A Comparison of Visual Pathways in Boston and Midwestern Siamese Cats

CARLA SHATZ 1
Department of Neurobiology, Harvard Medical School, 25 Shattuck Street, Boston, Massachusetts 02115

ABSTRACT A genetic mutation in Siamese cats causes retinogeniculate fibers representing roughly the first 20 degrees of ipsilateral visual field in each eye to cross aberrantly in the optic chiasm and terminate in the wrong lateral geniculate nucleus (LGN). Previous investigations have shown that in the visual cortex this extra representation of ipsilateral visual field can be organized into one pattern in Boston Siamese cats, another in Midwestern. This finding was confirmed here.

The possibility that the organization of the LGN might account for these two patterns was studied using combined anatomical and physiological methods. On the basis of microelectrode recordings from the visual cortex, 11 out of the 12 Siamese cats included here were Boston cats; one was Midwestern. The distribution of retinogeniculate terminals was examined in each cat using autoradiographic techniques following an eye-injection of 3H-proline. Overall, the LGN organization in Boston cats was similar to that of Midwestern: both lateral and medial normal segments of lamina A1 (mAl) were present. In Boston cats, however, the mAl was remarkably small and shifted ventromedially in the nucleus to allow for the fusion between the medial borders of lamina A and the abnormal segment of A1. In the Midwestern cat this fusion was not apparent and the medial normal segment of A1 was significantly larger.

These differences in organization of the LGN are consistent with those seen at the level of the visual cortex in Midwestern and Boston Siamese cats. It was not possible, however, to relate them clearly to the characteristic strabismus of these animals.

The mechanisms responsible for the normal development of connections within the visual system are unknown, but much can be inferred about them from studies in which development occurs abnormally. Among the factors responsible for abnormal development are, of course, genetic mutations and many neurological mutants have been identified (Sidman et al., '65; Hotta and Benzer, '73). One is the Siamese cat whose familiar and distinctive coat color is produced by a genetic mutation at the albino locus (Searle, '68). It is now known that this same allele somehow interferes with the normal development of connections in the visual system of these animals. In particular, Guillery ('69) has shown that the mutation causes some of the retinogeniculate fibers which would normally remain uncrossed to cross aberrantly in the optic chiasm.

To assess which fibers are misrouted, Guillery and Kaas ('71) removed one eye and studied the pattern of fiber degeneration in each lateral geniculate nucleus. Using this approach combined with physiological recordings from the LGN, they demonstrated that in addition to the usual crossed projection from the nasal retina, each LGN receives fibers which originate from the contralateral eye within a strip of temporal retina representing roughly the first 20 degrees of the ipsilateral visual field.

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2 Present address: Department of Neuroscience, Children's Hospital Medical Center, 300 Longwood Ave., Boston, Massachusetts 02115.
field. These aberrant connections are illustrated diagrammatically in figures 1A and B. The stippled area in geniculate lamina Al of figure 1B indicates one region which receives misrouted retinogeniculate fibers. Retinotopic order within this region is preserved: for instance, in figure 1B cells located at the medial border represent parts of the ipsilateral visual field close to the vertical midline, while cells located at its lateral edge represent a region situated roughly 20 degrees into the ipsilateral visual field.

Although the misrouting of retinogeniculate fibers is characteristic of all Siamese cats, evidently the manner in which the visual cortex subsequently deals with this aberrant input varies to some extent among these cats. It is on this basis that at least two types of Siamese cat have been distinguished. One, described by Hubel and Wiesel ('71) has since been designated the Boston variety. The other, reported by Kaas and Guillery ('73) is called the Midwestern variety. (These terms were not intended to refer to any known geographical distribution of Siamese cat types, but simply to the location of the two laboratories first reporting them.) By examining retrograde cell degeneration in the LGN following localized cortical lesions, Kaas and Guillery ('73) concluded that in the Midwestern Siamese cat as in the ordinary cat, cells lying opposite one another in each lamina of the LGN project to the same location in area 17 (Carey and Powell, '67; Glickstein et al., '67; Gilbert and Kelly, '75) (compare figs. 1A and 1C). But because some of these LGN laminae receive aberrant input from the temporal retina of the contralateral eye, a given cortical location should now represent two mirror-symmet-

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![Diagram](https://via.placeholder.com/150)

> Fig. 1 Diagram to show pathways from the retina to cortex in ordinary (A), Boston (B) and Midwestern (C) Siamese cats. In Siamese cats, abnormal projections are shown by dashed lines, and the participating abnormal regions within the retina, LGN, and the cortex which represent roughly the first 20 degrees of ipsilateral visual field are stippled. For simplicity, only connections between the right LGN and cortex have been indicated, and connections to the C-laminae and the medial normal segment of lamina A1 in the LGN have been omitted. Thus, in the LGN of both Boston and Midwestern cats, the abnormal segment of lamina A1 receives an abnormal representation of ipsilateral visual field from the contralateral eye (see also fig. 5 for more detail). But at the cortical level this abnormal representation is dealt with differently in the two varieties of Siamese cat. In Boston cats, a separate region at the anatomical 17-18 border is devoted to it, whereas in Midwestern cats, within the same region of cortex the abnormal representation of ipsilateral visual field is superimposed upon the normal representation of the contralateral visual field. Note that the connections from peripheral retina (beyond 20 degrees) are normal.
ric positions in the visual field: one located in the contralateral half of the visual field, as usual, and the other abnormally located in the ipsilateral hemi-field. Kaas and Guillery examined this by recording from areas 17 and 18 and found that, as in ordinary cats, vertical microelectrode penetrations entering the cortex near the anatomical 17-18 border first recorded from cells whose receptive fields were located at the vertical meridian (Kaas and Guillery, '73: fig. 3). When the electrode was advanced down the medial bank of the lateral gyrus into area 17, however, cells driven by the contralateral eye with receptive fields located abnormally in the ipsilateral visual field were encountered, but far more rarely than would have been expected. Thus they concluded that in Midwestern Siamese cats this abnormal input is usually suppressed at the cortical level.

