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"General Organization of Callosal Connections in the Cerebral Cortex"

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These are preliminary lecture notes, intended only for distribution to participants.

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General Organization of Callosal Connections in the Cerebral Cortex

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1. Introduction

The necessity of interhemispheric connections, and the nature of this necessity, are demonstrated by the following hypothetical event. An intelligent being from outer space lands on earth and is asked to design the brain of a cat. The being is intrigued to find that the body of a cat is bilaterally symmetric (he looks himself rather like a multieyed and multiwhiskered octopus).

After some deliberation, the being produces the following solution: the cat is given a bilaterally symmetric brain and different elements of each half brain are connected in a discrete, and more or less direct manner to different sensory and motor organs of the ipsilateral half body. For the integrated functioning of the whole, connections between different elements of the same hemisphere and similar connections between elements of different hemispheres are created.

A teleological approach may be useful to organize the quickly expanding knowledge on the organization of callosal connections of various mammals into a coherent picture, to place this picture into a broader framework of brain organization, and to generate hypotheses for future work. The teleological temptations become strongest when we consider the development of callosal connec-

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tions and try to justify that seemingly extravagant wastefulness. To these temptations I have succumbed consciously only once (Section 8).

This review is essentially restricted to aspects of callosal organization which have emerged over the last 12 years, especially from the use of new techniques for tracing connections. The excellent reviews of Berlucchi (1972, 1981), Doty and Negrao (1973), Gazzaniga and Ledoux (1978), Elberger (1982), as well as the papers on cerebral commissures, collected by Steele Russel *et al.* (1979), can complement several aspects of this work.

2. The Callosal Neurons

It has been possible to positively identify neurons projecting into the corpus callosum (callosal neurons) only since the introduction of retrograde transport methods for tracing neural connections. Identification of callosal neurons was, however, also tried, with modest results, by studying the consequences of transecting their axons (Pines and Maiman, 1939). With this approach, the large pyramids in layer III at the 17/18 border were recognized as a source of callosal axons in the monkey (Glickstein and Whitteridge, 1976), because these neurons seemed to disappear following callosal transection. They are also absent in human brains with agenesis of the corpus callosum (Shoumura *et al.*, 1975). The effect may, however, not be due to degeneration of the callosal neurons, but to shrinkage of their perikarya. Adult callosal neurons, or at least some of them, seem not to degenerate following transection of their axons since Asanuma and Okamoto (1959) and Clare *et al.* (1961) could record antidromic responses to the stimulation of the proximal stump of callosal axons severed several weeks earlier. And in normal development, and experimentally induced agenesis, many juvenile callosal neurons lose their callosal axons without degenerating (see Section 7).

Callosal neurons have now been studied with the retrograde tracer horseradish peroxidase (HRP), alone or bound to wheat-germ agglutinin (WGA), or with fluorescent tracers, in several species and areas (Table I).

2.1. Radial Distribution

As a general rule, in the anatomical studies, the largest fraction of callosal neurons has been found in layer III (Table I, Fig. 1). Callosal neurons, identified electrophysiologically by antidromic activation in the visual areas of the cat (Toyama *et al.*, 1974; Innocenti, 1980; Harvey, 1980) or of the rabbit (Swadlow and Weyand, 1981), and in somatosensory cortex of the cat (Miller, 1975), have also been preferentially found in layer III. Other layers also contribute to the corpus callosum, but differently, depending on the species and the area. For example, the second largest fraction of callosal neurons seems to be in layer V in rodents, and in layer VI in cats. Infragranular callosal neurons have been inconsistently found in the monkey, in either layer (Table I; see Jones, this volume). The

Table I. Radial Distribution and Morphology of Callosal Neurons

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Species	Method[a]	Area[b]		Layers[c]	Neuron type[d]	Authors
		Injected	Studied			
Rat	HRP/DAB	Motor, primary-sensory, association-sensory, auditory, primary-visual, association-visual, cingulate (29b, 29c, 23)	Motor, sensory-association, auditory	II, III, IV, V, VI	—	Jacobson and Trojanowski (1974)
Mouse	HRP/DAB	3/4/6 3, 18a, 17/18a/18b	—	II, III, IV, V, VI I (only in 29b)	SPy (II); MPy, LPy (III–V); Pl (VI)	Yorke and Caviness (1975)
	HRP/DAB-Co	MI	MI	III (20%), V (70%), VI	—	Porter and White (1983)
Rat	HRP/DAB	SI	SI	II, III, IV, V, VI	Py	Wise (1975)
	HRP/DAB	SI	SI	II, III, IV, V, VI (upper)	SPy, MPy	Wise and Jones (1976)
Mouse	HRP/DAB	PMBSF (SI)	PMBSF (SI)	II, III (75%), V (15%)	—	White and DeAmicis (1977)
Rat	HRP/TMB	Parietal	Parietal	II, III, IV, Va, Vb, Vc, VI (upper)	Py, Pl (VI)	Ivy *et al.* (1979) Ivy and Killackey (1981)
	TB	Parietal	Parietal	II, III, IV, V, VI	—	O'Leary *et al.* (1981)
Hamster	HRP/DAB	Auditory	Auditory	II, III, IV, V	Py	Ravizza *et al.* (1976)
	HRP/DAB	17/18a/18b	17, 18a, 18b	II, III, IV, V, VI	MPy	Dürsteler *et al.* (1979)
	HRP/TMB	17/18a/18b	17/18a	III, V, VI	—	Rhoades and Dellacroce (1980a)
Rat	HRP/TMB	Cingulate	29d 24b	II, III, V, VI II, III, V, VI	—	Vogt *et al.* (1981)

(continued)

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Table I. (*continued*)

Species	Method[a]	Area[b] Injected	Area[b] Studied	Layers[c]	Neuron type[d]	Authors
Rabbit (Dutch belted)	HRP/TMB, Electrophysiology	VI/VII	VI/VII	II, III, IV, V	SPy, MPy	Swadlow *et al.* (1978), Swadlow and Weyand (1981)
	HRP/TMB	17/18	17/18a	II, III, IV, V	—	Chow *et al.* (1981)
Cat	HRP/DAB	Frontal, suprasylvian–ectosylvian	—	II, III, IV, V, VI	—	Jacobson and Trojanowski (1974)
	HRP/DAB, TMB	SI	SI	II, III, IV, V, VI	—	McKenna *et al.* (1981)
	HRP/DAB	SI, SII	SI, SII	II, III, IV, V, VI	SPy, MPy, LPy, Pl (VI)	Caminiti *et al.* (1979)
	HRP/DAB	AI	AI	III, IV, V, VI	Py, Pl	Imig and Brugge (1978)
	HRP/DAB, TMB	AI	AI	III, IV, V, VI	—	Kelly and Wong (1981)
	HRP-WGA/DAB, PDC, TMB	AI	AI	III (71%), V–VI (29%)	Py, N-Py	Code and Winer (1983)
	HRP/DAB, ODN	Lateral gyrus (17, 18, 19)	17, 18	II, III, IV, V, VI	SPy, MPy, LPy, St, Pl (VI)	Innocenti and Fiore (1976), Innocenti (1980)
	HRP/DAB	Lateral gyrus (17, 18, 19)	17/18	III, IV, VI	Py, St	Hornung and Garey (1980, 1981)
	HRP/DAB	17/18	17	II–III, VI	Py, St, Pl (VI)	Shatz (1977b)
			18	II, III, IVa, VI		
			19	III, V, VI		
			LS	III, V, VI		
	HRP/DAB	Lateral gyrus (17, 18, 19)	17/18, 19	II, III, IV, V, VI	Py, St, Pl	Sanides and Donate-Oliver (1978)
			LS	III, VI		
	HRP/ODN	CC	17, 18	II, III, IV, V	Py, St, Pl	Segraves and Rosenquist (1982a,b)
			19	III, IV, V, VI		
			LS	III, IV, V, VI	Py, Pl	
	HRP/DAB	Middle suprasylvian	LS	III (+ deeper layers)		Maciewicz (1974)
	HRP/DAB, ODN	Lateral gyrus (17, 18, 19)	LS	II, III, IV, V, VI	Py, Pl (VI)	Keller and Innocenti (1981)
	HRP/DAB, DAB-	LS	LS	II, III, IV, V, VI	SPy, MPy, LPy	Keller and Innocenti (1981)

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	HRP/DAB	Middle suprasylvian	LS	III (+ deeper layers)		Maciewicz (1974)
	HRP/DAB, ODN	Lateral gyrus (17, 18, 19)	LS	II, III, IV, V, $\underline{\text{VI}}$	Py, Pl (VI)	Keller and Innocenti (1981)
	HRP/DAB, DAB-Co, ODN, TMB	LS	LS	II, $\underline{\text{III}}$, IV, V, VI	SPy, MPy, LPy	Keller and Innocenti (1981)
	HRP/DAB, ODN	CC	LS	II, $\underline{\text{III}}$, IV, V, VI	SPy, MPy, LPy, Pl (VI)	Keller and Innocenti (1981)
Rhesus	HRP/DAB	Arcuate sulcus	Arcuate sulcus	II, $\underline{\text{III}}$, IV, $\underline{\text{V}}$, VI	—	Jacobson and Trojanowski (1974)
	HRP/DAB	Prefrontal	Homo- and heterotopic	II, IIIa, $\underline{\text{IIIb}}$, V, VI	—	Jacobson and Trojanowski (1977)
	HRP/DAB, TMB, PDC	SI	3, 1, 2	$\underline{\text{IIIb}}$, VI	LPy	Jones *et al.* (1975, 1979), Jones and Wise (1977)
Aotus, Macaca fascicularis	HRP/TMB, DAB-GO, BDHC	Precentral/ postcentral	3b, 1, 2	$\underline{\text{III}}$ (deep), IV, V, VI	Py	Killackey *et al.* (1983a)
Rhesus	HRP/DAB	Inf. parietal lobule	Homo- and heterotopic	II, $\underline{\text{III}}$, IV, V, VI similar to above	MPy, LPy, Pl	Hedreen and Yin (1981)
Macaca nemestrina or *fascicularis*	HRP, HRP-WGA/ TMB	Sup. parietal lobule	Homotopic	IIIb, VI	Py, Pl	Caminiti and Sbriccoli (1983)
Rhesus	HRP/DAB	17/18	17/18	III (deep)	—	Winfield *et al.* (1975)
Macaca (3 species)	HRP	17/18, splenium	18	IIIa, $\underline{\text{IIIb}}$	SPy, MPy, $\underline{\text{LPy}}$	Lund *et al.* (1975, 1981)
Squirrel monkey	HRP/DAB	17/18	18	III (deep)	Py	Wong-Riley (1974)
Rhesus	HRP/BDHC, TMB	18, TE	18, 19, TE	IIIa, IIIb, $\underline{\text{IIIc}}$	—	Rockland and Pandya (1979)
Macaca fascicularis	HRP/DAB	CC	Visual areas	II, $\underline{\text{III}}$, IV, V, VI	SPy, MPy, LPy	Van Essen *et al.* (1982)

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[a] HRP, horseradish peroxidase; HRP-WGA, horseradish peroxidase coupled to wheat germ agglutinin; DAB, diaminobenzidine; DAB-Co, diaminobenzidine intensified with cobalt; DAB-GO, diaminobenzidine coupled to glucose oxidase; TMB, tetramethylbenzidine; BDHC, benzidine dihydrochloride; PDC, paraphenylene-diamine and catechol; ODN, *o*-dianisidine; TB, true blue.

