the visual cortex in normal Siamese cats

(A) The identification of the border between cortical areas 17 and 18

For the purpose of interpreting our results, the most critical region of the cortex is the 17/18 border where, in a normal cat, the zero vertical meridian is represented. Fig. 2 shows this region in a frontal section through the brain of one of our experimental Siamese cats. Similar pictures have been included in earlier studies of the architecture of the visual cortex of normal cats^{10,16,33,47,48,53} and it appears that there are no obvious cytoarchitectonic differences between normal and Siamese cats in the visual cortex. The criteria that have been used by others to distinguish areas 17 and 18 (see especially ref. 53) can also be used in Siamese cats. We have found that the

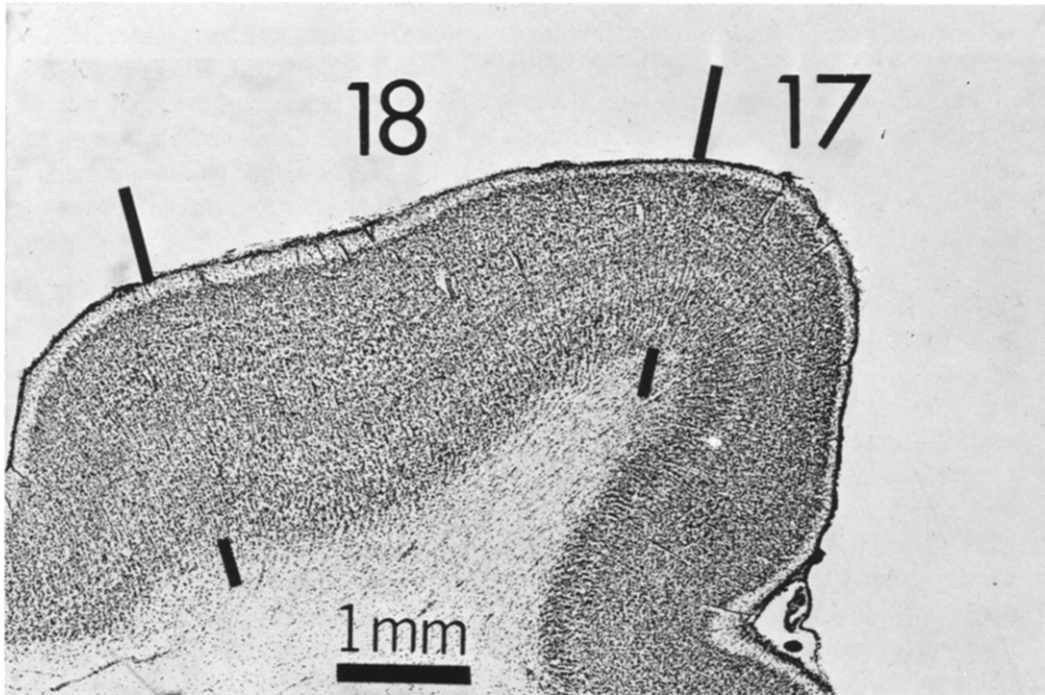


Fig. 2. Cytoarchitecture of cortical areas 17 and 18 of a Siamese cat used in the recording experiments. Nissl stain, frontal section.

most useful distinguishing features are seen at low magnifications, which show layer V as a lighter band, less densely packed with cells in area 17 than in area 18. Also, at the border, the deeper part of layer III, which corresponds to layer IVb of some investigators (see ref. 16), changes its character, having more loosely arranged cells which are more clearly distinct from layer IV in area 18 than in area 17. At higher magnifications one can see a scattering of large pyramidal cells in layer V of both cortical areas 17 and 18. However, close to the 17/18 border there are very few of these cells in area 17 and a marked increase of these cells is seen as one passes from area 17 into area 18. Similarly, an increased concentration of large pyramidal cells can be seen in the deeper part of layer III of area 18.

(B) *Evidence for the representation of the zero vertical meridian along the 17/18 border*

In a normal cat the position of the zero vertical meridian can be determined in a number of different ways. One can define it on the basis of the structure of the eye⁵, in terms of receptive fields recorded in the lateral geniculate nucleus^{40,52} or in terms of cortical records obtained from the region of the 17/18 border^{42,46}.

In the retina the vertical meridian corresponds to the line of decussation, which passes through the area of maximum cell density, the area centralis^{56,57}. The position of the area centralis has been carefully mapped by Bishop *et al.*⁵ for normal cats. Since human albino individuals commonly lack a fovea (see refs. 11 and 13) we have checked the position of the area centralis ophthalmoscopically and histologically and have found that in Siamese cats it lies in the appropriate part of the retina and appears to be normal. Two whole mount preparations of the retina of Siamese cats showed the

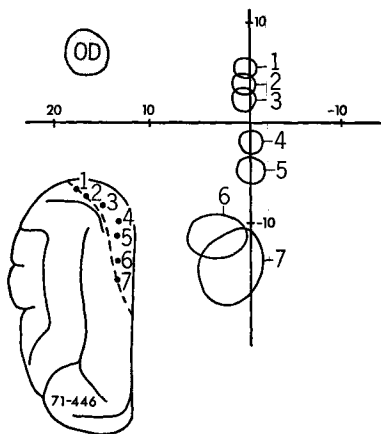


Fig. 3. Receptive fields for neurons along the dorsolateral border of area 17. Lower left: a dorsal view of the right cerebral hemisphere of a Siamese cat. The area 17/18 border is shown as a dashed line and electrode penetrations close to the border are numbered from 1 through 7. Upper and right: a portion of the visual field of the left eye, with temporal to the left. The optic disc (OD) is projected onto the visual field as a reference point. The numbered receptive fields were recorded from nerve cells in the first 2 mm of the corresponding electrode penetrations. These fields show displacements from the optic disc approximately the same as would be found in normal cats. A vertical line drawn through these receptive fields shows the estimated position of the zero vertical meridian. The horizontal meridian was estimated from the position of the optic disc⁴⁶.

expected dense accumulation of small ganglion cells 3.2 and 3.5 mm from the optic disc. This corresponds approximately to the position of the area centralis in a normal cat⁵.

Since in Siamese cats many of the fibers from the temporal retina are misrouted one cannot strictly speaking look for a line of decussation comparable to that of a normal cat. The abnormal fibers arise from a strip of retina that lies too close to the position of the line of decussation in a normal cat²⁶. However, layer A of the lateral geniculate nucleus receives a normal input, so that the vertical meridian can be defined by the position of receptive fields of neurons lying along the medial margin of this layer. We have found that this method gives similar results for normal and Siamese cats. Thus, on the basis of the ocular and geniculate structure the vertical meridian can be defined in the Siamese cat in exactly the same way as in normal cats.

In a normal cat the cortical representation of the vertical meridian lies along the 17/18 border, as it does in a wide range of mammalian species (see ref. 2 for review). In the Siamese cats studied by Hubel and Wiesel³⁶ the representation of the zero vertical meridian was displaced some distance from the 17/18 border, and the meridian 20° into the ipsilateral hemifield was represented at the 17/18 border. In all of the Siamese cats that we have studied electrophysiologically, the zero vertical meridian was represented at the 17/18 border as in normal cats.

Fig. 3 shows the 7 receptive fields that were obtained in one cat from electrode positions close to the 17/18 border, which is shown as an interrupted line. In this figure the estimated position of the vertical meridian has been drawn to pass as nearly as possible through the midpart of the smallest receptive fields, and it can be seen that this estimated vertical meridian has a normal displacement from the blind spot. Such an estimate, based on a similarly limited number of receptive fields in a normal cat might be in error by 1° or 2°, but this error would not be critical in determining whether or not receptive field positions were abnormal by about 20°.

Similar estimates of the position of the zero vertical meridian in relation to the

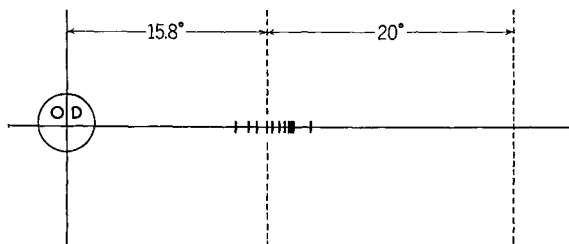


Fig. 4. The representation of the vertical meridian at the area 17/18 border in Siamese and normal cats. A portion of the visual field is shown, with the projection of the optic disc (OD) as a reference point. The left dashed line indicates the average displacement of the zero vertical meridian from the optic disc, determined by recording at the area 17/18 border in normal cats⁴⁶. The right dashed line indicates the approximate location of a meridian based on receptive fields for recording sites along the area 17/18 border that would be obtained from the Siamese cats described by Hubel and Wiesel³⁶. The short bars show the positions of the meridians obtained as in Fig. 3 by recording at the area 17/18 border in 11 hemispheres from Siamese cats. The position of the vertical meridian lies close to the value expected for normal cats.

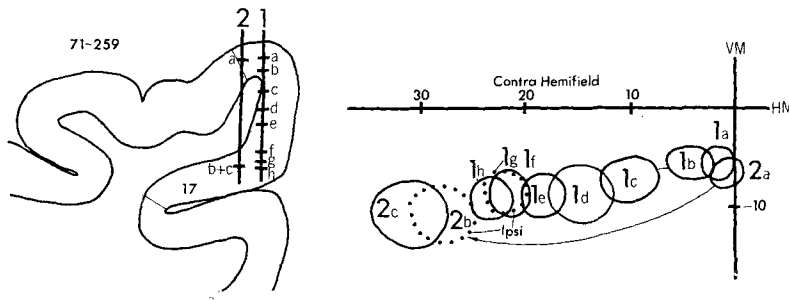


Fig. 5. Receptive fields for recording sites in area 17 of a Siamese cat. Electrode penetrations are shown on an outline of part of a frontal section of the right cerebral hemisphere. Lettered horizontal bars (a-h) mark the recording sites. The corresponding receptive fields are shown on the right, where part of the visual field is indicated by zero vertical and horizontal meridians. The temporal (to the left) progression of receptive fields, seen as recording sites lie successively farther from the 17/18 border, is like that seen in normal cats. However, most of the receptive fields shown here relate to the eye contralateral to the recording sites. Only the receptive fields that are marked as dotted outlines were obtained from the ipsilateral eye.

blind spot were obtained from cortical records in several other Siamese cats. Fig. 4 shows the results obtained by this method from 11 cerebral hemispheres of 8 Siamese cats. In normal cats the average displacement of the vertical meridian from the optic disc has been found to be 15.8° on the basis of such cortical recordings⁴⁶. Other estimates have been close to this value⁴². It is clear from Fig. 4 that for our Siamese cats, estimates of the vertical meridian representation based on recordings at the 17/18 border cluster around the expected normal, and do not approach a 20° nasal displacement.