In Boston Siamese cats, on the other hand, Hubel and Wiesel ('71) found that the geniculocortical projection undergoes a surprising rearrangement so that the abnormal geniculate laminae representing the ipsilateral visual field now project to their own strip of visual cortex which is separate but adjacent to the region receiving normal input from geniculate laminae representing the contralateral visual field (fig. 1B). In this case Hubel and Wiesel ('71) showed that the first cells recorded in vertical electrode penetrations entering the cortex near the anatomical 17-18 border were driven by the contralateral eye and had receptive fields within the ipsilateral visual field almost 20 degrees from the vertical meridian. As the electrode was advanced into area 17, the receptive-field positions of cells moved in an orderly progression towards the vertical meridian, then finally into the contralateral visual field. Figure 1B summarizes the general aspects of this organization. Thus in the Boston Siamese cat a continuous representation of visual field is preserved at the cortical level by inserting the extra representation of ipsilateral visual field between the normal contralateral representations in areas 17 and 18 in such a way that the anatomical 17-18 border now represents a region in the ipsilateral visual field located roughly 20 degrees from the vertical meridian. As a consequence, the representation of the vertical meridian is displaced from the border to positions within areas 17 and 18 proper.

In two of their Boston Siamese cats, Hubel and Wiesel ('71) found that in addition to a strip of cortex entirely devoted to the representation of the ipsilateral visual field a second feature of abnormal cortical organization was present. Within cortical regions concerned with the representation of the first 20 degrees or so of contralateral visual field, it was possible occasionally to record from groups of cells driven by the contralateral eye with receptive fields mirror-symmetrically placed in the ipsilateral visual field. Some cells even received simultaneous input from both the ipsilateral and contralateral visual fields. This pattern of projection, then, resembles what was found, also only occasionally, in the Midwestern variety.

Why more than one type of cortical organization exists (even in one cortex) is far from clear. Kaas and Guillery ('73) have suggested that some consistent anatomical difference in the organization of the lateral geniculate nucleus of Boston and Midwestern cats might account for the variation seen at the level of the visual cortex, and that the degree of squint could be a related factor. The aim of the present study was to examine these relationships directly in the same animal by injecting one eye of each Siamese cat with tritiated amino acids and using autoradiographic techniques to examine the distribution of retinogeniculate afferents. In addition, each cat was identified as Midwestern or Boston by making microelectrode recordings from the visual cortex.

METHODS

Six ordinary adult cats and 12 purebred adult Siamese cats were used (11 of these were from the same breeding colony). Most of the Siamese cats (8) were markedly cross-eyed when alert. Several others were
selected for study because they either showed no convergent squint, or even a mildly divergent one. After the animals were anaesthetized and paralyzed, the positions of the area centralis and optic disc in each eye were plotted on a tangent screen using a double-beam orthomicroscope (Hubel and Wiesel, ’59), and the angular separation between the two areas centrales was used as a measure of squint. Ten of the Siamese cats showed a convergent squint that ranged between 2 and 30 degrees. The remaining two cats showed 7 degrees and 35 degrees of divergent squint. In contrast, the eyes of three ordinary cats diverged by two-and-a-half to four degrees. This agrees well with the results of Hubel and Wiesel (’62) and of Bishop et al. (’62). Although in some Siamese cats the area centralis seemed clearly outlined, in others the fundus seemed abnormal and the areae centrales were not as clearly defined as in ordinary cats.

**Autoradiographic methods**

In all 12 Siamese cats, and in three ordinary cats, the vitreous of one eye was injected with 150-250 μCi ³H-Proline (New England Nuclear Corp., specific activity 37.3 Ci/mM; NET 323) in 100 μL 0.1 M phosphate buffer. The label was injected slowly through a 27 gauge 3/4 inch needle over a period of one half to one hour by an infusion pump (Harvard Apparatus). Animals were anesthetized with Ketamine HCl for this procedure.

Three days later, immediately following the conclusion of electrophysiological recordings, the animals were perfused with normal saline followed by 10% formol-saline. In most cases the lateral geniculate bodies were first separated from overlying visual cortex and then sectioned in the Horsley-Clarke plane at 15-20 μm. Sections were mounted on subbed slides, coated with Ilford K-2 or Kodak NTB2 emulsion, and exposed for six to eight weeks. After development in Kodak D-19, slides were lightly counterstained with thionin (Cowan et al., ’72; Hendrickson, ’72).

**Electrophysiological methods**

Ketamine HCl was used to facilitate insertion of an intravenous cannula. Thiopental sodium was administered intravenously to perform additional surgery and to maintain anaesthesia during the experiment. Animals were placed in a stereotaxic head-holder and eye muscles were paralyzed with a continuous infusion of succinylcholine, thus necessitating artificial respiration. Heart rate and CO₂ were monitored.

Techniques of stimulating and recording were similar to those of Hubel and Wiesel (’62). Pupils were dilated with atropine and corneas were protected with contact lenses of strength appropriate to focus the eyes on a tangent screen 57” away. The positions of the area centralis and optic disc in each eye were checked frequently during the course of an experiment.

Tungsten microelectrodes in a closed chamber (Hubel, ’57) were used to record single units from the visual cortex in all 12 eye-injected Siamese cats. Receptive fields were mapped using slits, edges, bars, and spots generated by a slide projector and, whenever possible, were classified as simple, complex, or hypercomplex according to the criteria of Hubel and Wiesel (’62, ’65). In a total of 21 penetrations made between Horsley-Clarke coordinates anterior 5.0 and 0.0, 446 cells were examined in detail. The primary aim in each penetration was to identify convincingly the extent of abnormal ipsilateral visual field represented in the visual cortex in order to classify each cat as either Midwestern or Boston. Eleven out of the 12 Siamese cats were of the Boston variety, the remaining cat being Midwestern.

Several electrolytic lesions (5-10 μA for 5-10 seconds) were made along the electrode track, and following perfusion blocks of visual cortex were either embedded in celloidin, cut at 26 μm, and stained with cresyl violet, or directly cut on the freezing microtome (30 μm) and stained with thionin. The Loyez stain for myelin was used to help locate the anatomical
17-18 border. Electrode tracks were reconstructed from serial sections.

RESULTS

The results are divided into three sections. Section I describes the similarities, as revealed by autoradiographic techniques, of organization in the lateral geniculate nucleus of the 11 Siamese cats classified as Boston on the basis of cortical physiology. As a preface to this section, examples of microelectrode recordings from the visual cortex of two Siamese cats are included to illustrate the determining characteristics of cortical organization in Boston Siamese cats. The remaining Siamese cat was classified Midwestern on the basis of cortical physiology and section II is devoted to a description of the particular characteristics which distinguished it from the Boston cats. Finally, in section III, the relationship of squint to organization in the LGN and visual cortex is examined briefly.