[b] A, M, S, V, auditory, motor, somatosensory, visual cortex; CC, corpus callosum; LS, lateral suprasylvian region; numbers, cytoarchitectonic fields; PMBSF, posteromedial barrel subfield; TE, subdivision of inferotemporal region; /, border between areas (e.g., 17/18).

[c] Underscores denote layers with heaviest concentration, as documented by descriptions and, when available, illustrations and/or counts.

[d] SPy, small pyramids; MPy, medium-size pyramids; LPy, large pyramids; Py, pyramids; N-Py, nonpyramidal neurons; St, stellate neurons; Pl, polymorphic neurons; —, not specified.

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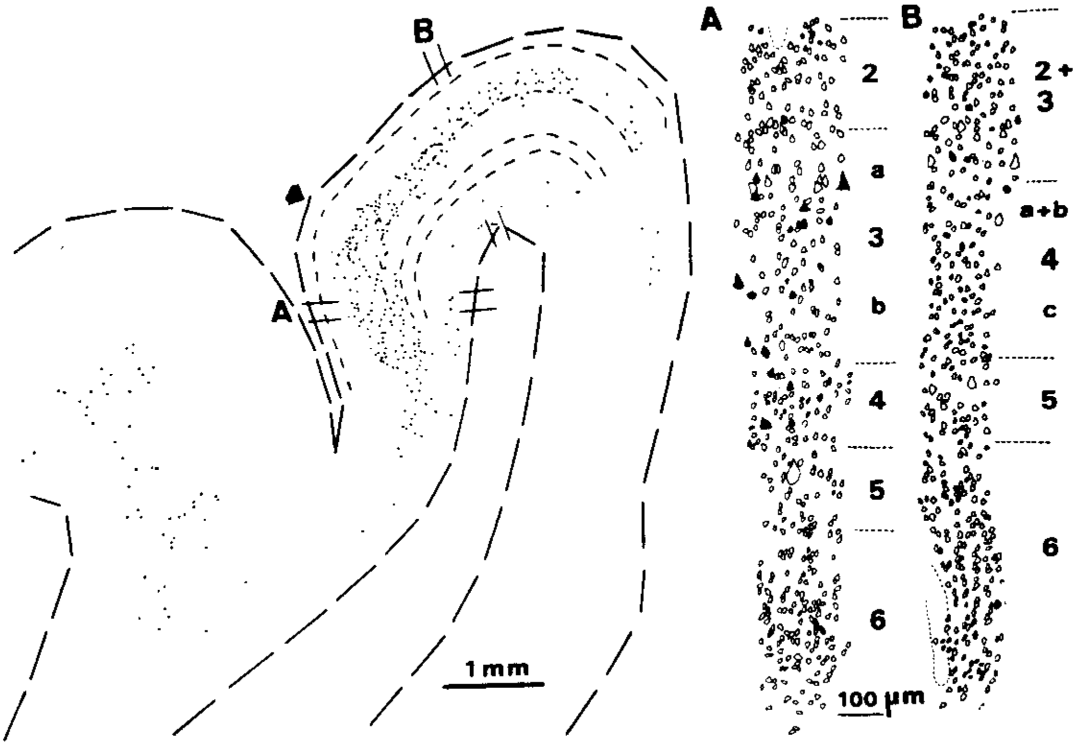

Figure 1. Radial and tangential distribution of callosal neurons in areas 17 and 18 of the cat, labeled by HRP injections filling most of the lateral gyrus. (Left) Computer-microscope chart of distribution of callosal neurons (dots) in an 80-μ-thick coronal section reacted with DAB. Thin dashed lines mark bottoms of layers 1, 3, 4, 5, 6; arrow points to the boundary between areas 17 and 18. A and B refer to the strips of cortex drawn on the right. (Right) Camera lucida-drawn outlines of HRP-positive (solid symbols) and HRP-negative (open symbols) neurons in areas 18 (A) and 17 (B). Layers and sublayers are indicated by numbers and letters, respectively. Outlines of major blood vessels are drawn with dashed contours. From Innocenti (1980).

relative contribution of the other layers is probably also a species-specific trait; it is small in monkeys and cats, large in rodents.

Areal differences in the radial distribution of callosal neurons have only recently been systematically explored (Jouandet *et al.*, 1985) but they can be exemplified by the relatively stronger contribution of infragranular layers to the corpus callosum in areas 19 and PMLS in the cat, as compared to areas 17 and 18 (Shatz, 1977b; Keller and Innocenti, 1981; Segraves and Rosenquist, 1982a). Infragranular callosal neurons seem to be relatively more frequent in motor cortex than in somatosensory cortex of the monkey (Zant and Strick, 1978; Killackey *et al.*, 1983a) and mouse (cf. White and DeAmicis, 1977; Porter and White, 1983). In the monkey, Van Essen *et al.* (1982) have reported a higher incidence of deep callosal neurons in parietal cortex than in striate and peristriate areas. These differences in the radial origin of callosal connections are interesting because they seem to challenge the homology of cortical layers across areas and species.

Each area projects callosal axons not only to homologous (homotopic) areas in the contralateral hemisphere, but also to heterologous (heterotopic) areas (see

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p. 309). These projections can originate from different layers. For example, the visual area PMLS of the cat projects to the contralateral homologue mainly from layer III, and to area 17/18 mainly from layer VI (Keller and Innocenti, 1981; Seagraves and Rosenquist, 1982b; Fig. 2).

2.2. Morphology

The average size of cell bodies of callosal neurons is very similar in SI of the monkey (259.5 µm^2; Jones and Wise, 1977) and several areas of the cat: SI (279.2 µm^2; Caminiti *et al.*, 1979), VI/VII (256.0 µm^2; Innocenti, 1980), AI (278.9 µm^2; Code and Winer, 1983). In cats and monkeys, the callosal neurons are, on the average, larger than the other neurons in the same layer. This is not the case in rodents (unpublished). The prominent size of callosal neurons is acquired

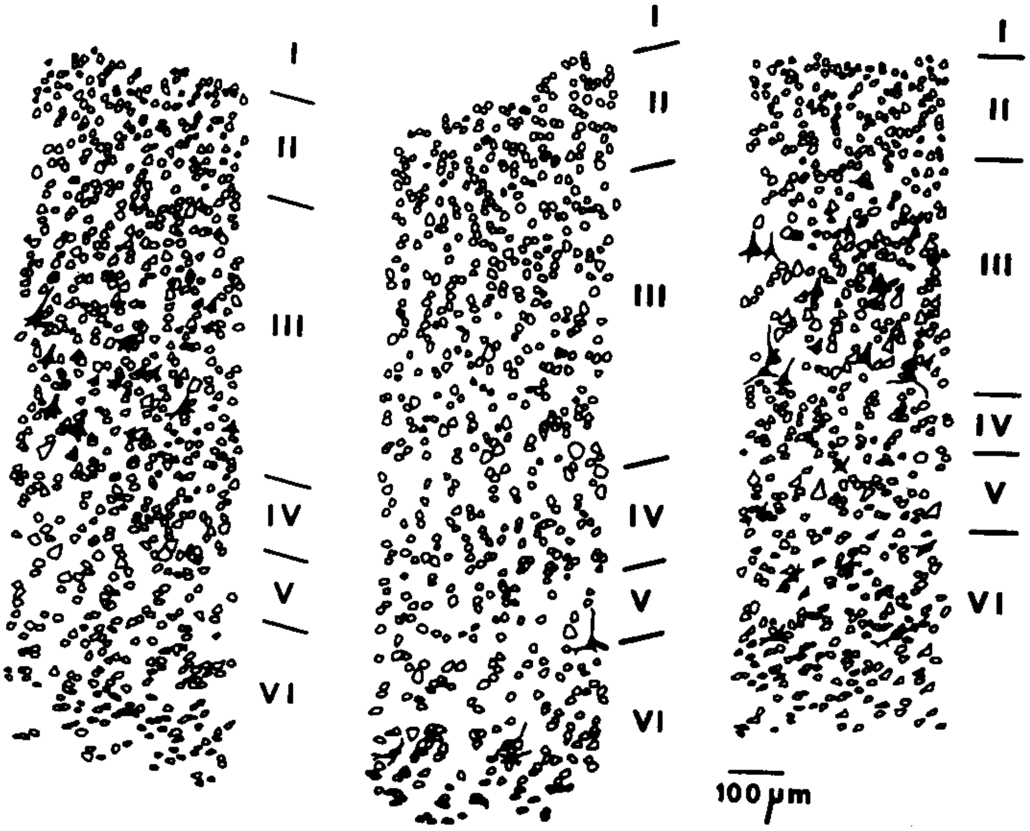

Figure 2. Radial distribution of callosal neurons in area PMLS of the cat, labeled by HRP injections into the homotopic cortex (left), areas 17 and 18 (middle), and application of HRP to the corpus callosum (right). Camera lucida-drawn outlines of HRP-positive (solid symbols) and HRP-negative (open symbols) neurons in 80-µm-thick coronal sections reacted with DAB. Layers are indicated by roman numerals. The choice of the regions shown in these drawings emphasizes the difference in the laminar distributions of homotopic and heterotopic callosal neurons; occasionally, a few homotopic callosal neurons can also be found in infragranular layers and a few heterotopic ones in supragranular layers. Modified from Keller and Innocenti (1981).

postnatally in the cat (Innocenti and Caminiti, 1980) and it may reflect either the progressive elongation of the callosal axons due to the volumetric increase of the brain, or the elaboration of telodendria.

Only recently has the sensitivity of retrograde transport methods become adequate to resolve the morphology of callosal neurons. Across areas and species, pyramids are by far the commonest type of callosal neuron (Table I, Fig. 3). Polymorphic neurons (Table I) and, occasionally, inverted pyramids (Van der Loos, 1965; Innocenti, 1980) in layer VI also contribute to the corpus callosum in several areas and species.

The contribution of layer III and IV spiny stellate cells to the callosum was demonstrated in areas 17 and 18 of the cat (Innocenti and Fiore, 1976; Shatz, 1977b; Sanides and Donate-Oliver, 1978; Innocenti, 1980; Hornung and Garey, 1980, 1981; Figs. 3, 4). This was somewhat unexpected, since there has been a tendency to consider stellate neurons as the source of exclusively intracortical axons, in spite of older evidence to the contrary from Golgi studies (Ramón y Cajal, 1911; Sholl, 1955). The contribution of stellate cells to the corpus callosum may be restricted to visual cortex and, possibly, to the cat (see Table I), in which species this cell type has now also been identified as the source of ipsilateral projections from area 17 to area 18 (Meyer and Albus, 1981).