(C) *The representation of the visual fields in area 17 and 18*

In the normal cat the contralateral hemifield is represented in a topologically organized manner in area 17 and a distorted mirror reversal of this representation is found in area 18⁶². A representation of the temporal periphery of the visual field has not been demonstrated in area 18³³. The visual cortex receives inputs through the contralateral eye from all of the contralateral visual hemifield, which extends about 90° laterally from the zero vertical meridian to the temporal periphery. Through the ipsilateral eye the cortex receives from a contralateral visual field that extends only about 45° nasal to the vertical meridian³⁸.

In all of the Siamese cats that we have studied electrophysiologically the representation of the contralateral visual field via the contralateral eye shows a normal distribution over the surface of areas 17 and 18. This normal pattern is dominant in the records. In addition there is an input from the ipsilateral eye that is markedly reduced compared to normal, and there is a small abnormal input from the ipsilateral hemifield via the contralateral eye. The pattern we have seen is most readily interpreted as a normal geniculo-cortical projection from layers A and C and a reduced or suppressed projection from layers A1 and C1.

(1) *The normal cortical projection through layers A and C.* The pattern of the

normal projection from the contralateral eye is clearly shown in Fig. 5. A succession of receptive fields recorded through the contralateral eye starts with 2a at the vertical meridian, and progresses steadily towards the temporal periphery as the recording sites lie further from the 17/18 border. Within this portion of area 17, which extends into the splenial sulcus and reaches close to the border between area 17 and the limbic cortex, about 35° of the total contralateral visual field representation is seen to be organized in a systematic manner entirely consistent with expectations based on normal cats^{62,63}.

Other recordings from Siamese cats show the same mediolateral organization within area 17. Further, they show that the upper visual field is represented caudally and the lower field rostrally, as in a normal cat. There is no indication of any rostro-caudal displacement of the visual field representation in comparison to the normal pattern (see ref. 36).

The same normal representation of the contralateral visual field through the contralateral eye has been found in area 18. Fig. 7 shows an example of the normal receptive field progressions that were encountered as recording sites moved medio-laterally through area 18. Receptive fields near the lateral border of area 18 were up to 45° from the zero vertical meridian, but a representation of more temporal parts of the visual field was not found in area 18. As in area 17, the upper visual field is represented caudally and the lower field rostrally and in this, too, the Siamese cat does not differ from the normal cat. Only a few receptive fields were obtained from cells in area 19 (see Fig. 7). So far as we could determine, the distribution of these fields in the contralateral hemifield did not differ from the normal distribution³³.

(2) *The cortical projection through the normal segments of layers A1 and C1. We*

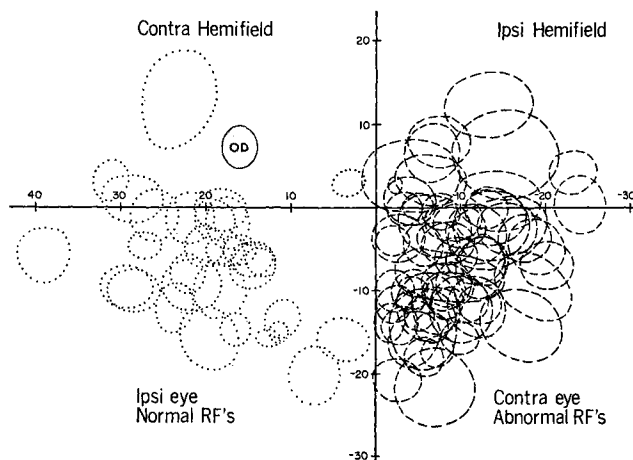


Fig. 6. The locations of two types of receptive field recorded in the cortex of 8 Siamese cats. Receptive fields with abnormal locations in the ipsilateral hemifield are for the eye contralateral to the recording sites and are marked by dashed outlines. Normally located receptive fields for the ipsilateral eye are marked by dotted outlines. The much greater number of normally located receptive fields for the contralateral eye are not shown. Note that most of the abnormally located receptive fields are within 20° of the zero vertical meridian, while most of the receptive fields for the ipsilateral eye are 15° or more away from the vertical meridian.

have shown that, in the lateral geniculate nucleus of Siamese cats, neurons that receive afferents from the ipsilateral eye are largely confined to a vertical strip of the contralateral hemifield extending from a line 15–20° nasal to the vertical meridian and reaching to about 45°, which is the edge of the binocular visual field^{26,50}. These neurons are found in the lateral normal segment of lamina A1. The small medial normal segment, which receives from parts of the visual field close to the vertical meridian, is not easily demonstrated electrophysiologically, although it can be seen clearly when retino-geniculate fiber degeneration is studied. This segment is largest in the rostral parts of the lateral geniculate nucleus and correspondingly, responses from areas near the vertical meridian come through the ipsilateral eye primarily from the lower parts of the visual field.

The responses of cortical neurons seen when the ipsilateral eye is stimulated fit the known topography of the geniculate connection pattern. That is, most of the receptive fields are in the 15–45° strip of the visual field (see Fig. 6). A few lie within the 0–15° strip, and these are found mainly in the lower visual field.

The cortical sites that were activated by the ipsilateral eye were abnormal, because generally they did not have a binocular input as do most of the cortical neurons in a normal cat³¹. Thus, the great majority of cortical recording sites could be activated by one eye or by the other, but not by both. There were a few exceptions, such as recording sites 2b and 2c in Fig. 5, but since the electrode was recording the activity of several neurons at this point, it is possible that no single neuron was activated through both eyes. The evidence we have suggests, but does not prove, that there were no binocularly driven cells in our cats. We saw very few binocularly driven cell groups, and we never saw a binocularly driven unit, although we did record from a number of single cells.

A second abnormal feature seen in our Siamese cats was that even in the cortical segments corresponding to the normal segments of the lateral geniculate nucleus there were relatively few cortical neurons activated through the ipsilateral eye. On the basis of the geniculate records one would expect to find the cortical input from the two eyes to be approximately equal in these normal segments. Instead, within the segments of areas 17 and 18 that represent the 20–45° visual field strip the amount of the ipsilateral input is markedly less than the contralateral.

An accurate estimate of the ratio of ipsilateral to contralateral input is not possible on the basis of the methods we have used. We only recorded receptive fields when they showed a change in position or in the eye of activation (see Methods). Our method thus tended to record relatively more of the cortical neurons that were a minority in terms of ocular dominance. In many cortical penetrations there would be no change in eye dominance and we then recorded only major changes in receptive field position. However, of the 66 cortical sites that gave records for the 20–45° visual strip in area 17 of 5 Siamese cats, 57 were activated through the contralateral eye and only 9 were activated through the ipsilateral eye. The corresponding figures for area 18 were 16 and 2. Lateral to area 18 only 5 recording sites had receptive fields 20–45° from the vertical meridian, and these were all activated through the contralateral eye.

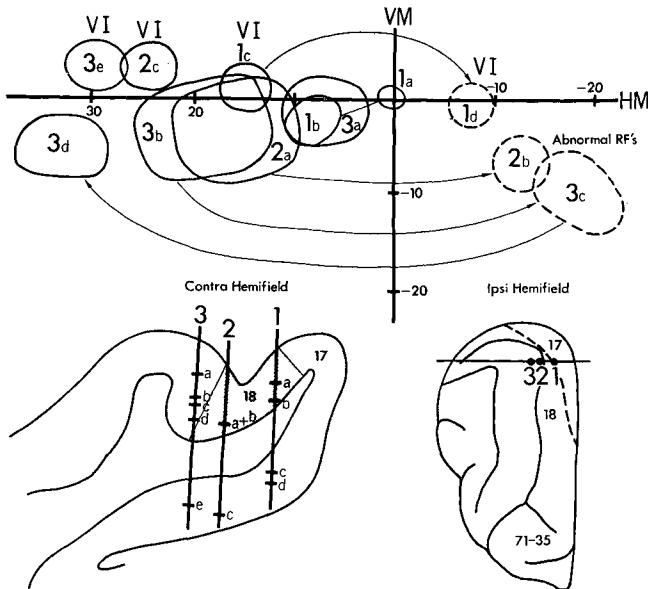


Fig. 7. Abnormally and normally located receptive fields for 3 subdivisions of the visual cortex in a Siamese cat. Above: a portion of the visual field showing the zero vertical meridian (VM), the horizontal meridian (HM), and labeled receptive fields. Four receptive fields (marked VI) were recorded from area 17. All receptive fields are for the eye contralateral to the recording sites. Below: a dorsal view of the right cerebral hemisphere is shown on the right with 3 numbered electrode penetrations indicated by dots. A dashed line marks the border between architectonic areas 17 and 18 and a horizontal line indicates the plane of the frontal brain section shown to the left. The 3 electrode penetrations are numbered on the section and lettered horizontal bars (a-e) show recording sites. Area 18 is shaded.

In general, the responses evoked through the ipsilateral eye were weaker than those evoked through the contralateral eye, and it must be concluded that, given the bias of our recording method, cortical neurons activated through the contralateral eye must greatly outnumber those that receive ipsilateral afferents.

The topological mapping of the visual field upon the cortical surface obtained through the ipsilateral eye in general matches that obtained through the contralateral eye. For example, in Fig. 5 receptive field 1g is very close to 1f and 2b is close to 2c. There is a slight difference in the position of these fields, and this may be due, at least in part, to small errors in estimating the position of the vertical meridian for the two eyes. However, when allowance is made for such errors, there remain a number of instances in which receptive fields for the two eyes are obviously out of alignment, and in this Siamese cats differ from normal cats³⁶. The implications of these misalignments are discussed below.