I. The Boston Siamese cats

Cortical recordings

A cortical penetration made in a typical Boston Siamese cat, 7D2, is shown in figure 2. The histological reconstruction of this electrode track is shown to the right. An
arrow indicates the approximate location of the anatomical 17-18 border as determined according to the criteria of Otsuka and Hassler ('62). In most of the Siamese cats used in this study the exact location of the 17-18 border as determined histologically seemed less distinct than usual, but was nevertheless in about the same position as in the ordinary cat. In the electrode track of figure 2, for example, the border was medially placed as expected for more anterior levels. In this Siamese cat, however, the representation of the vertical meridian did not coincide with the 17-18 border as it does in the ordinary cat (Hubel and Wiesel, '65), but instead with a cortical region located part way down the medial bank of the lateral gyrus. The 17-18 border, on the other hand, represented a region in the ipsilateral visual field roughly 22 degrees from the midline. In this Siamese cat there was no evidence of patches of cortex which received mirror-symmetric input from the ipsilateral visual field interspersed within cortical regions otherwise devoted to the representation of contralateral visual field. Since these characteristics of cortical organization are the same as those described in detail by Hubel and Wiesel ('71), it is reasonable to conclude that Siamese cat 7D2 is of the Boston variety.

A cortical area devoted exclusively to the representation of ipsilateral visual field was found inserted between the normal contralateral representation in areas 17 and 18 in 11 of the 12 Siamese cats studied. In five, including cats 6U5 (fig. 6) and 179 (fig. 9), cortical organization was remarkably similar to that of the cat just described. In particular, the amount of ipsilateral visual field represented at the cortical level was rather constant, ranging between 20 and 25 degrees. In four other Siamese cats, including cat 5R6 (fig. 8), another feature of cortical organization was present in addition to the insertion of ipsilateral visual field at the 17-18 border. An exam-

![Diagram](image)

Fig. 3 The first penetration in the right hemisphere of Siamese cat 5W1 at Horsley-Clarke level anterior 3.0 to demonstrate a slightly different pattern of cortical organization present in some Boston Siamese cats. Conventions as in figure 2. Just as in cat 7D2 the receptive fields of the first units (1-7) were located in the ipsilateral visual field as the electrode entered the cortex in area 18 near the 17-18 border. After the electrode passed through white matter and entered area 17, receptive fields moved out into the contralateral visual field in an orderly progression up to unit 12. However, background activity in the contralateral eye then shifted abruptly to a region located about 22 degrees into the ipsilateral visual field where unit 13 was recorded. When the electrode was withdrawn slightly to unit 14, receptive fields jumped back into the normal contralateral visual field. Next, readvancement of the electrode to units 15 and 16 confirmed that within the normal contralateral representation of visual field a mirror-symmetric patch of ipsilateral visual field was also present (as indicated by units 13, 15, 16). All units were driven by the contralateral eye with the exception of unit 16, which was driven only by the ipsilateral eye as indicated by the dashed lines.
ple of a penetration from one of the four, cat 5W1, is shown in figure 3. Just as in the cat of figure 2, the 17-18 border coincided with the representation of a region of the ipsilateral visual field located approximately 20 degrees from the midline (units 6 and 7). In addition, patches of input from the ipsilateral visual field in the contralateral eye (units 13, 15, 16) were interspersed within cortical regions otherwise devoted to the representation of the contralateral visual field (units 8-22). These patches were also seen in Siamese cat 5R6 and in its two littermates (5R2 and 5R5). The pattern of cortical organization exhibited in these four cats is virtually identical to that of two Siamese cats (see particularly kitten No. 7) studied by Hubel and Wiesel ('71). As shown in the Family Tree of figure 4, kitten 7 was a close relative of the cats used here. These cats also belonged to the Boston variety since the characteristic feature distinguishing them from Midwestern cats, namely the presence of a strip of cortex entirely devoted to an abnormal representation of ipsilateral visual field, could be demonstrated. On this basis, therefore, 11 of the 12 Siamese cats could be identified as members of the Boston variety.

**Autoradiography of the lateral geniculate nucleus**

Figure 5 is a schematic diagram showing the general aspects of laminar organization in the LGN of Siamese cats. The figure is based on results of Guillery ('69) and Guil- lery and Kaas ('71), who used fiber degeneration techniques following enucleation, and physiological recordings from the

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**Fig. 4** Family Tree to show how 11 of the 12 Siamese cats used in this study (indicated by asterisks) are interrelated. (Siamese cat 5R1 was not a member of this breeding colony.) In cats designated by numbers and letters, the first number followed by a letter refers to the litter, and the last number to the particular cat within the litter. Thus cats 151 and 120 were mated on two separate occasions and produced a 5A-litter and a 5R-litter.
LGN, to study abnormal LGN organization in what were presumably Midwestern Siamese cats. For simplicity in this diagram, connections between the C-laminae and the retinas have been omitted. As in the ordinary cat, lamina A receives afferents from the nasal retina of the contralateral eye. In Siamese cats, however, each eye also contributes extra misrouted fibers from what is presumed to be a strip of temporal retina representing the first 20 degrees or so of the ipsilateral visual field to lamina A1 of the contralateral (wrong) LGN. Thus lamina A1 is fragmented into at least three cell islands, each representing either the ipsilateral (normal) or contralateral (abnormal) eyes. Guillery termed the large medial island receiving aberrant input from the contralateral eye (fig. 5: stippled area) the abnormal segment of lamina A1 (abA1). The other two islands receive what remains of the normal input from the ipsilateral eye to lamina A1: the most lateral island, termed the lateral normal segment of lamina A1 (fig. 5: lnA1), receives the usual projection from peripheral regions of the temporal retina of the ipsilateral eye. The small medial island, the medial normal segment of lamina A1 (fig. 5: mnA1) receives a projection from a group of ganglion cells which apparently are spared the genetic defect and project ipsilaterally despite their more central location within the temporal retina.