In visual cortex of the cat, the heterogeneity of morphological types corresponds to the heterogeneity in the receptive field properties of callosal neurons, and fits the structure–function relationships discovered for this part of the brain. Visual callosal neurons have "simple," "complex," and "hypercomplex" receptive fields (Hubel and Wiesel, 1967; Berlucchi *et al.*, 1967; Shatz, 1977a; Innocenti, 1980; Harvey, 1980) and, in layers III and IV of area 17, "simple" receptive fields correlate with the stellate morphology whereas cells with "complex" receptive fields are usually pyramids (Kelly and Van Essen, 1974; Gilbert and Wiesel, 1979).

Callosal axons give rise to initial collaterals which either ascend toward the pial surface or run tangentially for up to 500 μm and possibly farther (Innocenti, 1980). Other collaterals arise from more distal parts of the axons, probably contributing to the projection from layer III to layer V (Lund and Boothe, 1975).

The possibility that callosal neurons may send axon collaterals to ipsilateral cortical, or subcortical, targets (Ramón y Cajal, 1894) or to different contralateral areas, has been tested electrophysiologically (Toyama *et al.*, 1974; Miller, 1975; Catsman-Berrevoets *et al.*, 1980; Swadlow and Weyand, 1981), or by using double retrograde tracer techniques (Catsman-Berrevoets *et al.*, 1980; Wong and Kelly, 1981; Schwartz and Goldman-Rakic, 1982; Graziosi *et al.*, 1982; Segraves and Innocenti, 1982; Weber *et al.*, 1983; Herron and Miller, 1983). Few such neurons have been found so far, on an average about 1% of the total callosal neurons labeled in an area, but this figure can be expected to vary considerably depending on the combination of injection sites, layer, area, and, possibly, species. For

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Figure 3. Phase-contrast photomicrograph (A) and camera lucida drawing (B) of callosal neurons (one pyramid and two stellate cells) in area 18 of the cat, stained in a Golgi-like way by HRP injected into the contralateral lateral gyrus. A horizontal bar in A and a dashed line in B mark the bottom of layer 3. In B bottom of layer I is also indicated. The section was 80 μm thick, reacted with DAB. From Innocenti (1979).

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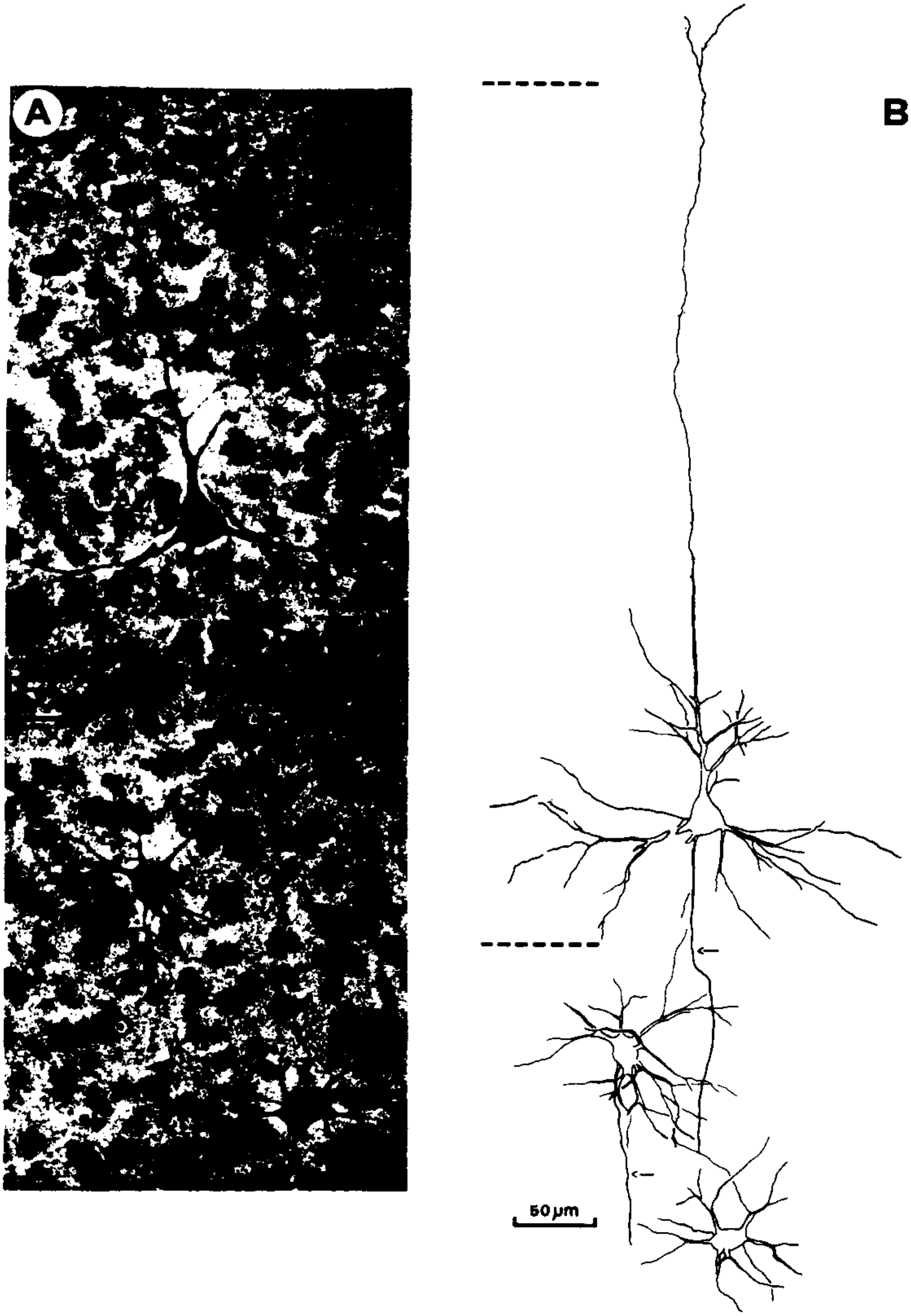

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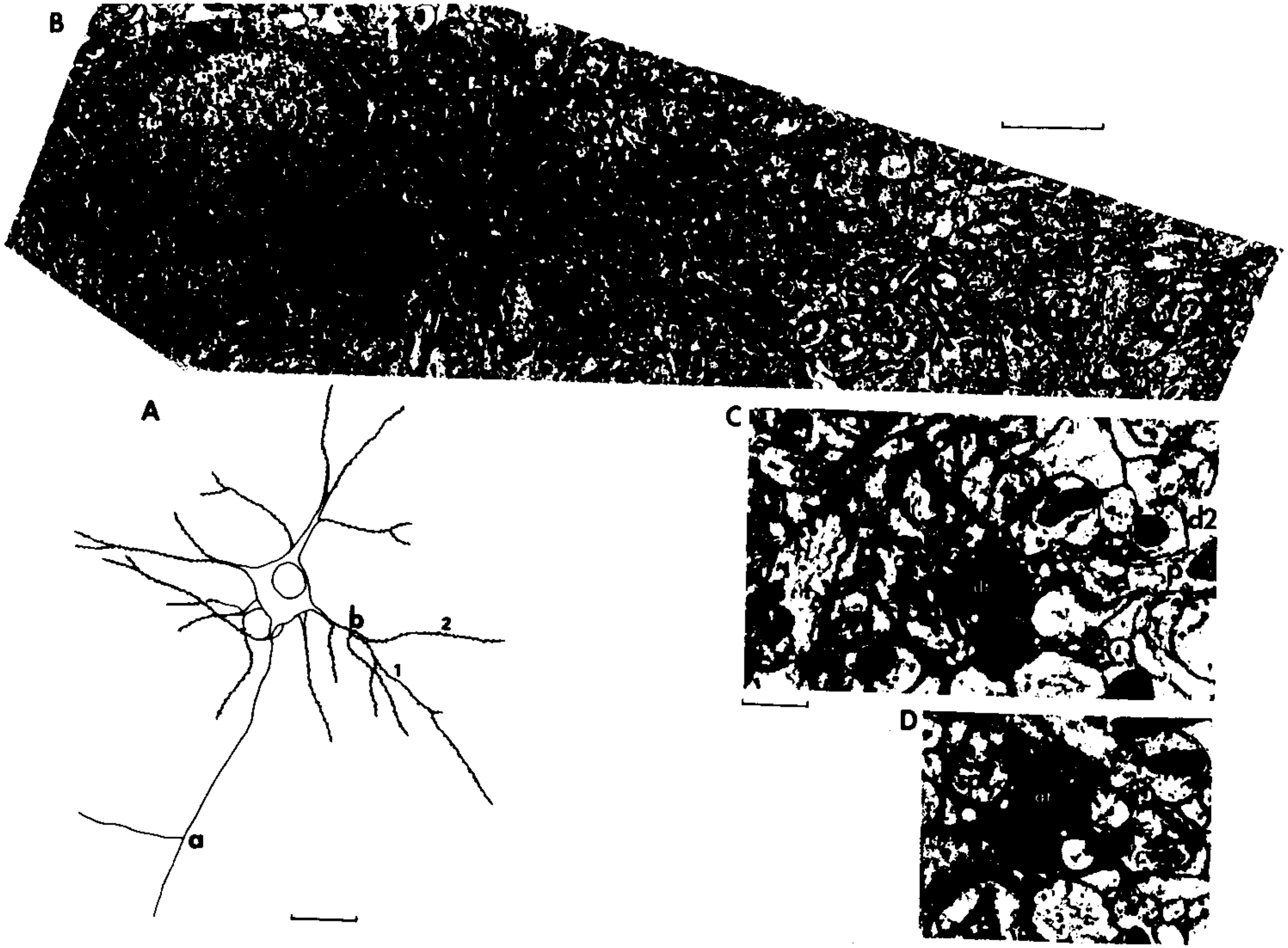

Figure 4. (A) Drawing of a stellate neuron in layer IV at the area 17/18 boundary, retrogradely labeled by HRP injection in the contralateral visual cortex. The pial surface is toward the top of the drawing. a, Axon; b, branching of the dendrite illustrated in B; 1 and 2 indicate the position of the degenerating thalamocortical terminals. Bar = 20 μm. (B) Montage of electron micrographs through the soma and initial dendrite of the neuron in A. Note the granules of reaction product in the cytoplasm including that of small dendritic segments (arrows). b, Branching indicated in A. Bar = 5 μm. (C) Degenerating terminal (dt) contacting a labeled spine (sp1) at position 1 in A, with an asymmetrical postsynaptic thickening. The spine belongs to the marked dendrite (d1). The terminal also contacts an unmarked spine (sp2) from another cell; this spine is in continuity through its pedicle (p) with its parent dendrite (d2). Bar = 0.05 μm. (D) Subsequent section of the same terminal (dt) contacting the marked (sp1) and unmarked (sp2) spines. Scale as in C. From Hornung and Garey (1980).