(3) *The cortical projection through the abnormal segments of layers A1 and C1.* As would be expected from the known connections of the lateral geniculate nucleus, there are some cortical recording sites with receptive fields in the ipsilateral visual hemifield. Almost all of these receptive fields lie within 20° of the zero vertical meridian (see Fig. 6) and they all correspond to the contralateral eye.

Fig. 7 shows 3 such abnormally located receptive fields, one for area 17, one for area 18, and one for cortex lateral to area 18. Within area 17, receptive fields 1c, 2c, and 3e show the progression of receptive fields towards the temporal parts of the upper visual field that one also sees on the tentorial surface in a normal cat. However, the receptive field for cortical site 1d, instead of being close to that for 1c, lies about 8° into the ipsilateral hemifield. Similarly, within area 18, the positions of receptive fields 1a, 1b, and 2a reflect the normal visual field representation for this area. However, the receptive field 2b, which was defined at the same recording site as 2a, was more than 10° into the ipsilateral hemifield. Finally, receptive fields 3a, 3b, and 3d show a progression similar to that reported previously for area 19 by Hubel and Wiesel³³, but 3c is not a part of this progression. Instead it shows a receptive field centered nearly 20° into the ipsilateral hemifield.

Although we have found such abnormally placed receptive fields in the ipsilateral hemifield, their number was surprisingly small in relation to the number that were found in the lateral geniculate nucleus²⁶. One might expect, on the basis of the known retino-geniculate connections in Siamese cats, to find that the number of abnormal fields in a 20° strip on one side of the vertical meridian would be approximately equal to the number of normal fields in a similar strip on the other side. Instead, the vast majority of the cortical recording sites that were activated through the contralateral eye, and whose receptive fields were within 20° of the vertical meridian, had normal receptive fields in the contralateral hemifield. In 5 Siamese cats we found 142 normal receptive fields within 20° of the vertical meridian, and only 38 abnormal receptive fields in the ipsilateral hemifield. It is to be noted, again, that our method of recording was biased to give relatively too low a value for the normal receptive fields (see p. 71).

The abnormal receptive fields generally mirrored the normal receptive fields that were obtained from the same or closely adjacent recording sites. Thus, if the normally located receptive field was 10° contralateral to the vertical meridian, the corresponding abnormal receptive field was approximately 10° ipsilateral to the vertical meridian and close to the same horizontal level. However, the abnormal receptive fields were sometimes out of alignment, as in Fig. 7, and the asymmetry was occasionally even more pronounced, especially for peripheral fields. A similar misalignment has been noted by Hubel and Wiesel³⁶.

The degree to which receptive fields for layers A and A1 are not precisely aligned in the lateral geniculate nucleus of the Siamese cats has been noted before²⁶. It was found that within the abnormal segments of layer A1 the abnormal receptive fields were not precise mirror images of the normal receptive fields recorded from neurons in closely adjacent parts of layer A. Presumably, the cortical cells reflect this geniculate property. A similar lack of correspondence has also been found for the parts of the cortex that receive from the normal segments of the lateral geniculate nucleus (see above), even though no such lack of alignment was noted in the corresponding parts of the geniculate nucleus. This may be because the electrode punctures generally passed obliquely to the normal parts of the geniculate layers and, thus, it was more difficult to make judgements about the expected alignments.

The extent to which the normally matched activity in adjacent geniculate layers can interact at geniculate or cortical levels may determine the accuracy with which the visual field representations can be aligned during development. The lack of alignment may reflect the lack of interaction that is shown by our cortical records.

(Part II) Electrophysiological studies of the visual cortex in Siamese cats raised with one eye shut

In the visual cortex of normal cats most neurons are activated by either eye^{31,32}. This balanced binocular input can be altered by raising a kitten with one eye closed. It is found that visual stimuli delivered to the eye that was closed during early development will activate only few cortical cells in these cats⁶⁰. In addition, geniculate cells that are innervated by the closed eye grow less than normal⁵⁹. It has been suggested that there may normally be a balanced binocular competition controlling the development of ocular dominance patterns in the cortex and also controlling the growth of geniculate cells. Thus, when one set of geniculo-cortical cells is deprived of a normal patterned input, it tends to be replaced in the cortex by the normally innervated set^{24,25,30,59,60}.

In Siamese cats there is a large segment of the geniculo-cortical system which receives its afferents from one eye only, and in these abnormal parts there can be no binocular competition. It thus becomes of interest to study the effects that closing one eye has upon the development of the parts of the geniculo-cortical system in Siamese cats. Here we are concerned only with the effects that can be demonstrated electrophysiologically in cortical neurons. The effects upon geniculate cell growth will be considered separately.

In the normal segments of the geniculo-cortical system of Siamese cats one can expect a lid suture to have the same effect as it has in a normal cat. That is, in the cortex opposite the sutured eye, the number of neurons activated by the normal ipsilateral eye through lamina A1 should increase. Since in the normal Siamese cats that we have studied the input to the cortex through layer A1 is markedly reduced (see p. 71), it was of interest to determine the extent to which a lid suture would change this pattern of input.

In the abnormal segments of the geniculo-cortical system the input from layer A1 is also much weaker than the input from layer A. The mechanism that produces this unbalanced input from the contralateral eye to the cortex is not understood (see p. 89). However, our evaluation of the developmental processes that produce the adult pattern will depend to some extent upon the changes if any, that can be produced by a lid suture.

(A) Changes in the normal segments of the geniculo-cortical system

Recordings have been obtained from 3 Siamese cats that were raised with one eye closed. Two had one eye sutured on postnatal day 19 and survived until they were 4.5 months old. The third had one eye sutured when it was 8 days of age and this animal was kept for 4 months. Since inputs from the ipsilateral eye are limited to relatively small parts of the cortex in all Siamese cats, most neurons in these 3 cats were

activated from the contralateral eye. However, the difference in the amount of ipsilateral activation seen on the two sides of the brain was revealing. Out of a total of 19 recording sites activated by the ipsilateral eye from all parts of the visual field, in these 3 cats 17 were activated through the eye that had been left open. Thus, closing one eye clearly changed the pattern of activation that developed in the cortex opposite that eye, so that much more ipsilateral input from the normal eye was seen. Although there was this change of ocular dominance in the expected direction, it was surprising to find that in the region of cortex containing most of the ipsilateral input (approximately 15–45° of visual field representation) considerably more than half of the recording sites still responded to activation of the contralateral eye that had been sutured (26 contralateral; 14 ipsilateral).

Although we can demonstrate that the ocular dominance was changed in cortex contralateral to the closed eye, we cannot demonstrate any change ipsilaterally. We obtained only a very weak ipsilateral input in the cortex of normal Siamese cats, and our samples are too small to demonstrate clearly that this weak input is further reduced by lid suture.

(B) Changes in the abnormal segments of the geniculo-striate system

In the 3 cats that we have studied after lid suture we recorded many more sites with abnormal receptive fields than would be expected in a normal Siamese cat. All, of course, were in the ipsilateral hemifield and came from the eye contralateral to the cortical recording site. Each of these cats differed noticeably from the normal Siamese cats. Whereas about one-third of the receptive fields were abnormal in the lid sutured animals, only about one-sixth were abnormal in the normal cats when all parts of the visual field were considered (58 out of 162; 38 out of 231). It should be emphasized that the dominant influence was that of the normal contralateral input, and that our sampling methods favored the recording of abnormal receptive fields.

Contrary to expectations, we found no asymmetry in the distribution of the cortical sites with abnormal receptive fields. That is, the number of cortical sites receiving input from the normal eye was almost the same as the number that received from the previously closed eye (30 and 28 respectively). Thus, it might appear that the unilateral lid suture has reduced the suppression of the abnormal input on both sides of the brain. The interpretation of this curious result is discussed on page 92.

(C) The visuotopic organization of the abnormal input

The relatively large number of abnormal receptive fields found in these 3 cats served to show the organization of the abnormal input in rather more detail than in the normal Siamese cats. The visuotopic organization was the same as in normal Siamese cats, and the same mirror reversal of the representation of the ipsilateral hemifield was present. In Fig. 8, recording site 1a was in area 18 close to the 17/18 border. Its receptive field was abnormal, just within the ipsilateral hemifield. Site 2a was just within area 17, and the receptive field was normal, in the contralateral hemifield close to the vertical meridian. Recording sites 3a–d and 2b continue the sequence of abnormal receptive field positions, progressing through the ipsilateral hemifield

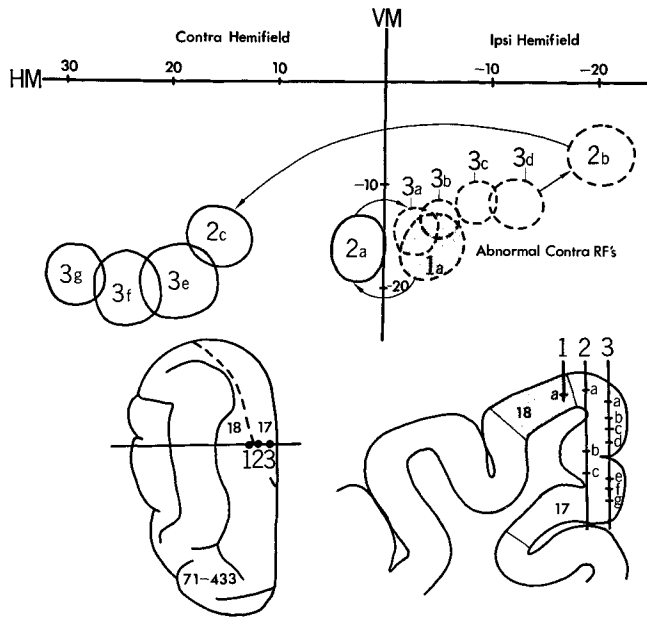


Fig. 8. Sequences of abnormally and normally located receptive fields obtained in 2 electrode penetrations in area 17 of a lid sutured Siamese cat. Conventions as in Fig. 7. Note that as the recording sites in area 17 are further from the area 17/18 border, the normally located receptive fields are more to the left (temporal) and the abnormally located receptive fields more to the right (nasal) in the visual field of the contralateral eye. Area 18 and a receptive field for area 18 are shaded. All receptive fields were obtained from the contralateral eye.

away from the vertical meridian. These receptive fields show a mirror reversal of the sequence formed by the normal receptive fields 2c and 3e-g.