In the present study autoradiographic techniques were used to reveal abnormal organization in the LGN of all 12 Siamese cats classified as Midwestern or Boston on the basis of cortical physiology. Since the overall pattern of LGN organization in these animals also conformed to that outlined above, the terminology of Guillery (‘69) and Guillery and Kaas (‘71) is adopted here. For example, figures 6C and D show autoradiographs of frontal sections through the midportion of the nucleus ipsilateral and contralateral to an intraocular injection of tritiated proline in a typical Boston Siamese cat (6U5). Comparable sections from an ordinary cat (Norm. 43) are included in figures 6A and B. In these and all subsequent darkfield photographs radioactively labeled retinogeniculate afferents appear bright white. For clarity, layers not receiving labeled afferents are delineated by dotted white lines drawn from the brightfield thionin-stained view of the same section. In the ordinary cat it is possible to divide the LGN into several discrete cell laminae from dorsal to ventral which Guillery has designated A, A1, C, C1, and C2. Hence, in figures 6A and B, layers A, C, and C2 receive afferents from the contralateral eye while layers A1 and C1 are innervated by the ipsilateral eye. These results agree with previous studies (Hayhow, ‘58; Laties and Sprague, ’66; Stone and Hansen, ’66; Garey and Powell, ’68; Guillery, ’70). In addition, it was possible to confirm a recent observation of Hickey and Guillery (’74) who, using similar autoradiographic techniques, were able to identify yet another lamina, C3, the ventralmost label-free lamina in figures 6A and B, which does not receive clear, direct input from either eye. Each retina also projects to a region immediately adjacent and medial to the LGN: the medial interlaminar nucleus (fig. 6A: MIN) (Laties and Sprague, ’66; Garey and Powell, ’68; Kinsman et al., ’69). Despite the absence of clear lamination within this nucleus, the two

Fig. 6. Autoradiographs of frontal sections from the lateral geniculate nucleus ipsilateral (A,C) and contralateral (B,D) to an injection of tritiated proline into the right eye of Normal cat 43 (A,B) and a typical Boston Siamese cat, 6U5 (C,D). Darkfield optics. In this and all subsequent darkfield photos, regions with radioactively labeled retinogeniculate terminals appear bright white. Dotted white lines delineate the structure of the unlabeled laminae which receive afferents from the un.injected left eye. Lines were drawn from the brightfield, nissl-stained view of the same section. Abbreviations: O.T., optic tract; abA1, abnormal segment of lamina A1; mnA1, medial normal segment of lamina A1; lnA1, lateral normal segment of lamina A1. In D, the most dorsal (upper) short arrow indicates the lateral normal segment of lamina C1, which is only faintly visible. The ventral short arrow indicates lamina C3 which is apparently unaffected by the genetic defect (compare figs. 6B and D). Also in D, the small interruption in labeling which runs vertically just medial to the lateral border of the abnormal segment of lamina A1 was due to injury of the retina during the eye injection. Calibration, 1 mm.
Figure 6
eyes are again restricted primarily to separate areas of termination (compare figs. 6A and B).

A comparison of autoradiographs of the LGN from Siamese cat 6U5 in figures 6C and D with those of Norm. 43 in figures 6A and B shows that in the Siamese cat, within each LGN, the number of terminals from the contralateral retina is greatly increased at the expense of the ipsilateral retina. For example, in figure 6D the LGN is almost entirely filled with labeled terminals from the contralateral (injected eye), while regions normally receiving afferents from the ipsilateral (uninjected) eye are drastically reduced to a few isolated label-free cell islands. The two largest islands are clearly visible in figure 6D and correspond to the lateral normal segment of lamina A1. Separating them is a region, also a part of lamina A1, which receives abnormal input from the contralateral eye and is therefore the abnormal segment of lamina A1.

A reduction of afferents from the ipsilateral retina likewise occurs in lamina C1 of the lateral geniculate nucleus (upper black arrow in fig. 6D). This diminution can be seen best in figure 6C, the LGN ipsilateral to the eye injection. As in the ordinary cat, lamina C1 is characteristically narrow and radioactively labeled afferents from the injected eye have a rather patchy distribution. In addition, in figure 6C only the most lateral portion of lamina C1 is present in the nucleus; it is therefore called the lateral normal segment of lamina C1. Although by analogy with the disruption in lamina A1 a medial normal segment might be expected in lamina C1 also, none was observed with one possible exception shown from Siamese cat WR1 in figure 10A (arrow). This finding is consistent with Guillery and Kaas' ('71) observation that the expression of the abnormality within the C-laminae is quite variable. The presence of such an abnormality nevertheless suggests that the genetic lesion affects all classes of retinal ganglion cells including W-cells which are known to project selectively to the C-laminae (Cleland et al., '75; Wilson and Stone, '75).

Only a small medial island of the ipsilateral retinogeniculate projection remains within the medial interlaminar nucleus, located at its ventromedial border as shown in figure 6C. In all of the Siamese cats studied here, the MIN and the medial normal segment of lamina A1 were closely associated: the medial normal segment was displaced ventromedially, away from the abnormal segment of lamina A1 and toward the lateral border of the MIN (figs. 6C, 8A,B, 9A). Hence it was often difficult to decide whether the medial normal segment indeed belonged to lamina A1, as suggested by Guillery ('69), or instead to the adjacent MIN. To clarify the question, progressive changes in shape of the medial normal segment of lamina A1 were examined in frontal sections taken at intervals throughout the rostrocaudal extent of the nucleus, as shown in figure 7. At extreme rostral levels only one cell island, designated A1 (stippled area), receives afferents from the ipsilateral (normal) eye (figs. 7A,B). Slightly further caudally, however, this single island evidently fragments into several smaller areas. Soon one of these can be recognized as the lateral normal segment of lamina A1 (fig. 7C). In figure 7D the medial normal segment emerges: here the fiber plexus surrounding both the medial and lateral normal segments of lamina A1 is continuous. It is therefore reasonable to suppose that the medial normal segment is itself derived from lamina A1 in a manner similar to the lateral normal segment.