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example, in area PMLS of the cat at least 15% of the callosal neurons projecting to contralateral 17 and 18 also send an axon collateral to ipsilateral 17 and 18 and these neurons are most numerous in layer VI (Segraves and Innocenti, 1982, 1985). With these limitations, and even though the available techniques may fail to visualize a fraction of the callosal neurons with bifurcating axons, the picture emerging is that distinct neuronal sets project from supragranular layers to different contralateral areas or to areas in the two hemispheres. Interestingly, this is not a general rule for all telencephalic commissural systems: in the hippocampus, commissurally projecting neurons often have long ipsilateral collaterals (Laurberg and Sørensen, 1981).

2.3. Synaptology

The response latency of somatosensory (Innocenti *et al.*, 1974) and visual (Toyama *et al.*, 1974; Harvey, 1980) callosal neurons in the cat has indicated that at least some of them are monosynaptically excited by thalamic afferents.

Ultrastructural studies have confirmed that thalamic afferents synapse on callosal neurons in areas 17/18 of the cat (Hornung and Garey, 1980, 1981) and in somatosensory cortex of the monkey (Hendry and Jones, 1980, 1983; see Fig. 31 of Chapter 4). In both areas, the thalamic terminals form asymmetrical contacts with spines and shafts of basal dendrites of callosal neurons in layers III–IV (Fig. 4). In visual cortex, both pyramidal and stellate callosal neurons receive the thalamic afferents. Callosal neurons also receive symmetrical synapses on their somata, proximal parts of the dendrites and initial axon segments. Interneurons specialized in axoaxonic connections give rise to the symmetrical synapses on the initial axon segment of callosal neurons in area 18a of the rat (Somogyi *et al.*, 1979).

3. The Callosal Tract

The adult corpus callosum consists of myelinated and unmyelinated axons (Fig. 15). The former comprise 43–69% of the total (a figure which represents different authors, species, and methods; Table II). There is a wide range of axon diameters; some of the axons are as thin as 0.08 μm while the thickest can exceed 5 μm (Table II). However, electron microscopic studies in rabbits and cats show that very few axons are thicker than 1 μm (Fleischhauer and Wartenberg, 1967; Waxman and Swadlow, 1976).

The wide range of axon diameters corresponds to a wide range of conduction velocities. Naito *et al.* (1970) reported two classes of conduction velocities for somatomotor callosal axons in the cat: slow axons (3.0–4.3 m/sec; mean 3.6 m/sec) and fast axons (6.4–15.8 m/sec; mean 10.3 m/sec). Axons of these two classes synapse, respectively, with slow and fast pyramidal tract neurons. Miller (1975) estimated conduction velocity of somatosensory callosal axons of the cat to range from less than 1 m/sec to 10 m/sec, irrespective of the layer location of the parent neuron. The conduction velocity of callosal axons from visual areas

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spine belongs to the marked dendrite (d1). The terminal also contacts an unmarked spine (sp2) from another cell; this spine is in continuity through its pedicle (p) with its parent dendrite (d2). Bar = 0.05 μm. (D) Subsequent section of the same terminal (dt) contacting the marked (sp1) and unmarked (sp2) spines. Scale as in C. From Hornung and Garey (1980).

Table II. Morphology and Number of Callosal Axons[a]

Species	Method	Myelinated % of total	Diameter (μm)	Number × 10^6	Authors
Rat	Nonidez, Ehrlich	66.6	—	1.1	Cumming (1969)
	EM	53.6	—	—	Seggie and Berry (1972)
Rabbit	EM	55	0.08–0.6 (um) 0.3–1.85 (m)	—	Waxman and Swadlow (1976)
Cat	EM	—	0.3–6	—	Bishop and Smith (1964)
	EM	60	—	—	Fleischhauer and Wartenberg (1967)
	EM (rostral CC)	100[b]	0.3–6.4 (mean 1.2)	—	Naito *et al.* (1971)
	EM	43–58	—	23	Koppel and Innocenti (1983)
Macaca (*rhesus* and *fascicularis*)	EM (splenium)	69	0.08–0.5 (um)[c]	—	Swadlow *et al.* (1980)
Man (male)	Weigert, Haeggquist	56–64	0.5–5 (mode = 1)	174.7–195.47	Tomasch (1954)

[a] Abbreviations: EM, electron microscopy; m, myelinated; um, unmyelinated.
[b] Photomicrographs do, however, show unmyelinated axons.
[c] Most myelinated axons are less than 1 μm.

17 and 18 ranges between 0.5 and 8.25 m/sec (median: 2.8 m/sec) in rabbits (Swadlow and Weyand, 1981) and between 1.4 and 30 m/sec (median: 14–15 m/sec) in cats (pooled data from Toyama *et al.*, 1974, and Harvey, 1980). Variations in latency of antidromic responses of up to 22% of the control value can be observed with paired stimulations, suggesting that activity can modify the conduction velocity of callosal axons (Swadlow and Waxman, 1976). Swadlow *et al.* (1979) have discussed the implications of these figures for the assessment of commissural transmission time in man.

There is but scanty information regarding the number of callosal axons. Counts derived from light microscopic studies (for references see Doty and Negrao, 1973; see also Table II) must be seriously questioned since they probably missed many small unmyelinated callosal axons. In an electron microscopic study, we have recently counted an average of 23 million axons in the adult cat, i.e., nearly 5 times more than the previous light microscopic figure (Koppel and Innocenti, 1983; Fig. 18). Unfortunately, this seems to be the only estimate of the number of callosal axons using a modern technique. [Note added in proof: La Mantia and Rakic (1984) have counted 45 million axons in the adult rhesus.]

Which proportion of cortical neurons gives rise to callosal axons is also not known with certainty. In earlier work with diaminobenzidine (DAB)-visualized HRP, I estimated that 10–15% of the layer III–IV neurons in the most heavily projecting parts of areas 17/18 of the cat send axons to contralateral 17/18 and 19 (unpublished). It is probable that, if callosal neurons projecting from 17/18 to the contralateral suprasylvian region were included and, especially, if more sensitive substrates for HRP visualization were used, this figure would be considerably augmented.

Few studies have thus far tried to correlate the topography of the corpus callosum with that of the hemispheres (Sunderland, 1940; Luttenberg and Marsala, 1963; Pandya *et al.*, 1971b; Innocenti, 1980; Seltzer and Pandya, 1983). Sunderland (1940) concluded his Marchi study on the macaque with this statement: "The localization in the corpus callosum is of a very general type. Not only are the commissural fibres from some cortical areas diffusely spread over the corpus callosum but there is also an overlap of fibres coming from different areas in the same lobe, and also, apparently, from areas in different lobes."

This statement is still appropriate. More precisely though, in cats and monkeys, the rostrocaudal axis of the corpus callosum corresponds roughly to that of the hemisphere while the dorsoventral callosal axis does not seem to correspond to a mediolateral trajectory on the hemisphere (Innocenti, 1980; Seltzer and Pandya, 1983). The differences in the dorsoventral and rostrocaudal topography of the callosum may be due to the existence of numerous heterotopic connections between medial areas in one hemisphere and lateral areas in the other. The elimination of at least 70% of the callosal axons in development (Koppel and Innocenti, 1983) may contribute to blur the callosal topography.

The topography of axons in the corpus callosum is interesting for at least two very different reasons. Sidtis *et al.* (1981) have demonstrated that different parts of the corpus callosum transfer the sensory and semantic attributes of a visual stimulus. It would be important to know which area-to-area connections are responsible for these two performances. On the other hand, sex-related differences in the shape of the corpus callosum have been found in human

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brains (De Lacoste-Utamsing and Holloway, 1982) and may also exist in the monkey (De Lacoste and Woodward, 1983). Women seem to have a more bulbous and larger splenium than men, which may indicate differences in the connectivity of specific cortical areas in the occipital, temporal, or parietal lobes. Along the same lines, it is interesting that left-handers seem to have a larger corpus callosum (at equal brain weight) than right-handers (Witelson, 1983).

4. The Termination of Callosal Axons

Table III combines the descriptions of the radial distribution of terminating callosal axons in a selected group of recent papers which have devoted special attention to it. Some precautions are necessary in interpreting Table III. The results derive from studies with different techniques. However, probably only the few electron microscopic studies could distinguish, with certainty, terminals from preterminal or "en passage" axons. In addition, some studies have involved localized cortical lesions or tracer injections, and others transections of the corpus callosum. These two approaches may not always lead to identical results. Finally, in many areas callosal connections terminate in a "columnar" pattern (see Section 5.3). A "column" may assume different widths in different layers (see Jones *et al.*, 1979). It was not possible to include these details (which are not available in all studies) in Table III.

In spite of these potentially confusing factors, comparisons of the radial distribution of callosal terminals in different species and areas can be attempted.

Callosal terminals to corresponding areas seem to acquire a more strict radial segregation from rodents to cats and monkeys. Concomitantly, the bulk of the terminations assume a deeper position in the granular and supragranular layers. Thus, near the area 17/18 border, the densest callosal termination was usually found in rodents in layers I–III but many terminations were also found in V and VI, and a few in IV. In the same region, most callosal axons were found in layers III–IV in the cat but also a few in other layers. In monkeys the distribution is similar to that found in the cat, although callosal terminals seem to become less numerous in the upper part of III.

In theory, the differences in the radial distribution of callosal connections at the 17/18 border of rodents, cats, and monkeys could be related to the different organization of the visual pathways. However, similar differences also seem to exist for other areas (Table III; see also Jacobson and Marcus, 1970).

Areal differences in the radial distribution of callosal terminals have been noticed since the early studies of callosal connections (Heimer *et al.*, 1967), but remain incompletely described. One of the best documented areal difference is at the transition between areas 17 and 18 in rat, cat, and monkey: callosal terminals are in all layers in area 18 but in 17 they become restricted to supra- and infragranular layers (Fisken *et al.*, 1975; Shatz, 1977b; Cusick and Lund, 1981; Innocenti *et al.*, 1985).

With these limitations, the general rule seems to be that granular and supragranular layers are the main, and most constant, recipient of callosal axons. Exceptions to this rule seem to be areas 17 and 18 of *Aotus* and *Galago* monkeys

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(Newsome and Allman, 1980) and the limbic area 29 of the rat (Vogt *et al.*, 1981), where granular–infragranular layers are the main callosal recipients.

Single callosal axons to parietal cortex of the mouse have been anterogradely traced with HRP (Hartenstein and Innocenti, 1981; Fig. 5). These axons, which may represent but a subclass of all callosal afferents to this area, were found to form their terminal arborization in granular or supragranular layers, but they often gave off short collaterals in deeper layers. The terminal arborization occupies, in the coronal plane, a triangular space with a 100 to 200-μm-wide base toward the pial surface and a height not exceeding 200 μm. In SI of the monkey a callosal axon with a more elaborate terminal arbor has been described (Hendry and Jones, 1983; see Fig. 31 of Chapter 4). This axon, unlike in the mouse, does not seem to give rise to infragranular collaterals but to two distinct terminal arbors at the layer IIIb/IV border and in IIIa. The widest of these arbors spans 100–150 μm, tangentially, just as in the mouse. Given the enormous difference in the surface of neocortex in these two species, this possibly circumstantial similarity is nevertheless striking, especially since the distribution of callosal terminals may be the expression of a general modular pattern of neocortical organization (see Section 5.3).