Other but shorter mirror reversed sequences of abnormal receptive fields were found in area 17 and in area 18. We conclude that in normal Siamese cats the abnormal input is superimposed as a mirror reversal upon the normal pattern of visual field representation, that the abnormal input activates fewer neurons than does the normal input, and that the relative strength of the abnormal input is increased bilaterally in the kittens that we have raised with one eye sutured.

(Part III) Anatomical studies of the geniculo-cortical interconnections

In order to demonstrate the pattern of geniculo-cortical projections in Siamese cats, we have made lesions in the visual cortex of 12 Siamese cats, and studied the retrograde changes produced in the lateral geniculate nucleus. Since the visual field representations in the lateral geniculate nucleus of normal cats are well defined^{26,38,50} and those in the cortex are also known in detail^{58,62,63}, it is a relatively simple matter to make a number of cortical lesions and determine whether the geniculo-cortical projection pattern demonstrated by retrograde degeneration in the lateral geniculate nucleus is abnormal.

On the basis of the electrophysiological results reported for our Siamese cats in

the previous sections, one would expect the segments of retrograde degeneration in such Siamese cats to have a normal distribution in the nucleus. That is, the borders of the degenerative segments should always correspond in position to the lines of projection that can be defined in a normal cat (see ref. 38 and Fig. 9A). However, if the reduced functional connections from layers A1 and C1 to the cortex reflect an actual reduction in geniculo-cortical connections, rather than a modification of intra-cortical connections, then it is possible that in each geniculate segment the retrograde degeneration would involve layers A1 and C1 little, if at all, while the usual retrograde changes would be found in layers A and C (see Fig. 9A).

If the altered pattern of cortical organization reported by Hubel and Wiesel³⁶ is the result of changes in geniculo-cortical projections, one would expect these changes to be revealed by the distribution of the geniculate retrograde degeneration as shown in Fig. 9B. The segments of retrograde degeneration within adjacent geniculate layers should be out of register when abnormal parts of the nucleus are involved. That is, when within any geniculate segment layers A and A1 do not represent the same part of the visual field, then they would be expected to project to 2 different zones of the visual cortex in these cats, and a cortical lesion could not produce a zone of retrograde degeneration with borders that correspond to the normal lines of projection.

Cortical lesions produce not only retrograde degeneration in the geniculo-cortical pathways, but also anterograde degeneration in the cortico-geniculate fibers.

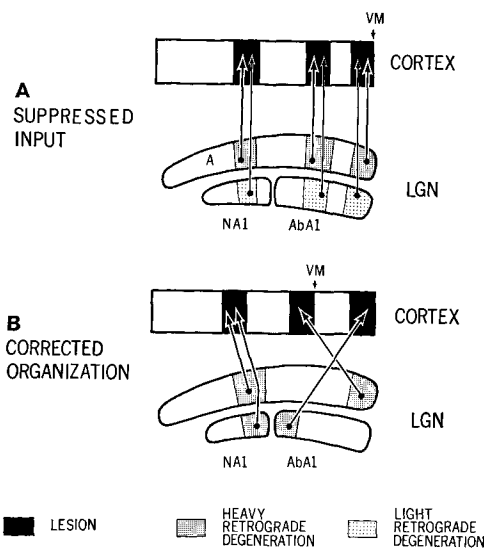


Fig. 9. Schema to show the patterns of retrograde degeneration that would be expected in the lateral geniculate nucleus after a lesion in the visual cortex of Siamese cats. Scheme A shows the degeneration that would be expected on the basis of the electrophysiological results described here, while B shows the degeneration expected on the basis of Hubel and Wiesel's³⁶ results. The cats shown in B would not show columns of retrograde degeneration passing through all the layers of the lateral geniculate nucleus for every lesion, while in the cats shown in scheme A the degeneration in layer A1 might be less severe (light stipple) than that in layer A (dark stipple). Only layers A and A1 are shown here for simplicity.

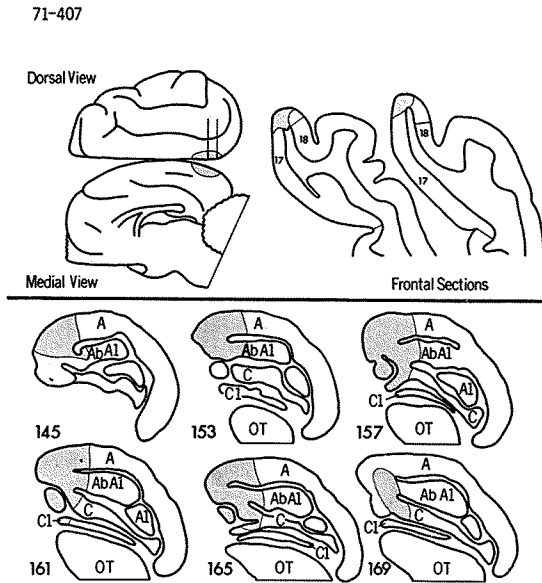


Fig. 10. The retrograde degeneration in the lateral geniculate nucleus after a lesion of area 17 of a Siamese cat. Above: the location of the cortical lesion (shaded area) on surface views of the right cerebral hemisphere. The 2 lines indicate the locations of the 2 frontal brain sections on the right. The area 17/18 border is marked by a line. Below: drawings of the lateral geniculate nucleus from serially numbered 50 μ m frontal brain sections. The zone of retrograde degeneration is shaded. Laminae A, A1, C, and CI are labeled; Ab A1, abnormal segments of layer A1; OT, optic tract.

We have used 6 of the Siamese cats to study these pathways. These animals survived 10–12 days postoperatively, which is long enough to show marked retrograde cell changes and also short enough to allow staining of the degenerating cortico-geniculate axons by silver methods. One can reasonably anticipate that the cortico-geniculate feedback might relate retinotopically equivalent parts of the cortex and lateral geniculate nucleus, and that, therefore, this fiber system might also be modified in accordance with the changes that occur within the cortex of the Siamese cats.

(A) *The topological organization of the geniculo-cortical projection in Siamese cats*

The cortical lesion and the resulting retrograde degeneration shown in Fig. 10 demonstrate that in this Siamese cat the medial parts of the lateral geniculate nucleus project to the dorsolateral parts of area 17, close to the 17/18 border. The anterior and posterior margins of the lesion are within area 17 and do not quite reach the 17/18 border. In the lateral geniculate nucleus, the anterior and posterior parts of the degenerative zone do not quite reach the medial border of layers A and A1. In the largest, midportion of the lesion, however, some of the white matter is damaged, and thus some of the axons passing to the medial part of area 18 and to the adjacent 17/18 border are probably also damaged. Correspondingly, the midportion of the degenerative zone includes the most medial parts of the nucleus. Figs. 10 and 11 show that the lateral border of the degenerative zone passes through the lateral geniculate nucleus approximately along the lines of projection and at the appropriate distance from the

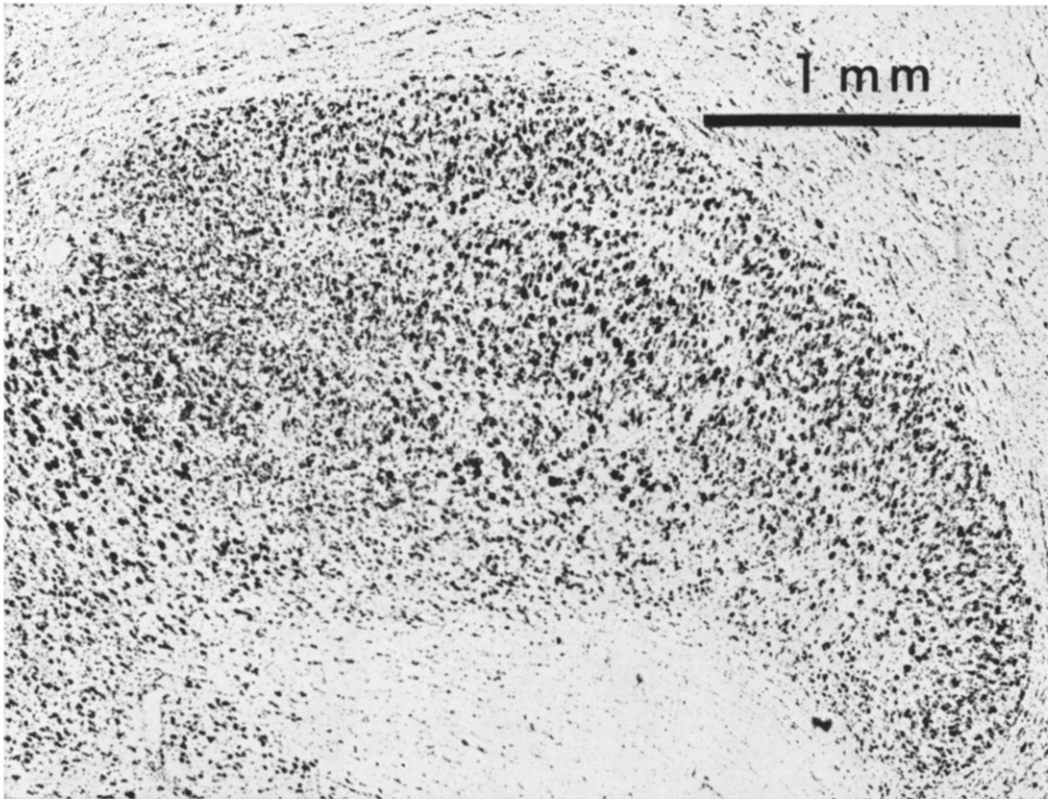


Fig. 11. Retrograde changes in the lateral geniculate nucleus of the Siamese cat illustrated in Fig. 10. Section 153; Nissl stain.

medial border of the nucleus. It is especially important to note that this lateral margin of the degenerative zone passes straight through the abnormal segment of lamina A1, thus indicating that this segment projects to the same part of the cortex as does the adjacent layer A.