As sections through the nucleus progress more caudally the medial normal segment shifts further medially, thus increasing its distance from the lateral normal segment (figs. 7E,F). Finally in the caudal extremity, the medial normal segment is quite close to the MIN (figs. 7G,H). The only exception to this pattern was the one Siamese cat, 6C2, identified as Midwestern on the basis of cortical physiology. As shown in figure 13A, the medial normal segment was much larger and extended laterally until it almost joined the lateral normal segment of lamina A1, thus lending further support to the notion that (at least in this instance) it
Fig. 7 Diagram to show the distribution of labeled terminals in a series of frontal sections taken from the LGN of Siamese cat 6U5. The sections A-H run rostral to caudal and in each diagram medial is to the left. Regions receiving afferents from the ipsilateral eye are indicated by stippling. Arrows mark the medial normal segment of lamina A1 in each section, with two exceptions: in A, it points to the tail of label which streams medially and dorsally from the medial interlaminar nucleus (MIN) in sections A-F and is presumably associated with the lateral pulvinar. In H, the most dorsal (upper) arrow points to a region belonging to the lateral normal segment of A1. Abbreviation in H: O.D., optic discontinuity. Note that medially lamina A and the abnormal segment of A1 are fused in all sections. Section F is identical to figure 6D.
was indeed a part of lamina A1 rather than the MIN.

Although the shape and size of the medial and lateral normal segments of lamina A1 varied throughout the anteroposterior extent of the LGN as shown in figure 7, there was surprising uniformity when frontal sections taken from a fixed anteroposterior level (approximately Horsley-Clarke Anterior 6.6) were compared among the Boston Siamese cats. For example, figures 8A and B show autoradiographs of frontal sections through the LGN of two other Boston Siamese cats (7D2 and 5R6). Compared with figures 6D and 7F, there was no significant difference in the size and shape of the ipsilateral retinogeniculate projection to lamina A1, and only a slight variation in the size and medial extent of lamina C1. (These similarities are perhaps surprising in view of the slight differences in cortical physiology of these particular cats, as reported in the preceding section.)

Another feature common to the Boston Siamese cats studied here was the definite cellular continuity and absence of a clear interlaminar plexus between the medial borders of lamina A and the abnormal segment of lamina A1. In autoradiographs of the nucleus contralateral to the injected eye (figs. 6D, 9A) this fusion of lamina A and the abnormal segment of A1 can be seen directly. The entire dorsomedial region of the LGN forms a uniform sea of label in which the medial normal segment of lamina A1 sits as an island. Figure 8C, a brightfield cresyl violet-stained section taken immediately adjacent to the autoradiograph of figure 8A, and figure 9B adjacent to 9A, confirmed that the observed fusions were indeed real fusions of the cytoarchitectonically defined laminae and not simply due to accidental distribution of radioactive label over the interlaminar plexus which, in the ordinary cat, typically separates lamina A from A1 as shown in figure 8D. The relative lack of radioactive label over the interlaminar plexus is consistent with the notion that most of the label arrives at the LGN in the rapid phase of axoplasmic transport and is therefore distributed primarily within axon terminals (Hendrickson, '72).

Although the fusion between the medial part of lamina A and the abnormal segment of lamina A1 is most evident in sections taken through the midportion of the nucleus, it is also commonly present throughout the anterior two-thirds of the LGN as shown in figures 7A to G. In posterior sections such as that of figure 7H, however, layer A itself is interrupted due to the representation of the optic disc (Guillery and Kaas, '71). This interruption, plus the extreme curvature of the cell laminae, makes it difficult to interpret the relationship between the medial regions of lamina A and the abnormal segment of A1. Nevertheless, it seems likely that the fusion persists well into the posterior third of the nucleus.

Often not only the medial region of lamina A but also a corresponding region at the medial tip of lamina C appeared to fuse with a small overlying part of the abnormal segment of lamina A1. This particular fusion can be seen best in figure 9B, and it is also present in figures 6C and D and 8C. In contrast, there was never any indication of fusion between the most lateral portion of the abnormal segment of lamina A1 and laminae A and C, again with the possible

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Fig. 8  A, B. Darkfield autoradiographs of frontal sections from the LGN ipsilateral to an eye injection in two other Boston Siamese cats, 7D2 and 5R6, to show the similarities in size and shape of the lateral and medial normal segments of lamina A1 despite the differences seen at the level of the visual cortex, and in the degrees of squint in these animals. (7D2 was 7 degrees divergent and 5R6 was 10 degrees convergent.) Compare also with figures 6C and D. Arrow in A indicates the lateral normal segment of lamina C1. C. Brightfield photo of the same section as in A. Nissl stain. Large arrow indicates the medial normal segment of lamina A1. Small arrows indicate the lateral normal segment of A1. Note the clear fusion between the medial portion of lamina A and the abnormal segment of A1, and the separation of the lateral border of the abnormal segment from the adjacent region of lamina A. D. Brightfield photo of the LGN of a normal cat. Cresyl violet stain. Compare the obvious separation between laminae A and A1 medially with figures 8C and 9B. Calibration, 1 mm.
exception of the Midwestern Siamese cat. Indeed, throughout the anterior two-thirds of the nucleus the separation between the lateral edge of the abnormal segment from overlying regions of lamina A was remarkably distinct (figs. 6C, 7A-G, 8C, 9A,B).

Although the fusion between lamina A and the abnormal segment of lamina A1 may be related to the size of the medial normal segment (DISCUSSION), it did not appear to be affected by the size of the lateral normal segment of lamina A1. In cat WR1, the one Boston Siamese not a member of our breeding colony, the fusion persisted despite the presence of a lateral normal segment twice as large as the average (fig. 10, table 1). The small increase in the size of the medial normal segment is hardly significant. On the other hand, the increase in size of the lateral normal segment of A1 in cat WR1 occurs at the expense of the abnormal segment as seen in the shortening of the mediolateral extent of the abnormal segment in figures 10A and B. Since the abnormal segment receives its input from that part of the contralateral retina representing the first 20 degrees of the ipsilateral visual field (fig. 5; Guillery and Kaas, '71), one consequence of this shortening should be to diminish the extent of the representation of ipsilateral visual field. In Boston Siamese cat WR1, this expectation was fulfilled at the level of the visual cortex. An electrode penetration traversing the 17-18 border recorded receptive fields within the ipsilateral visual field as expected, but they did not progress beyond about ten degrees from the vertical meridian.