Callosal axons terminate with "boutons" containing round vesicles and forming asymmetrical synapses mostly on spines (Jones and Powell, 1970; Lund and Lund, 1970; Fisken *et al.*, 1975; Sloper and Powell, 1979; Hendry and Jones, 1983; Cipolloni and Peters, 1983) which, in auditory cortex of the rat, belong to apical or basal dendrites of pyramidal cells (Cipolloni and Peters, 1983). A few callosal terminals contact dendritic shafts or cell bodies.

5. Corticotopic Organization of Callosal Connections

The two key concepts which underlie the present understanding of the topographical (corticotopic) organization of callosal connections were established in the 1940s, especially by the electrophysiological studies of compound potentials evoked across the corpus callosum by electrical stimulation of the cortex or topical application of strychnine (Curtis and Bard, 1939; Curtis, 1940; McCulloch and Garol, 1941; Bailey *et al.*, 1941, Garol, 1942).

These concepts are that (1) callosal axons connect most strongly corresponding (homotopic) but also, less strongly, noncorresponding (heterotopic) cortical points and (2) the density of callosal connections varies across the cortex. Parts of some areas, most typically of the primary sensory areas, lack callosal connections.

The absence of callosal afferents in large parts of the visual, somatosensory, and auditory fields was definitively established by Myers (1962) and Ebner and Myers (1962, 1965) using the Nauta method in monkey, cat, and raccoon. The essential points of their descriptions were confirmed by Jones and Powell (1968, 1969), Diamond *et al.* (1968), Garey *et al.* (1968), and Pandya and Vignolo (1968, 1969); the latter group also provided the first precise anatomical information on the area-to-area relations established by the commissures.

These studies remain the foundations of current views on the corticotopic

Table III. Radial Distribution of Callosal Afferents

Species	Method[a]	Area[b]		Layer[c]						Types of terminals and targets[d]	Authors
		Origin	Termination	I	II	III	IV	V	VI		
Hedgehog	F-H	striate (large)	striate/ parastriate	+	+ + + +	= = = =	– – – –	– – – –	– – – –		Gould and Ebner (1978)
Rat	^{3}H	SI	SI	+	+ + + +	+ + + +	– – – –	= = = =	– – – –		Wise and Jones (1976)
	F-H	CC	SI	+	+ + + +	+ + + +	– – – –	= = = =	= = = =		Akers and Killackey (1978)
	F-H	CC	41	– +	+ + + +	+ + + +	– – – –	+ + – –	+ + + +		Vaughan (1983)
			20, 36	+	+ + + +	+ + + +	+ + + +	+ + – –	+ + + +		
	EM	CC	41	+	+ + + +	+ + + +	+ +	= =	= = = =	As; Sp(95%), Sh(5%)	Cipolloni and Peters (1983)
	F-H	CC	17, 18a, 18b, 7, 36, 41, 20, 39	+	+ + + +	+ + + +	+ +	= =	= = = =		Cipolloni and Peters (1979)
	N-G, F-H, EM	17–18a	17/18a	+	+ + + +	+ + – –	– – – –	= = = =	= = = =	RAs; Sp, Sh, Cb	Lund and Lund (1970)
Mouse	F-H	CC	several areas	+	+ + + +	+ + + +		= =	= = = =		Yorke and Caviness (1975)
						(regional differences)					
	F-H	17–18a (I–IV)	17/18a	+	+ + + +	+ + – –					
Rat, mouse	F-H	CC	17/18a	+	+ + + +	+ + + +	– – – –	+ + + +	+ + + +		Cusick and Lund (1981)
Hamster	^{3}H	17, 18a, 18b	17/18a	+	+ + + +	+ + + +	– – – –	+ + + +	+ + + +		Rhoades and Dellacroce (1980a)
Rat	F-H, EM	CC	24b	+	+ + + +	+ + + +		– = = =	= = = =	Sp, Smd	Vogt *et al.* (1981)
			29c	–	= = = =	= = = =	= = = +	+ + + +	+ + + +		
Cat	N-G	SI, SII	SI, SII	– –	= = = =	= = + +	+ + + +	– – – –	– – – –		Jones and Powell (1968)
	EM	SI, SII	SI, SII	+	– – – –	– – + +	+ + + +	– – – –	– – – –	As; Sp	Jones and Powell (1970)
	N-G	AI, AII, EP	AI, AII	– –	– – – –	– – + +	+ + + +	– – – –	– – – –		Diamond *et al.* (1968)
	^{3}H	AI	AI	+ +	– – – –	+ + + +	– – – –	+ + – –	= = = =		Imig and Brugge (1978)
						(individual and local variations)					
	N-G	17, 18	17, 18, 19			+ +	+ + + +				Garey *et al.* (1968)[f]
	N-G, F-H	17, 18, 19	17/18	–	= = = =	= = + +	+ + + +	– – – –	– – – –		Shoumura (1974)
	N-G, F-H, EM	17/18	17		– – – –	– – – –		– – – –	– – – –	RAs; Sp(76%), Sh(24%)	Fisken *et al.* (1975)
			18		– – – –	– – + +	+ + + +	– – – –	– – – –		
	^{3}H	17/18	17	–	+ + + +	+ + + +			= = = =		Shatz (1977b)
			18	–	= = = =	+ + + +	+ + – –	– – – –	= = = =		

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	N-G, F-H	17, 18, 19	17/18	– –	–	= = + +	+ + + +	–	– – – –		Shoumura (1974)
	N-G, F-H, EM	17/18	17		– – – –	– – – –		– – – –	– – – –	RAs; Sp(76%), Sh(24%)	Fisken *et al.* (1975)
			18		– – – –	– – + +	+ + + +	– – – –	– – – –		
	³H	17/18	17	–	+ + + +	+ + + +			= = = =		Shatz (1977b)
			18	–	= = = =	+ + + +	+ – –	– – – –	= = = =		
	³H	17, 18, 19, PMLS, ALLS	17, 18, 19, PMLS, ALLS		+ + + +	+ + + +	+ + + +	– – – –	– – – –		Segraves and Rosenquist (1982b)
Rhesus	³H	Fr	Fr	– –	= = = =	+ + + +	+ + + +	+ + + +	+ + – –		Goldman and Nauta (1977)
Macaca fascicularis	³H	4	4, 6	+ +	– – – –	+ + + +	– – – –	– – – –	+ + + +		Künzle (1976)
Rhesus	EM	S–M	SI (3b)	+ –	– – – –	+ + – –	– – – –	= = = =	= = = =		Sloper and Powell (1979)
			M	+	+ + – –	+ + – –	– – –	= = = =	= =		
	F-H	SI, SII	SI, SII	– –	– – – –	+ + + +	+ + + +	– – – –	– – – –		Jones and Powell (1969)
Saimiri, rhesus	³H	SI	SI, SII	–	– – = =	= = – –	+ + + +	– – – –	– – – –		Jones *et al.* (1975, 1979)
Aotus, *Macaca*	³H, HRP/TMB	precentral/ postcentral	3b, 1, 2	– –	= = = =	= = = =	+ + + (regional differences)	– – – –	– – – –		Killackey *et al.* (1983a)
Aotus	³H	AI, R	AI, R			+ +	+ + + +				Fitzpatrick and Imig (1980[f]
Saimiri	F-H	18	18(OBg)	–	– – = =	= = + +	+ + + +	+			Tigges *et al.* (1974)
Macaca	N-G, F-H, EM	17/18	17		– – – –	– – – –		– – – –	– – – –	RAs; Sp(72%), Sh(28%)	Fisken *et al.* (1975)
			18		– – – –	– – – –	+ + + +	– – – –	– – – –		
Rhesus	³H	18, 19	18, 19	– –	= = = =	= = = =	+ + + +				Rockland and Pandya (1979)
Aotus, *Galago*	W	splenium	17/18		– – – –	– – – –	+ + + +	+ + + +	+ + + +		Newsome and Allman (1980)
Macaca nemestrina	F-H	CC	18	– –	= = = =	= = + + + + + +					Lund *et al.* (1981)

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[a] N-G, Nauta–Gygax; F-H, Fink–Heimer; W, Wiitanen; ³H, radioactive amino acids; EM, electron microscopy; HRP, horseradish peroxidase; TMB, tetramethylbenzidine.

[b] A, M, S, V, auditory, motor, somatosensory, visual cortex; Fr, frontal and/or prefrontal; EP, posterior ectosylvian region; R, rostral field; numbers, cytoarchitectonic fields; PMLS, ALLS, subdivisions of lateral suprasylvian cortex; CC, corpus callosum; /, border between areas (e.g., 17/18).

[c] +, Heavy density; =, intermediate density; –, light density. Symbols schematize the relative densities in the various layers, or sublayers, as they were documented by the descriptions and, when available, by illustrations or, rarely, by counts. Only two symbols are used when only two different densities were documented.

[d] As, Asymmetrical terminals; RAs, asymmetrical terminals with round vesicles; Sp, spines; Sh, dendritic shafts; Cb, cell bodies; Py, pyramids; Smd, smooth dendrites.

[e] Layer IV does not exist in this area.

[f] Only regions of maximal density are indicated; for details, see original paper.

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organization of callosal connections. Over the last 10–15 years, however, important progress has been made in the definition of (1) the interhemispheric interrelations of several cortical areas, (2) the relationships of the callosal connections with the functional maps of several areas, and (3) the fine architecture of callosal connections.

5.1. Area-to-Area Interrelations

The information on the transcallosal interrelations of the various cortical areas is incomplete and requires a critical evaluation far beyond the goals of this review. Indeed, although the classic cytoarchitectonic and myeloarchitectonic studies still provide an invaluable framework for the parcellation of cerebral cortex, recent electrophysiological mapping studies have considerably refined the classic definition of several areas. On the other hand, the continuing, rapid increase in the sensitivity and selectivity of pathway tracing techniques implies a continuous revision of the connectional schemes.