Several lesions were placed well within the borders of area 17, and the zone of retrograde degeneration that was produced in the lateral geniculate nucleus passed

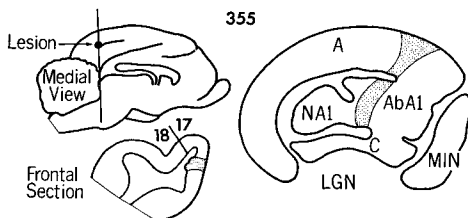


Fig. 12. The retrograde degeneration in the lateral geniculate nucleus (LGN) after a small lesion in striate cortex on the medial wall of the cerebral hemisphere. MIN, medial interlaminar nucleus. Other conventions as in Fig. 10.

through the nucleus as would be expected in a normal cat. Fig. 12 shows a small lesion in the medial wall of the cerebral hemisphere. In a normal cat this lesion would be in cortex that represents an area 4° or 5° from the vertical meridian, just in the lower visual field⁶⁰. The corresponding column of retrograde degeneration passes through the geniculate sector that would also represent the lower visual field $4-5^\circ$ lateral to the vertical meridian in a normal cat^{26,50}. Fig. 12 thus demonstrates that the geniculo-cortical projection in this cat was normal. Since the zone of retrograde degeneration also passes through the abnormal segment of layer A1 this, again, shows that the abnormal segment of layer A1 projects in a completely normal manner, in register with its neighbors. This small lesion produced no clearly identifiable changes in the C layers.

Most of the hemispheres show patterns of degeneration similar to the above. The rostrocaudal position of the lesions varies considerably and the rostrocaudal position of the cell degeneration varies accordingly. In some, the borders of the degenerative zone pass through the abnormal segment. In all of these hemispheres, except for the two that are described on p. 82 (see Figs. 13-16), the locus of the geniculate degeneration corresponds, in terms of the retinal representation, to the position of the cortical lesion. However, the extent to which the separate geniculate layers are involved varies (see below).

(B) Differences in the severity of the degeneration in the individual geniculate layers

There is evidence that the retrograde degeneration may be less severe in layer A1 than in layer A in some Siamese cats. With relatively large cortical lesions, such as the one illustrated in Fig. 10, the degeneration in layer A1 sometimes appears less marked than that in A, but this difference is neither pronounced nor consistent. Of the 5 smaller cortical lesions only the one illustrated in Fig. 12 produced retrograde degeneration that is approximately the same in layers A and A1. In the other 4 cases the cellular degeneration in layer A was more severe than that in layer A1. In 2 cases there is no detectable degeneration in layer A1 at all even though layer A shows clear retrograde changes.

Although this difference between layers A and A1 is what would be expected on the basis of the electrophysiological records, the cellular changes should not yet be treated as confirming our expectations to any significant extent. It appears from the pictures published by Niimi and Sprague⁴⁵ that there may be a similar difference between the two A layers in a normal cat.

The changes in the C layers are generally milder and more difficult to evaluate than those in the A layers. The cells of layer C1 are small and the borders of the layer are poorly defined in a normal brain, so that retrograde degeneration only shows up clearly when it is heavy. Although many of the cells of layer C are large, they are irregularly distributed and a number survive after lesions confined to area 17 (see ref. 17). In addition, the degenerative pattern in these two C layers varies considerably between cats, and does not seem to be related to the postoperative survival period. We have found no clear evidence of degenerative changes in layer C2. In summary, although there are many lesions in the present series that have produced no clear degeneration in

layer C1, the changes in layer C are so variable, and evidence about the changes that would be expected in a normal cat so limited, that we cannot conclude that the laminar distribution of the degeneration in the C layers is abnormal in Siamese cats.

Cat 463 merits a separate description since the arrangement of the layers in this cat differs from the usual Siamese pattern. In the rostral part of the nucleus layer A1 looks normal and does not show any disruption or fusion with adjacent layers. In the midportions of the nucleus the characteristic disrupted structure of layer A1 can be seen, but in the caudal half of the nucleus layer A1 cannot be clearly recognized; it appears to have fused with layer A completely. A fairly large cortical lesion on the right produced a zone of degeneration that passes through the fused layers A and A1. The smaller lesion on the left is further rostral in area 17, and is one of those (see above) that produced retrograde degeneration in layer A but no clearly recognizable changes in layer A1.

(C) An exceptional pattern of geniculate degeneration

Finally, there is one animal of this series (72-290) which is, perhaps, the most interesting. In this animal we found the pattern of retrograde change that would be anticipated on the basis of the cortical records reported by Hubel and Wiesel³⁶. Fig. 13 shows that on the left the cortical lesion and the corresponding retrograde degeneration fit the expected pattern precisely. The lesion lies on the medial wall of the hemisphere, some distance from the 17/18 border. The degeneration spares the abnormal segment of layer A1 and the most medial part of layer A. It is to be noted, however, that there is a considerable segment of retrograde change in the part of layer A that lies dorsal to the unaffected abnormal segment of layer A1 (see Figs. 13 and 14). That is, in the medial parts of the nucleus the borders of retrograde change do not correspond to the normal lines of projection. Figs. 13 and 14 show that in the lateral parts of the nucleus, where the normal segment of layer A1 lies opposite the degenerate segment of layer A the borders of the zone of retrograde degeneration do correspond to the lines of projection, exactly as expected.

On the right side of the brain the retrograde degeneration in cat 72-290 also fits the pattern expected from the type of cortical organization reported by Hubel and Wiesel³⁶ (see Figs. 15 and 16). The lesion lies in area 17 along the 17/18 border rostrally, but caudally it leaves a strip of undamaged area 17 adjacent to the 17/18 border (Fig. 15a and b). From the schema (Fig. 15c), it is apparent that given the altered cortical organization, this type of lesion would affect the abnormal projection from layer A1 more than the normal projection from layer A, and that the lateral borders of the zones of retrograde degeneration in the two layers would be out of register wherever the lesion did not extend symmetrically on either side of the representation of the zero vertical meridian. The degeneration in the lateral geniculate nucleus was found, as expected, in all but a lateral fringe of the abnormal segment of layer A1 rostrally (Fig. 15d, sections 32-26), while further caudally much of the lateral part of this segment is spared (sections 40-48). Correspondingly, more of layer A is affected in the caudal sections than in the rostral sections. This shows that the medio-lateral sequence of the geniculo-cortical projection from the abnormal segment of layer A1 is

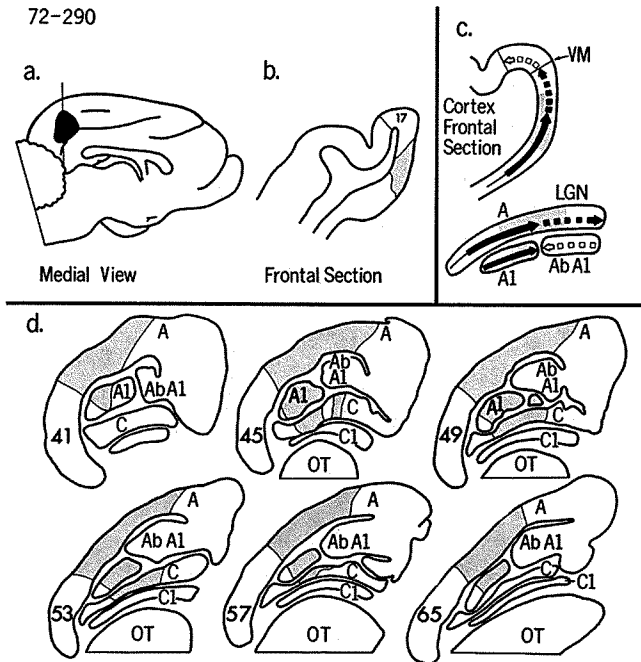


Fig. 13. Retrograde degeneration in the left lateral geniculate nucleus of cat 72-290. The pattern of degeneration found here resembles that shown in scheme B of Fig. 9. The cortical lesion is shown above (a and b) and the retrograde degeneration below (d). In c an interpretation of this result is shown. In the upper part of c is the representation of the visual field described by Hubel and Wiesel³⁶ and in the lower part is a simplified schema of the visual field representation found in the lateral geniculate nucleus of Siamese cats^{26,36}. The shading shows the position of the lesion and of the retrograde degeneration. Note that there is no degeneration in the abnormal segment of layer A1 lying ventral to the degeneration in layer A. The line labeled VM shows the cortical representation of the vertical meridian, the other line shows the area 17/18 border.

a reversal of the normal order and a reversal of the sequence present in the projection of layer A. A photomicrograph showing the retrograde degeneration in one of the sections in this series is illustrated in Fig. 16.

Thus, it appears that there are 2 quite different patterns of geniculo-cortical projection in Siamese cats. Whereas all of the other animals that have been studied have shown a pattern of retrograde degeneration that is not strikingly different from normal, in cat 72-290 the two A laminae in the abnormal segment of the nucleus must project to different cortical areas.