It seemed reasonable to expect that some systematic relationship between the size of the lateral normal segment of lamina A1 and the amount of ipsilateral visual field represented at the cortical level should hold not only for cat WR1, but for all Siamese cats studied here. To examine this possibility, the cross-sectional area of the lateral normal segment was measured in a representative frontal section through the midportion of the nucleus (at approximately Horsley-Clark anterior 6.5) in each Siamese cat. These areas were expressed as a percentage of the total cross-sectional LGN area to facilitate comparison among cats. Finally, the percentage cross-sectional area of the lateral normal segment was plotted against the extent of ipsilateral visual field represented in the visual cortex as determined from physiological recordings in each cat. In figure 11 the results show the expected trend: the
Fig. 10 Darkfield autoradiographs of frontal sections through the LGN ipsilateral (A) and contralateral (B) to an eye injection in a Boston Siamese cat in which the details of LGN organization differed somewhat from figures 6 to 9. Note the large size of the lateral normal segment and consequent decrease in the size of the abnormal segment of lamina A1. The arrow in A indicates a likely candidate for the medial normal segment of lamina C1. This particular Boston cat was not a member of our breeding colony. Calibration, 1 mm.

Fig. 11 A plot of the area of the lateral normal segment of lamina A1 against the extent of ipsilateral visual field represented in the visual cortex as determined from physiological recordings to show that there is a rough correlation between the two variables (correlation coefficient = -0.72). The cross-sectional area of the lateral normal segment was measured in a representative frontal section through the LGN and expressed as a percentage of the total LGN cross-sectional area in each cat. Line drawn is the regression line. Code of letters and numbers beside each point refers to each cat.

larger the area of the lateral normal segment, the smaller the amount of ipsilateral visual field represented in the visual cortex. The correlation coefficient was -0.72, not unacceptable in view of the crudity of measurements here, and the small sample. A similar loose correlation might also be expected between the area of the medial normal segment of A1 and the amount of ipsilateral visual field, since the areas of the two segments were roughly interrelated. Indeed, the area of the medial normal segment was found to increase concurrent with a decrease in the amount of ipsilateral visual field represented in the visual cortex in almost exactly the same fashion as above; the correlation coefficient was also about the same: -0.74.

II. The Midwestern Siamese cat

Cortical recordings

In one of the 12 Siamese cats, 6C2 (disconcertingly enough, a member of our own breeding colony, as shown in fig. 4), organization at the cortical level was clearly not of the Boston variety. In figure 12 the location of four electrode penetrations made in the right hemisphere are shown with respect to the anatomical 17-18 border (dashed line). A fifth penetration was made
in the left hemisphere. The left-hand side of the figure shows the receptive-field positions of the first units encountered in each penetration. In the second penetration, the electrode entered the visual cortex in area 17 almost directly adjacent to the border, yet receptive fields were located close to the vertical meridian slightly within the contralateral visual field. As the electrode was advanced down the medial bank of the lateral gyrus, receptive fields moved progressively further out into the contralateral visual field with no hint of a mirror-like representation within the ipsilateral visual field. Next, the electrode was withdrawn and moved one millimeter further lateral for the third penetration, so that it entered the cortex in area 18, just lateral to the border. Again the first receptive fields were right at the vertical meridian, and when the electrode was advanced, thus traversing the border, they moved out into the contralateral visual field as before. The first few receptive fields may have extended slightly into the ipsilateral visual field, but were always within the two or three degrees associated with the error in locating the area centralis, with the normal functioning of the corpus callosum (Berlucchi et al., '67) and with the usual naso-temporal overlap in the retinogeniculate projection (Stone and Hansen, '66; Sanderson, '71).

The general pattern of cortical organization in this Siamese cat clearly conformed to the Midwestern pattern on the basis of these experiments, since a cortical region exclusively devoted to the representation of ipsilateral visual field was not present. Even within the normal representation of contralateral visual field, however, there was no hint of mirror-like patches of ipsilateral visual field representation. This was somewhat unexpected, but is consistent with Kaas and Guillery's ('73) description of Midwestern cats in which they too only rarely encountered such patches. Thus, the only feature with distinguished
The size of the ipsilateral retinogeniculate projections to lamina A1 compared among the Siamese cats studied here

<table>
<thead>
<tr>
<th></th>
<th>% area lateral normal segment</th>
<th>% area medial normal segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average (10 Boston Siamese cats)</td>
<td>5.22% ± 1.21%</td>
<td>1.35% ± 0.46%</td>
</tr>
<tr>
<td>WR1 (Boston) 1</td>
<td>10.23%</td>
<td>2.37%</td>
</tr>
<tr>
<td>6C2 (Midwestern)</td>
<td>11.27%</td>
<td>4.38%</td>
</tr>
</tbody>
</table>

The cross-sectional areas of the lateral and medial normal segments were measured in a frontal section through the mid-portion of the LGN (Horsley-Clarke anterior 6.5) in each cat and expressed as a percentage of the total cross-sectional LGN area.

1 This Siamese cat was not a member of our breeding colony.

this Midwestern cat from normal cats was the absence of any significant input from the ipsilateral eye.

Autoradiography of the lateral geniculate nucleus

As compared with the Boston cats, clear and consistent differences in the size and shape of the projection from the ipsilateral retina to lamina A1 were evident in Midwestern cat 6C2, as shown in figure 13. The medial normal segment of lamina A1 was unmistakably wider and in some regions of the nucleus it extended laterally until it almost joined the medial edge of the lateral normal segment, which was also somewhat enlarged. As before, these trends could be roughly quantified by measuring the percentage cross-sectional area of the lateral and medial normal segments and comparing them with the average values for all other Siamese cats. The results of table 1 show that in cat 6C2 the medial normal segment was almost four times larger than average, the lateral normal segment was about two times larger, and both of these size increases were well outside the variation seen among the ten other cats.

Another distinguishing feature of LGN organization in the Midwestern cat was the presence of a clear discontinuity between lamina A and the abnormal segment of lamina A1. This can be seen best in figure 13C, a brightfield photograph of the section of figure 13A. The abnormal segment of lamina A1 (arrows) lies directly dorsal to the unusually large medial normal segment of lamina A1, and is separated from overlying lamina A by a fiber plexus. (The abnormal segment itself may be fragmented into two islands, one of which lies medial to the other.) Perhaps the unusually large size of the medial normal segment of lamina A1 is related to the lack of cellular continuity between lamina A and the abnormal segment of lamina A1. This possibility will be considered in more detail in the DISCUSSION.