Data on the transcallosal interrelations of the sensory-motor areas can be found in other chapters in this volume and in a series of articles on prefrontal

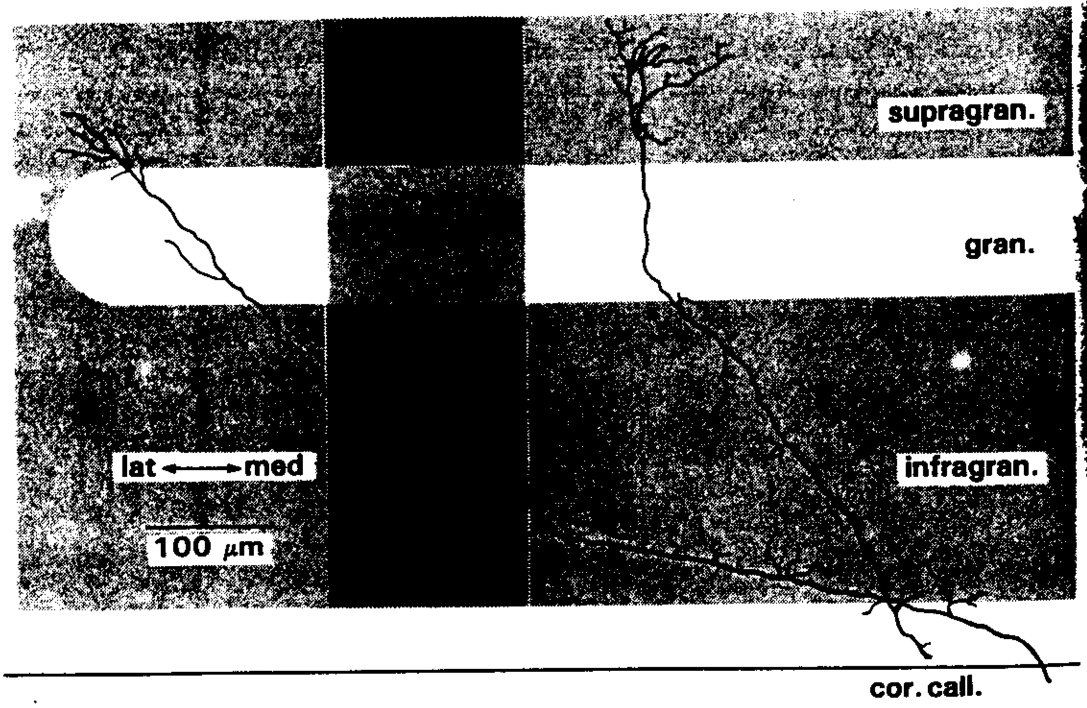

Figure 5. Camera lucida drawing of three callosal axons from different sections and cortical locations (from the left, areas 40, 17/18, 3) in a mouse injected with HRP in the contralateral hemisphere. The section (100 μm thick) was reacted with DAB and cobalt chloride. Shading schematically corresponds to regions containing diffuse distribution of anterogradely transported HRP. Two of the axons formed their terminal arborization in layers II and III, one in layer IV (within a "column" of anterograde transport). Note the nearly tangential trajectory of one of the axons in layer VI and the collateral arborizations in this layer of all three axons. From Hartenstein and Innocenti (1981).

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or motor cortex of the monkey (Pandya *et al.*, 1971a; Pandya and Vignolo, 1971; Jacobson and Trojanowski, 1977; Künzle and Akert, 1977; Künzle, 1978; Matsumura and Kubota, 1979; Jenny, 1979), cat (Cavada and Reinoso-Suárez, 1981), and rat (Beckstead, 1979), parietal cortex of the monkey (Pandya and Vignolo, 1969; Kaas *et al.*, 1977; Hedreen and Yin, 1981), somatosensory cortex of the monkey, cat, and mouse (Jones and Powell, 1968, 1969; Pandya and Vignolo, 1968, 1969; Jones *et al.*, 1975, 1979; White and DeAmicis, 1977; see Jones, this volume), auditory cortex of the cat and monkey (Diamond *et al.*, 1968; Pandya *et al.*, 1969; Fitzpatrick and Imig, 1980; Imig and Reale, 1980), and visual cortex of the hedgehog (Gould and Ebner, 1978), cat (Hubel and Wiesel, 1965; Wilson, 1968; Heath and Jones, 1970; Shoumura, 1972; Kawamura, 1973; Luttenberg, 1974; Keller and Innocenti, 1981; Segraves and Rosenquist, 1982b; Cavada and Reinoso-Suárez, 1983), and monkey (Spatz and Tigges, 1972; Tigges *et al.*, 1974; Wagor *et al.*, 1975).

In a combined anatomical and electrophysiological study with anterograde and retrograde tracers, Segraves and Rosenquist (1982b) have analyzed the callosal connections of 13 visual areas in the cat. From their study and from the others mentioned above, some of the general features of the transcallosal interrelations of cortical areas in cats and monkeys can be envisioned. (1) Each area projects to, and receives from, a characteristic set of areas, always including the homotopic one.* (2) Connections with different areas of the set differ in their density; the densest connections are usually between homotopic areas. (3) Different neurons project from one area to different contralateral areas, although a few neurons project with bifurcating axons to more than one area (Segraves and Innocenti, 1982). (4) The connections between two areas are usually, but not always, reciprocal. For example, area 19 projects to several areas from which it does not receive. SI projects to contralateral SII from which, however, it does not appear to receive, neither in the cat (Jones and Powell, 1968; Caminiti *et al.*, 1979) nor in the monkey (Pandya and Vignolo, 1968; Jones and Powell, 1969). (5) Different portions of an area may be differently connected. For example, injections in parts of PMLS representing the periphery of the visual field labeled connections with contralateral PMLS but not with areas 17 and 18, whereas injections closer to the vertical meridian representation labeled connections with both regions (Segraves and Rosenquist, 1982b).

The five points mentioned above are not specific for callosal connections but apply also to intrahemispheric connections. Nevertheless, certain areas are only connected by interhemispheric connections (see, e.g., Jones and Powell, 1968; Hedreen and Yin, 1981). A point of considerable theoretical interest is that of which organizing principles underlie the selective intra- or interhemispheric connections of cortical areas, as will be further elaborated in relation to the development of callosal connections.

Although the corpus callosum contains mainly corticocortical axons, some

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* In rodents, callosal connections may link preferentially or exclusively homotopic points (Yorke and Caviness, 1975), although some heterotopic connections have been described (Wise and Jones, 1976: White and DeAmicis, 1977: Beckstead, 1979: Porter and White, 1983: Markowitsch and Guldin, 1983).

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of its axons connect the cortex to subcortical structures such as the claustrum (Künzle, 1975; Squatrito *et al.*, 1980; Berman and Payne, 1982; Minciacchi *et al.*, 1983; see Sherk, this volume) and the caudate nucleus (Ebner and Myers, 1965; Carman *et al.*, 1965; Garcia-Rill *et al.*, 1979; Berman and Payne, 1982; see Goldman-Rakic and Selemon, this volume). Not all crossed corticosubcortical connections go by way of the corpus callosum (for examples, see Berman and Payne, 1982; Macchi and Bentivoglio, this volume).

5.2. Callosal Connections and Peripheral Representations: Visual Areas

Three lines of evidence unequivocally demonstrate that, in the cat, the origin and termination of visual callosal connections are focused to the proximity of the representations of the vertical meridian of the visual field. Electrophysiological recordings from the corpus callosum have shown that the receptive fields of visual callosal axons straddle the vertical meridian (Berlucchi *et al.*, 1967; Hubel and Wiesel, 1967; Shatz, 1977a). Transcallosally evoked visual responses (Choudhury *et al.*, 1965; Berlucchi and Rizzolatti, 1968; Lepore and Guillemot, 1982), or responses to electrical stimulation of the commissural pathways (Toyama *et al.*, 1974; Harvey, 1980; Innocenti, 1980), can be recorded only from parts of areas 17 and 18, representing visual-field locations near the vertical meridian. Finally, combined anatomical and electrophysiological studies have directly determined which portion of the visual field is represented in the regions which send or receive callosal axons (Innocenti, 1980; Sanides and Albus, 1980; Segraves and Rosenquist, 1982a; Fig. 6).

In the cat, the number of callosal neurons progressively increases from area 17 (VI) to the 17/18 border, where the vertical meridian is represented, and then decreases again, progressing into area 18 (VII; Innocenti, 1980; see Fig. 6). The portion of visual field represented within the region containing callosal neurons (callosal efferent zone) in 17 has an azimuthal width of 2–3° near area centralis and progressively increases to 8–9° at an elevation of 25° below area centralis. A wider portion of visual field corresponds to the callosal efferent zone in areas 18 and 19 (Innocenti, 1980; Segraves and Rosenquist, 1982a) and it increases further in area PMLS (Segraves and Rosenquist, 1982a). In each of these areas, the region occupied by callosal terminals (callosal terminal territory) is also centered on the vertical meridian representation, but is slightly narrower than the respective callosal efferent zones (Sanides, 1978). The strict association between callosal connections and the representation of the vertical meridian is emphasized by the finding that bridges of callosal terminations spanning the mediolateral extent of area 18 correspond to the exaggerated representations of visual field locations near the vertical meridian characteristic of this area (Sanides and Albus, 1980).

In area 17, the progressive increase with elevation in the azimuthal angle represented within the callosal zone may correspond to the eccentricity-dependent increase in receptive field size (see Fig. 7). A similar relation to receptive field size could explain the increase in the azimuthal angle of the callosal efferent zones and terminal territories across areas. In fact, there are strong indications

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that the callosal neurons situated in parts of PMLS, representing the most peripheral parts of the visual field, have wide receptive fields extending as far as the vertical meridian (Antonini *et al.*, 1983).

Callosal connections originate and/or terminate selectively near the border between areas 17 (VI) and 18 in cats (VII; 18a in rodents), hedgehogs (Gould and Ebner, 1978), mice (Yorke and Caviness, 1975), hamsters (Rhoades and Dellacroce, 1980a; but see Dürsteler *et al.*, 1979), rats (Jacobson and Marcus, 1970; Lund and Lund, 1970; Cipolloni and Peters, 1979; Cusick and Lund,

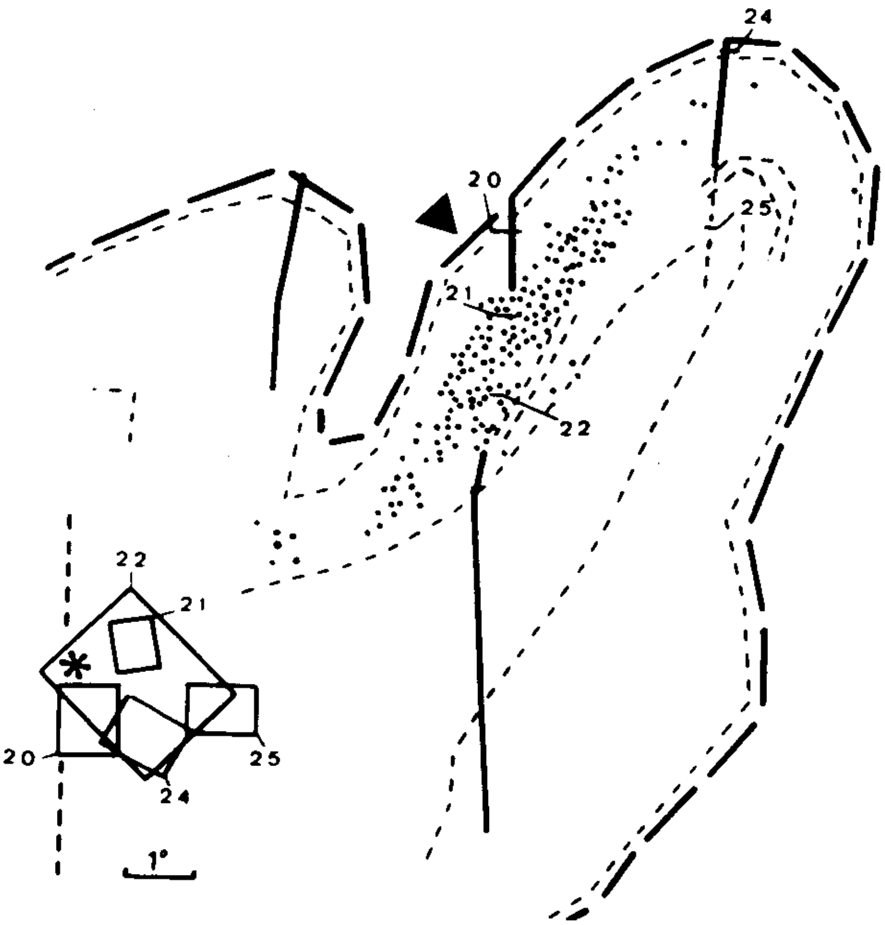

Figure 6. Example of a combined anatomical and electrophysiological experiment in cat visual cortex. Computer-microscope chart of a coronal section (80 μm thick, reacted with DAB) showing the distribution of callosal neurons (dots) labeled near the 17/18 border (triangle) by HRP injections in the contralateral, lateral, and postlateral gyri. Thin dashed lines mark the bottoms of layers I, IV, V, and VI. The lines crossing the cortex correspond to the trajectories of the microelectrode penetrations performed 24 hr after the HRP injections. The dashed portion of one of the penetrations was traced from a neighboring section; the line denoting one of the penetrations was interrupted in the region containing labeled neurons. Numbers along each penetration correspond to the receptive fields shown in the inset where the vertical meridian is indicated by a vertical, dashed line and area centralis (determined ophthalmoscopically) by an asterisk. From work partially described in Innocenti (1980).