(D) Cortico-geniculate projections

In general, the pattern of the cortico-geniculate fiber degeneration that is seen in Siamese cats does not differ significantly from normal (see ref. 20). The characteristic orientation of the fibers along the lines of projection within layers A and A1 can be seen in all these brains. However, the anterodorsal interlaminar plexus (see ref. 22), which is made up of axons that pass roughly parallel to the laminar borders, does not show clearly in the frontal sections. To some extent this occurs because layer A tends

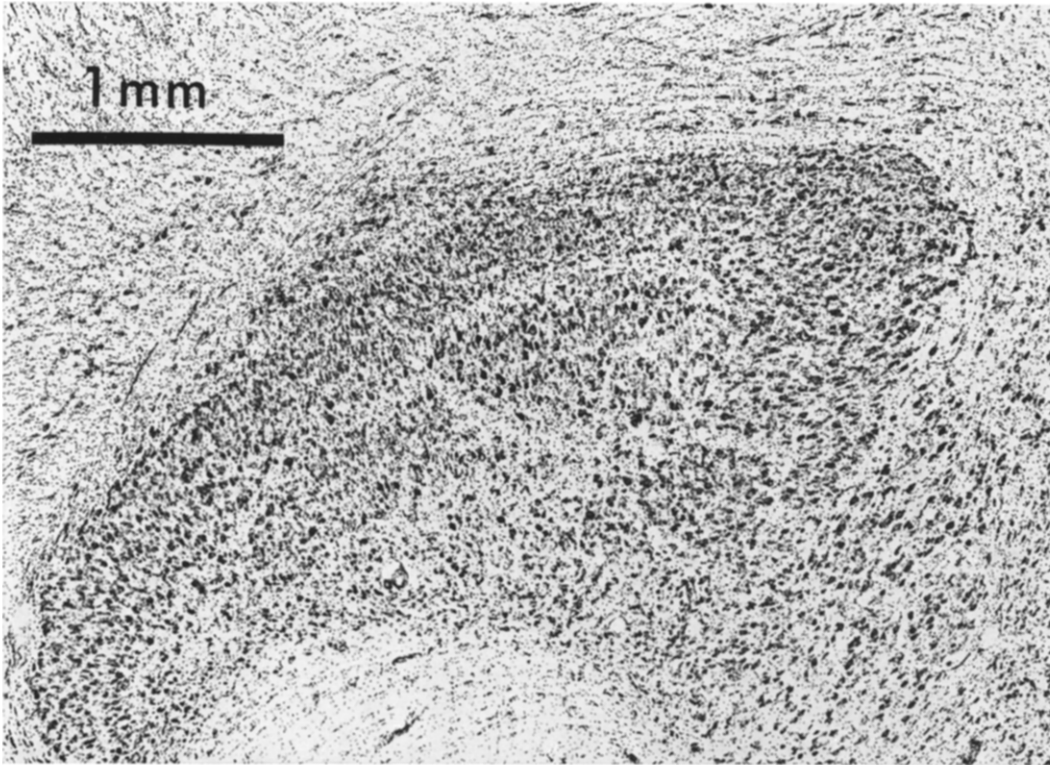


Fig. 14. Section 53 from the series illustrated in Fig. 13. Nissl method, showing the zone of retrograde degeneration in the lateral geniculate nucleus.

to fuse with the abnormal segment of layer A1, thus obliterating the interlaminar plexus. Most of the degenerating segments include the parts of the nucleus within which such an abnormal fusion occurs, but even where the Nissl sections show an apparently normal interlaminar region the silver sections show relatively few axons oriented along the plane of the laminae.

Only one animal shows a rich plexus of degenerating axons running in the interlaminar region and oriented in the plane of the laminae, and for this one animal the sections were cut parasagittally, not frontally, as were all the others. In this brain the interlaminar plexus is remarkably well shown, and the degenerating axons extend further than normal beyond the borders of the zone of retrograde degeneration.

It remains to be determined whether this is an individual Siamese cat with an unusual interlaminar plexus, or whether the interlaminar plexus in all Siamese cats has an abnormal orientation with most of the axons running in a parasagittal plane and few running frontally. Such a preferential orientation would be of considerable interest, for it would suggest that the cortico-geniculate feedback is well developed to deal with images that move up and down in the visual field, but is poorly developed for dealing with images that move horizontally. Since the Siamese abnormality disrupts the visual field representation along the horizontal axis, but leaves it undisturbed

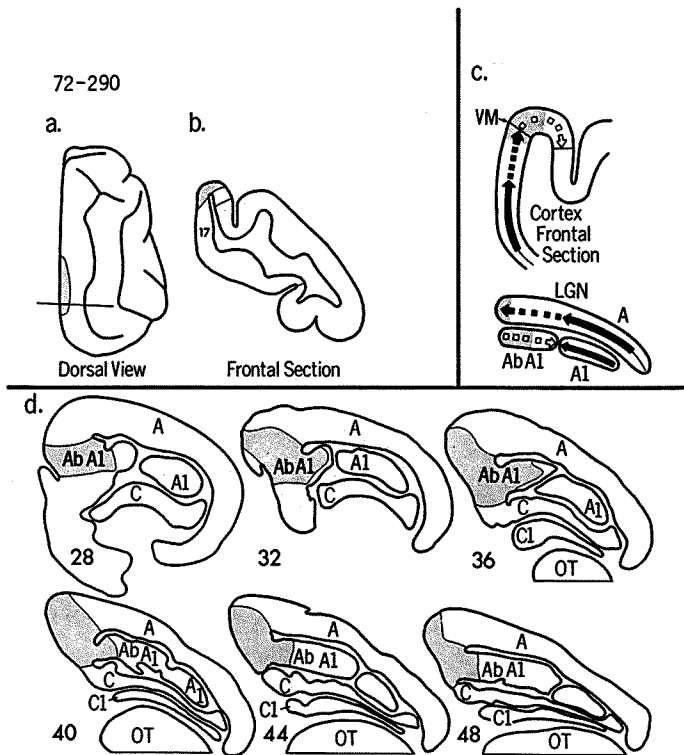


Fig. 15. Retrograde degeneration in the right lateral geniculate nucleus of cat 72-290. The pattern again resembles that of scheme B in Fig. 9. Conventions as in Fig. 13. The rostral part of the lesion, which extends close to the area 17/18 border and accounts for the retrograde degeneration in sections 28 and 32, is not shown in either b or c.

along the vertical axis, and since in some cats the abnormality is associated with a horizontal nystagmus (see below), this possibility merits further study.

One hemisphere (315R) shows a curious pattern of cortico-geniculate fiber degeneration that must be briefly mentioned. The geniculate fiber degeneration extends for a considerable distance lateral to the zone of retrograde cell degeneration. At first sight this would appear to be a grossly abnormal relationship. However, since the cortical lesion only includes a small portion of area 17 close to the 17/18 border and includes almost the entire extent of area 18, it is probable that the retrograde degeneration reflects the damage to area 17 while the fiber degeneration was produced primarily by the damage to area 18 (see ref. 17). We do not consider this brain as an example of an abnormal relationship between the lateral geniculate nucleus and the cortex.

Unfortunately cat 72-290, which showed the abnormal pattern of retrograde degeneration, was allowed a long postoperative survival and was not suitable for studying the cortico-geniculate fiber degeneration. Thus, we do not know whether the reorganized geniculo-cortical pattern was associated with a parallel modification of the cortico-geniculate projection.

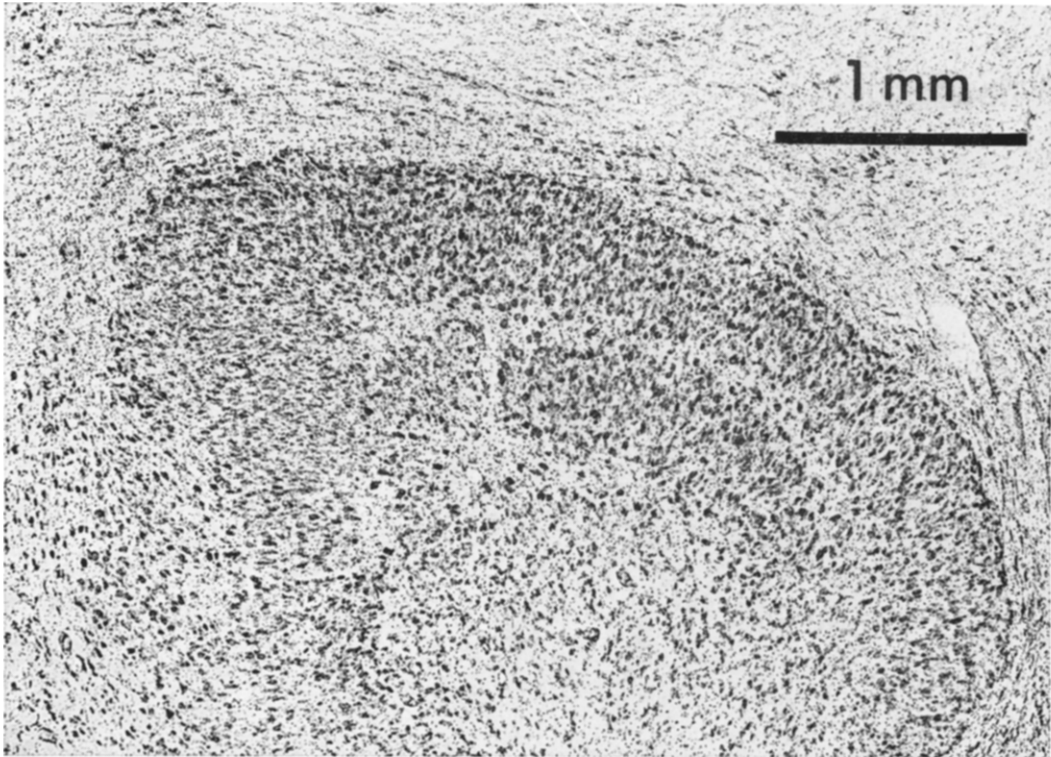


Fig. 16. Section 32 from the series illustrated in Fig. 15. Nissl method, showing the zone of retrograde degeneration in the lateral geniculate nucleus.

DISCUSSION

(A) The two geniculo-cortical projection patterns

The most striking conclusion that can be drawn from our studies of Siamese cats is that the cortex can deal with the aberrant geniculate input in 2 quite different ways. In one, the aberrant input is largely suppressed at the cortical level; in the other, the retino-geniculate projection is rearranged and the aberrant input forms a part of more extensive but sequential representation of the visual field.

In the cats studied by Hubel and Wiesel³⁶ an orderly sequence of visual field representations was recreated upon the cortical surface as indicated in Figs. 1 and 17, and this will be called the 'Boston' pattern. Only one of our cats, and this was studied anatomically, showed evidence of such a pattern. In all of the other cats that we have studied the topological arrangement of the geniculo-cortical projections appeared to be normal, while the input from the abnormal geniculate layers (A1 and C1) was suppressed (see Fig. 17). This will be called the 'Midwestern' pattern.