III. The relationship to squint

Of the 12 Siamese cats used in this study, the only cat with a cortical organization of the Midwestern type was 6C2. This cat also showed almost no squint (2 degrees convergent), suggesting that the extent of ipsilateral visual field represented in the visual cortex of Siamese cats might vary with the amount of squint. No clear correlation was found, however, in figure 14, when squint was plotted against the extent of the ipsilateral visual field representation (as determined from physiological recordings) for each cat. Both the correlation coefficient (r = 0.37) and the slope of the regression line (0.23) indicate that cats with a given representation of ipsilateral visual field may show considerable variation in the degree of squint.

Squint was also not correlated with any systematic variation in organization in the LGN. For instance, figures 9A and B show the LGN of Boston Siamese cat 179 contralateral to an eye injection. This cat was most strabismic of all (30 degrees con-
Fig. 13 To show the LGN organization in the Midwestern Siamese cat, 6C2. A, B. Darkfield autoradiographs of frontal sections ipsilateral (A) and contralateral (B) to the eye injection. Note the large size of both the medial and lateral normal segments of lamina A1. Calibration, 1 mm. C. Brightfield photograph of 13A to show directly the lamination pattern in a frontal section through the LGN. Nissl stain. Arrows point to the abnormal segment of lamina A1, which appears to be fragmented into two cell islands. Note particularly the discontinuity between the medial border of lamina A and the abnormal segment of lamina A1. Immediately ventral to the abnormal segment are the lateral and medial normal segments of lamina A1.
To obtain a rough correlation between the degree of squint and LGN organization, the cross-sectional areas of both the medial and lateral normal segments of lamina A1 were measured as before, and plotted against the degree of squint. For example, figure 15 shows such a plot for the medial normal segment. The solid line is the regression line. Despite the uniformity in the size of the medial normal segment (again with the exception of Midwestern cat 6C2), squint varied widely. There was consequently no clear correlation between the two variables (correlation coefficient = -0.40). There was also no correlation when the cross-sectional area of the lateral normal segment was plotted against squint. These results, taken together with the finding that there was also no correlation between squint and the extent of ipsilateral visual field represented in the visual cortex, suggest that squint, at least as measured in the anaesthetized, paralyzed animal, is not a reliable index of the abnormality either at the level of the LGN or visual cortex. Nor is the role of the neural abnormality in the etiology of squint evident, particularly since only ten of the 12 Siamese cats studied here had convergent squint, as has been commonly reported by other investigators (Hubel and Wiesel, '71; Berman and Cynader, '72; Kaas and Guillery, '73). The remaining two Siamese cats (7D1 and 7D2) had clear divergent squints, and one of the two (7D1) was obviously divergent when awake.

**DISCUSSION**

**Organization of the visual cortex in Boston and Midwestern cats**

This study has confirmed the existence of two types of Siamese cat, Boston and Midwestern, which differ from each other not only in their cortical physiology, as previously reported (Hubel and Wiesel, '71; Kaas and Guillery, '73), but also in the details of organization within the lateral geniculate nucleus. Microelectrode recordings from the visual cortex were used to identify 11 of the 12 Siamese cats...
studied here as members of the Boston variety since, as first described by Hubel and Wiesel ('71), a strip of visual cortex exclusively devoted to an abnormal but systematic representation of the first 20 degrees or so of ipsilateral visual field was present. In addition, in four of the 11 Boston cats, small infrequent patches of cortex which apparently received abnormal input from the ipsilateral visual field were found interspersed within the normal representation of the contralateral visual field. Cortical organization in these four cats was therefore similar to that of two Siamese cats described by Hubel and Wiesel ('71) and it is remarkable that in all six animals these mirror-like patches were encountered within cortical layers IV-VI only. A more extensive search of visual cortex concerned with the normal representation of contralateral visual fields in the other Boston Siamese cats might have revealed similar patches, especially if the search focused on the deeper cortical layers. Thus the presence of such patches may be characteristic of all Boston Siamese cats.

Since it is possible to find these patches also in the visual cortex of some Midwestern Siamese cats (Kaas and Guillery, '73), it is worth emphasizing that the major feature which distinguishes the two varieties of Siamese cat is the presence of a strip of cortex exclusively devoted to the representation of ipsilateral visual field in Boston cats. On this basis, the one remaining Siamese cat (6C2) studied here was classified as Midwestern.

**Organization of the LGN in the two varieties of Siamese cat**

At the level of the lateral geniculate nucleus, the details of organization as revealed here using autoradiographic techniques also differed significantly between Boston and Midwestern Siamese cats. In all 11 Boston Siamese cats, the medial normal segment of lamina A1 was distinctly smaller than either in the one Midwestern cat of this study (table 1) or in most of the Midwestern Siamese cats discussed by Guillery and Kaas ('69,'71). Indeed, without the help of autoradiography, it would have been virtually impossible to identify the medial normal segment of lamina A1. This difficulty was the reason why Kaas and Guillery ('73) did not identify the medial normal segment of lamina A1 in the one Siamese cat (cat 72-290: figs. 13-16) which they classified as Boston on the basis of the pattern of retrograde cell degeneration in the LGN following lesions of the visual cortex. From this particular cat they proposed that the medial normal segment of lamina A1 might be absent or extremely small if present in Boston Siamese cats. The present results suggest that it is simply very small.

The presence of the medial normal segment is in itself rather mystifying since it implies that some fibers from the ipsilateral eye which originate within the strip of temporal retina otherwise responsible for the misrouted retinogeniculate projection are spared the genetic defect and instead project to the correct LGN (fig. 5). From microelectrode recordings from the medial normal segment, Guillery and Kaas ('71) inferred that the sparing is probably restricted to a zone of temporal retina representing roughly the first two degrees of contralateral visual field. This particular zone may therefore give rise to a bilateral retinogeniculate projection. In the ordinary cat, a similar zone is responsible in part for establishing the central one degree of nasotemporal overlap in the LGN (Stone and Hansen, '66; Sanderson, '71). If a separate genetic program were required for a bilateral projection from this zone, then the class of ganglion cells located there might be spared the genetic defect in Siamese cats and consequently their retinogeniculate projection would produce the medial normal segment. Such an explanation, however, implies that the degree of sparing (and hence the size of the medial normal segment) should be relatively constant from one Siamese cat to the next, and it therefore cannot account adequately for
the distinct difference in size of the medial normal segment in Boston and Midwestern Siamese cats studied here.