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1981; Záborszky and Wolff, 1982), rabbits (Hughes and Wilson, 1969; Towns *et al.*, 1977; Swadlow *et al.*, 1978; Swadlow and Weyand, 1981; Chow *et al.*, 1981), and monkeys (Zeki, 1970; Karol and Pandya, 1971; Wong-Riley, 1974; Fisken *et al.*, 1975; Newsome and Allman, 1980; Van Essen *et al.*, 1982; Cusick *et al.*, 1983). Thus, in all of these species callosal connections between "primary" visual areas are also selectively concerned with the vertical meridian representation, as this seems to be invariably represented near the 17/18 border. The azimuthal angle corresponding to the callosal connections can, however, vary in different species. Rhoades and Dellacroce (1980a) have estimated that the callosal zone at the 17/18a border in the hamster encompasses 30–45° of the visual field representation. In the VI–VII region of the rabbit, Swadlow (1977) has found callosal neurons within parts of cortex ranging over 23° from the line of decussation of optic axons.

In the macaque, unlike in the other species, callosal axons originate only from 18 near the border with 17 but not from 17 itself (Lund *et al.*, 1975; Van

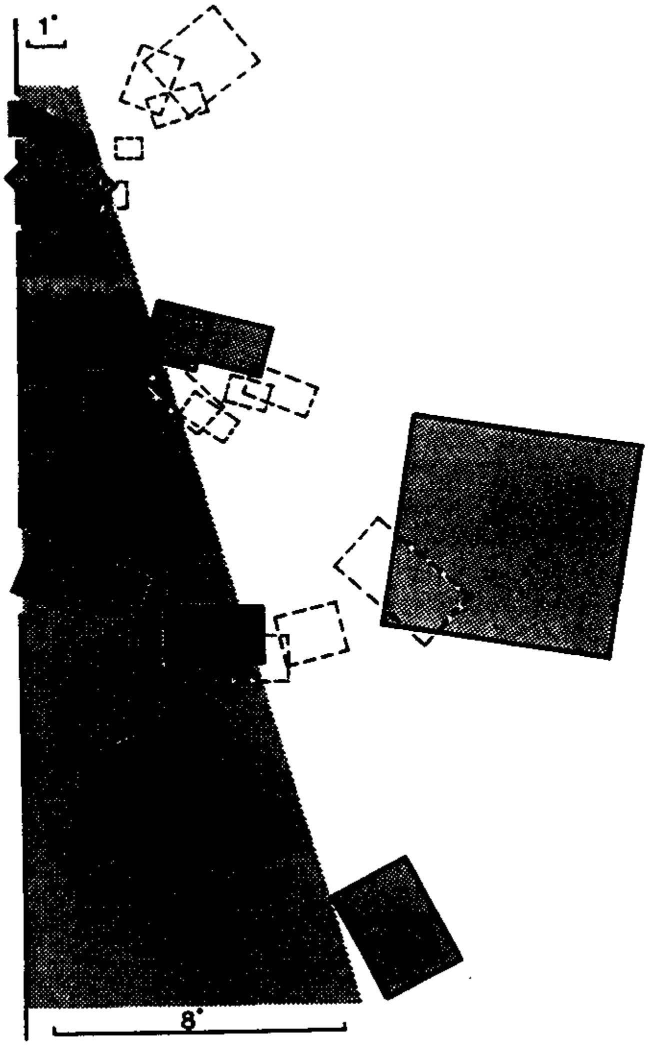

Figure 7. Visual field coordinates of the callosal zone in areas 17 and 18 of the cat. The vertical meridian is marked by a vertical line, area centralis (determined ophthalmoscopically) by a cross. Receptive fields of neurons met along microelectrode penetrations within the callosal zone in area 17 are indicated by solid rectangles; those met in the callosal zone in area 18 by hatched rectangles. Receptive fields of neurons outside the callosal zone are drawn with dashed contours. The hatched trapezoidal area extrapolates the data to indicate the portion of visual field within the callosal zone in area 17. Same experiment as shown in Fig. 6; 12 penetrations were performed at four rostrocaudal levels within the lower hemifield representation along the lateral and postlateral gyri. The receptive fields were plotted on a tangent screen in front of the animal. From work partially described in Innocenti (1980).

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Essen *et al.*, 1982), although they terminate on either side of the border (Fisken *et al.*, 1975; Van Essen and Zeki, 1978; Van Essen *et al.*, 1982).

The association between the callosal terminal territory and the vertical meridian representations can help to identify anatomically the borders between some of the "secondary" retinal representations in monkeys and in rodents (Zeki and Sandeman, 1976; Van Essen and Zeki, 1978; Newsome and Allman, 1980; Cusick and Lund, 1981; Van Essen *et al.*, 1982).

In spite of the work done thus far, it remains unclear whether callosal axons relate most specifically to the geometrical midline of the binocular visual field or to the border between nasal and temporal retinal moieties. It is this border which receives callosal afferents in the sheep, where it falls at 10–15° in the ipsilateral visual field, at the VI/VII boundary (Rao, 1979; Clarke *et al.*, 1979).

5.2.1. Somatosensory Areas

It has been believed for some time that similar principles underlie the relationships of callosal connections with visual and somatosensory maps. Studies with anterograde degeneration in the monkey, cat, raccoon, rat, and mouse have, in fact, emphasized the absence of callosal connections in regions of SI and of SII (Ebner and Myers, 1965; Jones and Powell, 1968, 1969; Pandya and Vignolo, 1968, 1969; Yorke and Caviness, 1975; Wise and Jones, 1976) representing distal segments of the limbs (but see Shanks *et al.*, 1975). Callosal terminals were, on the contrary, found within the representations of trunk and head, i.e., essentially in correspondence to the body midline. It should be stressed that these interpretations were based on comparisons of the patterns of anterograde degeneration with electrophysiological maps (with evoked potentials), which have now undergone profound revisions (see below).

The notion that tactile information from the distal limb segments has no access to the corpus callosum is difficult to reconcile with the behavioral evidence of transcallosal transfer of somatosensory information from the paws, and hands, apparently involving SII (Teitelbaum *et al.*, 1968). Furthermore, in the rostral part of the corpus callosum of the cat, focal potentials can be evoked by stimulation of distal fore- and hindlimb segments as well as of more proximally located body regions, and single units with receptive fields *restricted** to the distal limb segments can be found (Innocenti *et al.*, 1974; Lepore *et al.*, 1983b). Size and locations of receptive fields, latency, and modality specificity of the responses suggest that they are generated by impulses traveling along the lemniscal pathway and, at least in part, relayed monosynaptically through the cortex. The responses, including those evoked by stimulation of the distal limb segments, decrease in amplitude after ablation of SI and disappear entirely when SII is also ablated. Thus, both areas seem to relay input to the callosum from their representations of the distal limb segments. In fact, Robinson (1973) could identify, in SII, callosal neurons with contralateral receptive fields on the forepaws. Furthermore, experiments combining the retrograde transport of HRP and microelectrode re-

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* This is a crucial difference from what is observed in secondary visual areas, where receptive fields transmitted across the corpus callosum may extend into the periphery of the visual field, but they always include the vertical meridian or the neighboring visual space (Antonini *et al.*, 1983).

cordings have shown that in SI of the cat, a limited part of the forepaw representation has access to contralateral SII (Caminiti *et al.*, 1979), but perhaps also to contralateral SI (McKenna *et al.*, 1981). However, most callosal neurons projecting to contralateral SI seem to be restricted to two patches corresponding to the ventral and dorsal body midlines (Caminiti *et al.*, 1979; Manzoni *et al.*, 1980; McKenna *et al.*, 1981), while most of the forepaw and hindlimb representations are empty.

The conclusions that the paw representations in SII of the cat lacked callosal connections appear to have been due to the lack of resolution of the body maps of this area constructed with evoked potentials. Single-unit studies (Burton *et al.*, 1982; Clemo and Stein, 1983) have now indicated that SII contains three representations of the paws (Clemo and Stein, 1983). A combined anatomical and electrophysiological investigation has shown unequivocally that regions rep-