Each pattern provides an adequate solution to the problem set by the abnormal, disrupted, and reversed representation of the visual field that occurs in the lateral

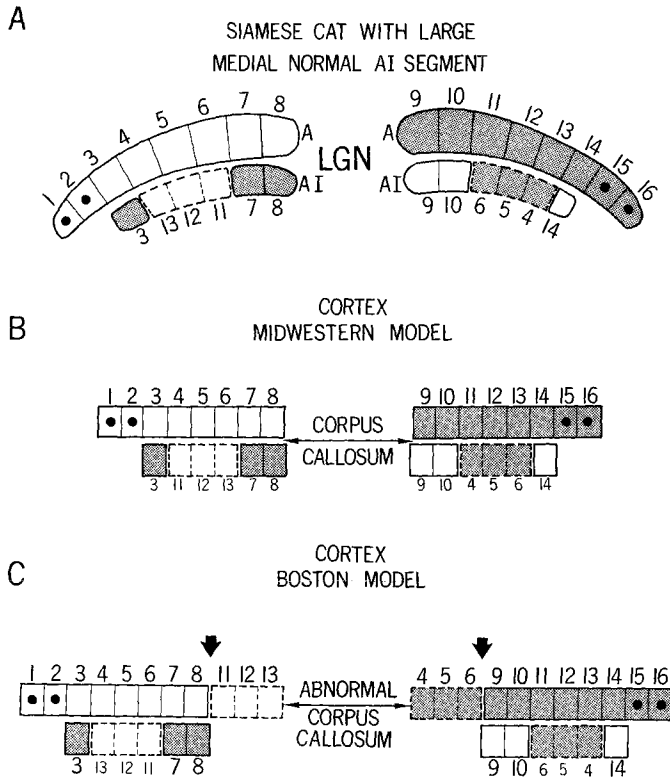


Fig. 17. Schema of the visual pathways in the 2 types of Siamese cat that have been studied, showing the retinotopic arrangement that would be seen in the lateral geniculate nucleus and cortex if there were a medial segment of lamina A1 that has normal connections (7 and 8 on the left, 9 and 10 on the right). The visual field (not shown) is a right-to-left series of segments, numbered 1–16, with 1–8 representing the right hemifield and 9–16 representing the left hemifield. In the figure the segments receiving from the left eye are shaded and those receiving from the right eye are unshaded. Segments with large dots (1 and 2; 15 and 16) receive from the monocular segments of the visual field. Geniculate and cortical segments that receive an abnormal input are outlined by dashed lines. Reduced or suppressed inputs to the cortex are indicated by the smaller numbers. Only layers A and A1 are shown; the C layers have been omitted for the sake of simplicity. Note that a medial normal segment would produce an interruption, indicated by the unlabeled arrows, in the sequential representation of the visual field in the Boston cats, but not in the Midwestern cats. In the Midwestern cats a normal set of callosal fibers would link the cortical representations of the hemifields as in a normal cat, but in the Boston cats a normal set of callosal fibers would be of doubtful value for visual functions.

geniculate nucleus of all the Siamese cats. Each solution produces an orderly sequence of visual field representations upon the cortical surface, and each allows reasonably full use of the available cortical tissue. Each must involve quite distinct developmental processes; whereas the Midwestern solution appears to be a relatively simple suppression of inputs that are abnormally arranged, the Boston solution is a sophisticated and elegant rearrangement of the whole input pattern. In the following discussion we will comment upon each of these solutions, and present a theory that may explain the difference.

It is necessary to postulate two different types of cortical organization in Siamese

cats, because the differences between our results and those reported by Hubel and Wiesel³⁶ cannot have been produced by different experimental methods. We recorded from large parts of the cortical surface and exposed a large area of visual cortex. As a result we have generally studied groups of neurons rather than individual cells. Hubel and Wiesel³⁶ used more restricted parts of the cortex for their studies and recorded the response properties of individual cells. Since the difference between their electrophysiological observations and ours concerns the position of receptive fields, not the individual properties of the receptive fields, the difference in the methods must be considered irrelevant. Neither method can produce an error of 15–20° in receptive field position and each can give a clear view of the medio-lateral arrangement of the visual field upon the cortical surface.

Our anatomical observations also show that there are two distinct patterns of geniculo-cortical projection, one of which fits with our electrophysiological results while the other fits those of Hubel and Wiesel³⁶. It is necessary to conclude that there are different sorts of Siamese cat, and that by chance of geographical distribution, or through different breeding patterns, Hubel and Wiesel obtained their results from one type of cat, while we obtained almost all of our results from another type. Cool and Crawford⁶ probably had some Midwestern and some Boston cats in their experiments, since the cortical representation of the vertical meridian appears not to have been the same in all their animals. However, the methods that they used give no evidence about the cortical arrangement of the retinal representations, and it is difficult to compare their results with ours or with those of Hubel and Wiesel³⁶.

The suppression of the normal geniculo-cortical projection is not complete in any of the Siamese cats. There are cortical regions in which the abnormal input from layer A1 overlaps the normal input from layer A, and there are some neurons or neuron groups that receive an input from two quite distinct parts of the visual field (see also ref. 36). That is, neither of the two patterns of cortical adjustment to the abnormal input is pure. Each exists together with remnants of a normal retinogeniculate projection.

(B) The Midwestern pattern

In the Midwestern Siamese cats the amount of cortical activity that can be attributed to afferents from the abnormal geniculate layers A1 and C1 is reduced. This reduction could be produced in several different ways. For example, the neurons in layers A1 and C1 could send abnormally few axonal branches to the cortex, the axons might fail to make synaptic connections in the cortex, or the geniculo-cortical projection system might be inhibited by other cortical neurons.

The electrophysiological recordings do not show which of these mechanisms is responsible for the reduced cortical activity. If we knew that a significant part of the recorded activity came from geniculo-cortical afferents we would have good evidence that these fibers have a reduced intracortical ramification. However, it is probable that the methods we have used do not record much activity from the afferent fibers, since in a normal cat most single neurons isolated by these methods have a binocular input and they must therefore be cortical cells (see ref. 31).

At present, the anatomical observations do not show how the reduced cortical activity is produced in the Midwestern cats. Cortical lesions do produce less severe retrograde reactions in layers A1 and C1 than in layers A and C, and this suggests that there is a reduced projection of geniculo-cortical afferents from the abnormal layers in the Midwestern cats. However, it is not certain that the Siamese cats differ from the normal cats in the pattern of the retrograde reaction (see Results, section B).

It is of some interest to compare the abnormality seen in a Midwestern cat with the changes that are produced when a normal cat is raised with one eye shut. In the latter, the input from the deprived eye to the cortex is markedly reduced, as is the input from the A1 and C1 layers in a Midwestern cat. The geniculate cells that receive their afferents from the deprived eye grow less than normal^{59,60}. The reduced geniculate cell growth of 25–40% appears to be closely related to the altered ocular dominance pattern in the cortex^{24,25,30}, and by analogy one might expect the geniculate cells in layers A1 and C1 in a Midwestern Siamese cat to be smaller than normal. At first sight, the cells within these layers appear normal and there is no indication that the A1 cells in the Midwestern cats are as much as 25–40% smaller than normal. However, the judgment cannot be made without extensive measurements. Since both geniculate nuclei are equally affected, one cannot compare the A1 laminae of the two sides. Further, a comparison with the adjacent normal A layers is complicated because in a normal cat the cells of the A layers are 15–20% smaller than those of the A1 layers²⁵. It is our impression that in the Midwestern cats the A1 cells are not significantly larger than the A cells; they may even be somewhat smaller. Measurements are being made to decide this point.

A second interesting comparison that can be made is between Midwestern Siamese cats and normally pigmented cats that have been raised with a surgically induced squint³⁴. In the cats with the induced squint the part of the visual field represented in layer A no longer matches that represented in adjacent parts of layer A1. In Midwestern cats the visual field representation in the abnormal segment of layer A1 does not correspond to the representation in the corresponding segments of layer A. Also, in the normal segments of the nucleus, the representations in layers A1 and A do not match to the extent that the Midwestern Siamese cat has a squint. In the cats with a surgically induced squint there is no cortical suppression of either of the two mismatched inputs³⁴, but in the Midwestern cats the whole of the input from the abnormal layer A1 is suppressed. This indicates that the cortical suppression cannot be attributed to the occurrence of non-matching visual field representations within adjacent geniculate layers. It is necessary to consider what mechanisms may be producing the cortical suppression that we have found in Midwestern cats and also to ask why it is that the suppression involves the inputs from the whole of layer A1, instead of being limited to the abnormal segments of this layer.

One difference between the Siamese cats and the cats raised with a squint is that the sequential representation of the visual field within layer A1 is disrupted and there is a reversal of a part of the visual field representation in the Siamese cats. This disruption and reversal may be critical in producing the suppression, since they do not occur in the normal cats that are raised with a squint. It is possible that static patterns

within the geniculo-cortical system that are not matched, or movements that are simply out of phase, can be dealt with by the cortex as two separate inputs that are kept distinct. It is only when movements across a single geniculo-cortical representation are disrupted that the cortical suppression occurs. That is, our results suggest that cortical mechanisms are not concerned simply with matching left eye inputs to right eye inputs; they are also concerned with establishing a complete sequential representation of the visual field within each of the geniculo-cortical pathways. A disrupted representation may be suppressed, even when a part of this representation fits with cortical patterns that are being successfully activated through the other geniculate layers.

The pattern of cortical activity that has been seen in the Midwestern cats indicates that there is little or no cortical vision for the temporal retina in these cats. When a Siamese cat is tested behaviorally one would expect to see no defects, except perhaps a lack of stereopsis, provided that the cat is tested with both eyes open. If the cat is tested with one eye open one would expect to be able to identify loss of cortical visual functions in the nasal visual field*.

(C) The Boston pattern

The modification of the geniculo-cortical pattern that occurs in Boston cats is shown in Figs. 1 and 17. We have only one of these cats, but the pattern of the retrograde degeneration seen in this animal fits extremely well with the changes one would expect on the basis of Hubel and Wiesel's³⁶ cortical records. It seems reasonable to regard our cat as having the same central modifications as their cats and to conclude that in their cats the modified cortical response patterns were produced by just such an altered geniculo-cortical projection.