How this distinct size difference arises is also unknown, and before further speculation the question of whether or not the variation in size of the medial normal segment is continuous must be decided. Table 1 suggests that the tendency if anything is toward two distinct groups: the 11 Boston cats on the one hand and the one Midwestern on the other. In this context it would be useful to know where the Midwestern cats studied by Guillery et al. ('71, '73) fall in relation to the measurements of Table I. Evidence supporting the existence of a projection from the medial normal segment of lamina A1 to the visual cortex is also rather sparse. In the present study, in agreement with Hubel and Wiesel ('71), there was no evidence for a representation in the ipsilateral eye of the first two degrees or so of contralateral visual field, although this would be expected if the medial normal segment were to project to the visual cortex. This finding was especially surprising in the one Midwestern Siamese cat, in which the medial normal segment as revealed by autoradiographic techniques was very large (fig. 13). Kaas and Guillery ('73) were able to obtain some evidence for a geniculocortical projection from the medial normal segment by examining retrograde cell degeneration in the LGN following lesions of areas 17 and 18. In at least one Siamese cat they were able to show that the medial normal segment underwent degenerative changes (see their fig. 10). Further, they recorded from three cortical units driven by the ipsilateral eye whose receptive fields were located within the first ten degrees of the contralateral visual field. The lack of physiological evidence for a projection from the medial normal segment in Boston cats could, naturally, be due to its extremely small size, but this would hardly be true in Midwestern cats such as 6C2. Instead it is possible that much of the projection from the medial normal segment is suppressed at the cortical level in a manner similar to that proposed by Kaas and Guillery ('73) for the abnormal segment projection in Midwestern cats.

Perhaps the most striking feature which characterized the organization of the LGN of Boston Siamese cats was the clear fusion between the medial borders of lamina A and the abnormal segment of lamina A1 (figs. 6-9). There was no evidence of similar fusions in the LGN of the one Midwestern Siamese cat studied here (fig. 13); indeed, the medial borders of the two laminae were clearly separated by an interlaminar plexus.

It is possible that the differences in the degree of fusion seen between laminae in the medial portions of the LGN of Boston and Midwestern Siamese cats are simply an indication of the extent to which the representation of visual field in the contralateral eye is continuous within lamina A and the abnormal segment of lamina A1. Certainly the arrangement of lamina A in the ordinary cat is a good precedent for such fusions according to the representation of visual fields or their absence. For example, in LGN layers innervated by the contralateral eye such as lamina A allowance is made for the retinal blind spot by interrupting the cellular continuity of lamina A at the position corresponding to its representation (Guillery and Kaas, '71; Kaas et al., '73). The grouping of cells in each LGN lamina therefore is accurately related to its retinal input and hence to equivalent positions within the visual field. Accordingly, in Midwestern Siamese cats, the absence of fusion between the medial edge of lamina A and the abnormal segment of A1 might indicate that the representation of visual field near the vertical meridian is not continuous, while the clear fusion in Boston cats could reflect a continuous, or nearly continuous, representation in the contralateral eye.

In Boston Siamese cats recordings from the visual cortex favor the hypothesis that the fusion between lamina A and the ab-
normal segment of lamina A1 reflects a continuous representation of visual field. In several (6) fortuitous microelectrode penetrations, one of which was shown in figure 2, the electrode remained entirely within grey matter during its traverse down the medial bank of the lateral gyrus. In those experiments, receptive fields in the contralateral eye progressed without any obvious interruptions in the representation from the ipsilateral visual field, towards the vertical meridian, and finally into the contralateral visual field. Two similar penetrations from Hubel and Wiesel ('71) support this observation. It seems quite likely, therefore, that the representation of visual field is continuous (or nearly so) in Boston Siamese cats. This continuity may not exist in Midwestern Siamese cats however, In figure 6 of Kaas and Guillery ('73) there is the suggestion that the first three degrees of the ipsilateral visual field in the contralateral eye may be somewhat underrepresented in the visual cortex, thus lending further support to the above hypothesis.

Relationship between the fusions and the size of the medial normal segment

If continuity across the midline and into the ipsilateral visual field is to be preserved and expressed at the level of the LGN as a fusion between lamina A and the abnormal segment of lamina A1, then most, if not all, retinogeniculate fibers originating within the abnormal strip of temporal retina representing the first 20 degrees of ipsilateral visual field in each eye might be expected to cross aberrantly in the chiasm. But some fibers from the strip, in particular those concerned with the representation of visual field within two degrees of the midline, in fact, remain uncrossed and are responsible for establishing the medial normal segment of lamina A1 (Guillery and Kaas, '71). One might imagine therefore that the size of the medial normal segment simply reflects the number of correctly routed fibers. The correct routing of fibers concerned with a midline representation of visual field, however, could only occur at the expense of the abnormal segment of lamina A1 (assuming that the total number of fibers from this area of temporal retina is more or less constant) and would consequently lead to an interruption in the representation of visual field in the contralateral eye. Such an interruption is likely in Midwestern Siamese cats, as mentioned earlier, and consistent with it is the presence of a large medial normal segment in these animals. Similarly, the extremely small size of the medial normal segment of lamina A1 and its shifted position within the LGN in Boston Siamese cats is also consistent with the notion that the representation of visual field in the contralateral eye is continuous, as first proposed by Kaas and Guillery ('73), and that the fusion between lamina A and the abnormal segment of A1 is a reflection of that continuity.

Relationship between organization in the LGN and visual cortex

It may be that during development, the characteristic differences in the organization of the LGN are directly responsible for producing a visual cortex of the Boston or Midwestern variety. If so, one crucial factor could be the degree of fusion between lamina A and the abnormal segment of lamina A1. In Siamese cats in which the representation of visual field in the contralateral eye is continuous within the LGN, it is possible that not only all of lamina A, but also most of the abnormal segment of A1 fused to it act as one complete “lamina” during development and project, as described by Hubel and Wiesel ('71), in fixed topographic order thus producing a visual cortex of the Boston variety (see also Gaze and Keating, '72). The gap between the medial borders of lamina A and A1 in Midwestern cats, on the other hand, could act as a signal for cells in corresponding regions of the adjacent laminae to project to the same cortical region, creating a Midwestern cortex as a consequence. (Similar considerations would apply to nor-
nogeniculate afferents themselves could have to be established first within the LGN. The pattern, in turn, would dictate the manner in which cells of the LGN then projected to the visual cortex. Retinogeniculate neurones of the cat. Brain Res., 91: 306-310.


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