The mechanism that controls the development of the Boston pattern is especially interesting. We do not know at what stage of development this pattern appears, and clearly it is important, if we are to understand the mechanism, to determine whether the geniculo-cortical axons are first organized as in a normal cat and are subsequently modified, or whether the Boston pattern of geniculo-cortical connections develops right from the start.

It is known that in a normal cat geniculo-cortical pathways are established at birth³². Hubel and Wiesel³⁶ have further shown that in a Siamese cat the Boston pattern can be developed even when an animal is raised with both eyes sutured. They have concluded that the development of the Boston pattern is independent of visual experience and is likely to be developed at birth. This would be a remarkable developmental achievement, since we know of nothing that labels the cells in the abnormal segment of layer A1 as abnormal other than their receipt of an abnormal sequence of stimuli from the visual field. The demonstrable retinal connections of these cells are normal apart from the left-to-right switch.

* *Note added in proof.* E. I. ELEKESY, J. E. CAMPION AND G. H. HENRY (personal communication) have recently demonstrated by behavioral testing that there is such a loss of the nasal visual field in normal Siamese cats.

It is conceivable that during development the cortex can use ordered sequences of retino-geniculate-cortical discharge patterns to establish the order in which geniculate layers are mapped onto the cortical surface. However, it is unlikely that suitably ordered sequences will be generated in the system in the complete absence of visual stimuli. It is possible that the very pale eyelids of a Siamese kitten allow enough light through for stimuli of alternating light and dark bars, which would be readily generated in a cage, to fall on the retina and produce orderly waves of activity within the lateral geniculate nucleus.

Thus, it becomes important to determine whether the Boston pattern is present at birth. This can be done by recording, or by making cortical lesions at birth, or shortly after. A more indirect method would be to raise a Siamese kitten completely in the dark. Only if the Boston pattern is found in such experiments would we need to look for a mechanism that allows the cortex to establish an orderly representation of the visual field in the absence of a visual field¹⁸. In order to interpret an experiment that failed to show the Boston pattern one would need to be sure that the experimental animal would have developed this pattern with normal visual experience. For this one needs to know that Boston cats and Midwestern cats breed true, and to have in-bred strains of each kind of cat.

While the discovery of two types of geniculate-cortical pattern raises some very interesting questions about the manner in which cerebral organization can be altered to compensate for an abnormally organized input, it complicates further advances. Almost any experiment in which the development of the visual system in a Siamese cat is modified will depend upon knowing which type of cat one had at the beginning, and that is not a decision that can be easily made by a brief preliminary study.

(D) The development of the two different cortical patterns

It is not known why there should be two quite distinct patterns of cortical organization in Siamese cats. We shall suggest that the size of the medial normal segment of layer A1 (see ref. 26 and Fig. 17) is a critical factor in producing a strabismus, that the presence of this segment can influence the development of the pattern of cortical organization, and that the Midwestern cats have a relatively large medial normal segment while the Boston cats have no such segment or an extremely small one.

The medial normal segment does not usually stand out clearly in a normal Siamese cat's brain. It can be seen best if the retino-geniculate fibers are degenerating. A medial normal projection to layers A1 and C1 was present in all the cats in which we studied the retino-geniculate fiber degeneration, but it was rather variable in size and smallest in the cat with the most marked strabismus²⁶. The afferents to the medial normal segment arise close to the area centralis. They are therefore likely to be critical in aligning the eyes, and one might expect that a medial normal segment of a certain size would be necessary for the development of a proper ocular alignment, and that without this segment a cat would be cross-eyed.

From the results reported by Hubel and Wiesel³⁶ it is not known whether their cats had a medial normal segment. However, most of their cats had a strabismus or were descended from strabismic parents. The only one of their cats that was adult and

not cross-eyed (their cat no. 6) showed a cortical pattern that bears some resemblance to the Midwestern pattern. Most of our cats have been obtained from dealers and probably come from a population that has been exposed to heavy selection against strabismus. Cross-eyed cats do not win prizes. From the account by Cool and Crawford⁶ it would also appear that the strabismic cats showed the Midwestern pattern.

There are, therefore, some indirect reasons for thinking that the medial normal segment may be absent or relatively small in the Boston cats. Fig. 17 shows that a continuous uninterrupted representation of the visual field can be recreated in the cortex only in the absence of a medial normal segment. If there were a significant medial normal segment, then the Boston pattern would show a disruption corresponding to the size of this segment. This hypothetical disruption is shown by the unlabeled arrows in Fig. 17, between segments 8 and 11 on the left and between segments 6 and 9 on the right. Thus, if the cortex does select geniculate input patterns that can recreate a continuous representation of the visual field, then, in the presence of a medial normal segment, it would necessarily have to suppress the abnormal input from the whole of layer A1. However, in the absence of the medial normal segment the cortex could recreate the visual field representation according to the Boston pattern.

The above explanation can be regarded as a reasonable way of accounting for the two patterns. However, two points that arise from our own material do not fit readily into this explanation. One is that the 3 Siamese kittens that were raised with one eyelid sutured showed the Midwestern pattern even though both parents were somewhat strabismic. The other is that the single animal in which we found the Boston pattern was not markedly cross-eyed. Extensive direct observations of the retino-geniculate and geniculo-cortical projections are required to demonstrate that the medial normal segment is indeed critical in the suggested manner, and to determine the precise relationship between the strabismus and the medial normal segment.

Fig. 17 shows that the callosal connections of the visual cortex are likely to be modified in the Boston cats but not in the Midwestern cats. If the callosal fibers link cortical areas that lie close to the 17/18 border as in a normal cat^{12,35,61}, then in a Midwestern cat these fibers would be linking parts of the visual field representation close to the zero vertical meridian as is normal. In a Boston cat, however, such normally distributed callosal fibers would link disparate parts of the visual field representation. It remains to be determined whether the callosal connections of Boston cats are modified or whether they are functionless. In view of the striking adaptation of cortical connections that exists in Boston cats it seems unlikely that there would be a significant callosal link between non-adjacent parts of the visual field representation. Preliminary studies of fiber degeneration in the corpus callosum have shown a relatively normal pattern of distribution of the callosal fibers, but it is not known whether the cats that have been studied so far were Midwestern or Boston cats⁶⁴.

(E) The effects of lid suture

The lid suture experiments were done primarily in order to study the changes in geniculate cell size, and the electrophysiological changes that we found were, to some extent, unexpected. While one would expect the cortical input from the non-deprived

normal segment of layer A1 to increase as a result of the lid suture, it was rather surprising to find that this input was still weaker than that from the corresponding segment of the deprived layer A. This demonstrates the extent to which the disrupted representation of the visual field in layer A1 tends to be suppressed at cortical levels. It also indicates that the cortical suppression seen in Midwestern cats depends upon mechanisms unlike those responsible for changing the input patterns from a sutured eye in a normal cat.

It is possible that the lid suture in the Siamese kittens was less effective than a suture in a normal cat because the Siamese kittens have unpigmented eyelids. However these lids must have eliminated from vision as effectively as the translucent occluders used by Wiesel and Hubel⁵⁹ and one would certainly have expected the cortex to receive its major input from the open eye if the only abnormality had been the sutured eye.

The observation that the input to the cortex from the abnormal segments of layer A1 was increased on both sides of the brain is difficult to explain without further experiments. It does not seem likely that the results we have obtained in these 3 cats arose by chance or that we were dealing with a particular line of cats in which the abnormal input was unusually strong. It seems difficult to believe that the bilateral change we saw was produced by a unilateral suture*. It is more reasonable to consider that our Siamese kittens grew up in a limited environment in which they had relatively little opportunity to make extensive sensorimotor coordinations that involved following movements of the eyes. This type of normal visual behavior during development would emphasize the weakness of the abnormal, disrupted input from layer A1, and it might thus appear that this is the type of activity necessary for the suppression of the input from layer A1.

Further observations of normal and abnormal visual development in Siamese cats are necessary to determine how this bilateral effect was produced.

General considerations

The preceding discussion has shown that the Siamese abnormality raises a number of interesting problems about the development of vision and about the modifiability of central neural connections. Siamese cats are likely to provide useful material for a number of new experimental approaches to the central visual pathways. Some of these experiments may prove complex, some will demand closely coordinated anatomical, physiological, behavioral and developmental approaches, and some may depend upon the development of inbred strains of cat that do not exist at present. However, the Siamese abnormality provides such an unusual and basically simple modification of a sensory pathway, and one which can be further modified by

* Note, however, that even this possibility is not entirely unreasonable. On each side the lid suture would reduce one of the two opposing sequences that lie in layer A1; on one side the normal sequence would be reduced and on the other the abnormal sequence. If the cortical suppression depends upon there being opposing activity sequences within a single layer, then a unilateral suture would produce the bilateral effect we have recorded.

relatively simple manipulations such as lid suture or dark rearing that extensive further studies seem well worthwhile.

It is not known to what extent the abnormalities that we have found in Siamese cats are also characteristic of other albino individuals. The details of the abnormal retino-geniculate pathways remain to be studied in most other species, while the geniculo-cortical projection has not been looked at in any other species. It will be of considerable interest to discover how the brains of different mammalian albinos deal with the abnormal visual input, and to find out more about the human abnormality in particular.

The human albino commonly has a strabismus⁴⁹, but albinism in man is more generally associated with a nystagmus¹¹. The cause of the nystagmus is not known, although it is generally thought to be produced because the albino individual lacks a fovea. The Siamese cats that we have studied from this point of view always had an area centralis, and among the experimental cats that have been available to us we have seen only two that had a slight and fleeting nystagmus, which appeared to be most marked when the cat was frightened. Neither of these cats was used in the present series of experiments. Three out of 6 Siamese cats that have been studied in England⁶⁴ had a marked horizontal nystagmus that was present consistently when the cat was paying attention to its surroundings. One of these cats appeared to have a normal area centralis when this was studied on a whole mount preparation⁵⁶.

It is possible, therefore, that the two modifications we have described here, the Boston pattern and the Midwestern pattern, do not cover all of the types of abnormality that can occur in Siamese cats. It may be that other patterns will be found and that the 'English' cat will prove to be a particularly useful model for understanding the human abnormality.

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