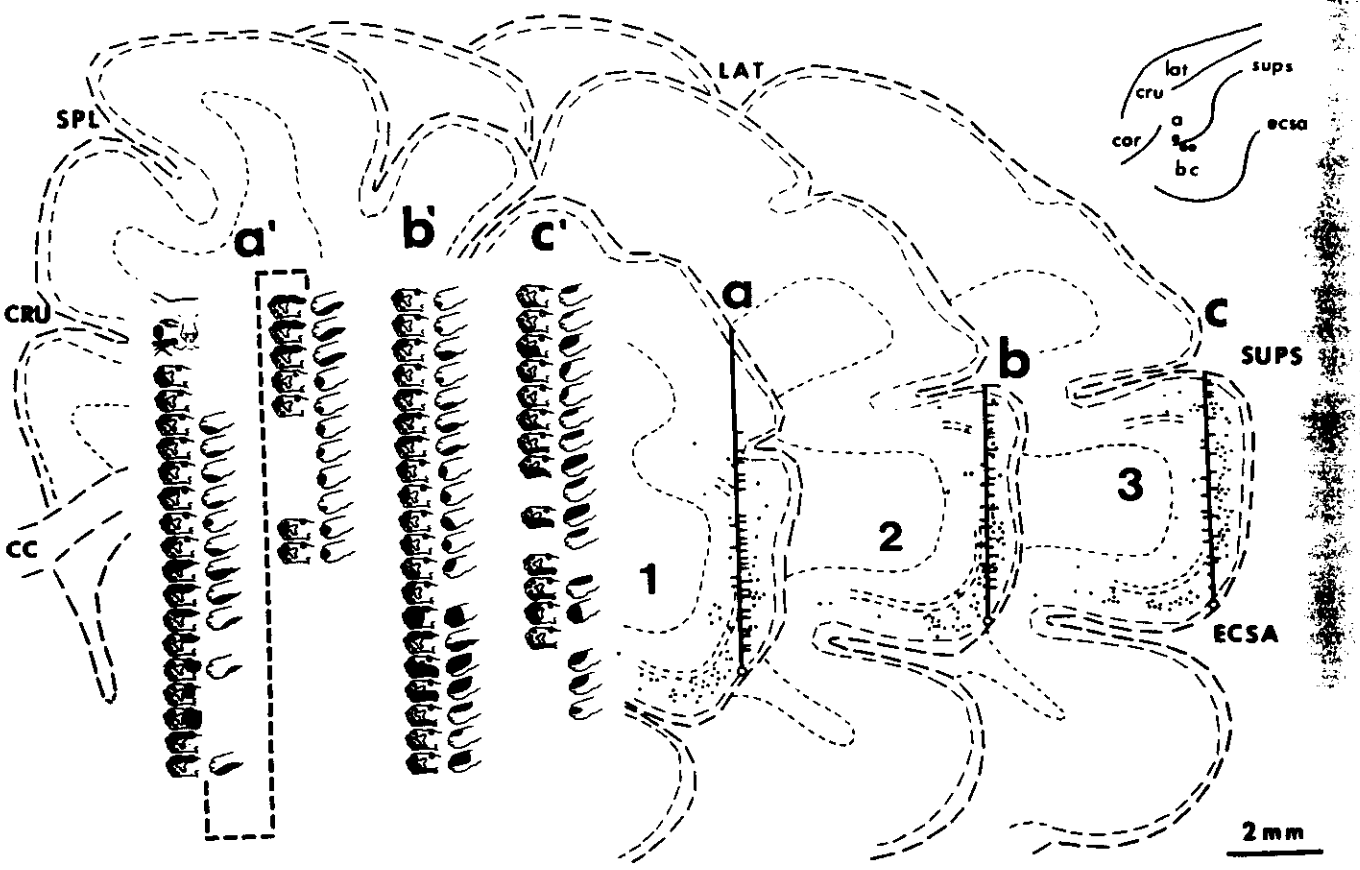

Figure 8. Relationship between the location of callosal neurons and the somesthetic representations in SII of the cat. Computer-microscope charts of coronal sections (80 μm thick, reacted with DAB) showing the distribution of HRP-labeled neurons (dots) and the reconstruction of three microelectrode penetrations performed 24 hr after injecting the HRP into the contralateral homologous area. Letters denote the beginning of each penetration, open circles the electrolytic lesion at the end. The microelectrode entered the brain at the positions indicated in the inset. Dashes along the electrode tracks correspond to the receptive fields, indicated by the filled surfaces on the sketches of cat paws (and head) and ordered in the sequence found during microelectrode advancement. In the sections, thin dashed lines denote the bottom of layers I, IV, V, and VI. From Caminiti *et al.* (1979).

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resenting the paws, and apparently corresponding to the two more lateral representations in SII, project heavily into the corpus callosum (compare Fig. 8 with Fig. 1 in Clemo and Stein, 1983). As already indicated by Jones and Powell (1968), the projection from SII reaches roughly homotopical portions of contralateral SII but not SI.

Combined anatomical and electrophysiological investigations in SI of the monkey have essentially confirmed that callosal connections of each of the three cytoarchitectonic fields of this area are restricted to the representations of body midlines and of the head, even though a few callosal neurons are also found in the hand representations, especially in area 2 (Killackey *et al.*, 1983a; see also Jones and Hendry, 1980). A similar approach has shown that the distal limb representations of the gray squirrel receive callosal afferents in SII but not in SI (Gould and Kaas, 1981).

The barrel field, the primary representation of the mystacial vibrissae in SI of rodents, sends a relatively weak projection to the corpus callosum; this projection seems to terminate in the homotopic area (White and DeAmicis, 1977). The primary representation of the mystacial vibrissae in the rat is also relatively acallosal (Wise and Jones, 1976; Akers and Killackey, 1978). In the rat, callosal terminations and callosal neurons surround individual barrels (each of which corresponds to one vibrissa) resulting in a tangential honeycomb pattern common also to the representations of other facial sinus hairs (Killackey *et al.*, 1983b). In the cat, several callosal axons were found to respond to stimulation of the whiskers (Innocenti *et al.*, 1974) and neurons within the whisker representations can be transsynaptically activated through the corpus callosum (Fadiga *et al.*, 1972). In the mouse, callosal neurons do not appear to hold preferential location with respect to the barrels (White and DeAmicis, 1977).

5.2.2. Motor Cortex

The relations of callosal connections to body representations have been usually found to be similar in motor and somatosensory cortex, i.e., in monkey primary motor cortex the hand area seems free, or relatively free, of callosal terminals (Pandya and Vignolo, 1971; Zant and Strick, 1978; Jones *et al.*, 1979; Gould *et al.*, 1983). Callosal connections originating and terminating in the hand representation were, however, traced by Goldman and Nauta (1977). Studies combining focal stimulation of motor cortex with the application of anterograde or retrograde tracers have confirmed the existence of homo- and heterotopic connections to, and from, the hand representation (Matsumura and Kubota, 1979; Jenny, 1979; Gould *et al.*, 1983). Jenny's work indicates that these connections arise from the representation of the thumb.

5.2.3. Auditory Areas

The proposition that in auditory cortex callosal connections may be denser in the regions of high-frequency representation and less dense or absent in the regions of low-frequency (2–12 kHz) representation (Diamond *et al.*, 1968) is difficult to substantiate with interanimal comparisons since there are multiple cortical representations of the cochlea and they vary in their precise location

(Merzenich *et al.*, 1975; Reale and Imig, 1980). In a combined anatomical and electrophysiological study of the high-frequency part of AI, Imig and Brugge (1978) have found that callosal connections are concentrated in the most dorsal parts of each isofrequency line but, apparently, this distribution cannot yet be related to the tonotopic organization of AI.

5.3. The Fine Organization of Callosal Connections

The first report of a discrete tangential organization of callosal connection of the sort now usually referred to as "columnar" (but see Cipolloni and Peters, 1979, for a discussion on terminology) was probably that of Heimer *et al.* (1967) showing the terminal distribution of callosal axons in rats subjected to ablations of large portions of neocortex.

A more detailed description of this pattern of termination came, however, from studies in somatosensory (Jones *et al.*, 1975) and motor cortex of the monkey (Künzle, 1976). "Columnar" distribution of callosal terminals was also described in sensory, motor, and association areas of monkeys, cats, and rats (Shanks *et al.*, 1975; Wise and Jones, 1976; Goldman and Nauta, 1977; Akers and Killackey, 1978; Imig and Brugge, 1978; Jenny, 1979; Jones *et al.*, 1979; Rockland and Pandya, 1979; Cipolloni and Peters, 1979; Fitzpatrick and Imig, 1980; Hartenstein *et al.*, 1980; Kelly and Wong, 1981; Segraves and Rosenquist,

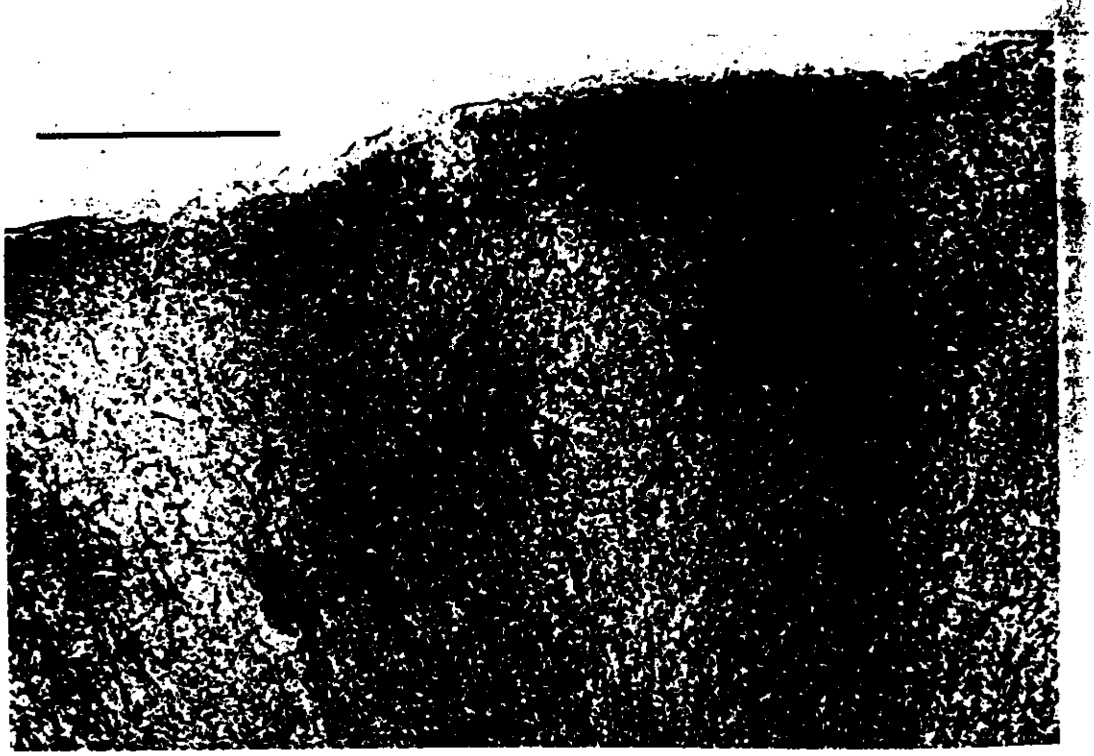

Figure 9. "Columnar" distributions of axon terminations in SII of the cat and of callosal neurons labeled by HRP injections in the contralateral homologous area. TMB reacted, 80-μm-thick coronal section. Bar = 500 μm.

1982b; Záborszky and Wolff, 1982; Caminiti and Sbriccoli, 1983). A discontinuous termination of callosal axons, parts of which could be described as "columnar," has been documented in the visual areas of monkeys (Van Essen and Zeki, 1978; Newsome and Allman, 1980; Van Essen *et al.*, 1982) and in the somatosensory areas of the squirrel (Gould and Kaas, 1981) and monkey (Killackey *et al.*, 1983a; see Fig. 30 of Chapter 4).

The callosal termination "columns" are 200 to 1000-μm-wide structures, perpendicular to the cortical surface and separated by empty spaces of approximately equal width (Figs. 9–11). When reconstructed from serial sections, or in tangential sections (Fig. 10), they appear to constitute systems of "bands" running tangentially through the cortex.

It should be emphasized that, in most of the cases where callosal connections have been documented by extensive tangential reconstructions, the regularity of the banding pattern shows great local variations. Individual "bands" can bifurcate or merge, sometimes into regions of more widespread termination. Along a "band," the density of terminals, their laminar location and tangential span can vary considerably. Consequently, it can become doubtful whether the pattern can still be accurately described as "columnar" or "striped." Indeed, different studies emphasize very differently the "columnarity" of the pattern of

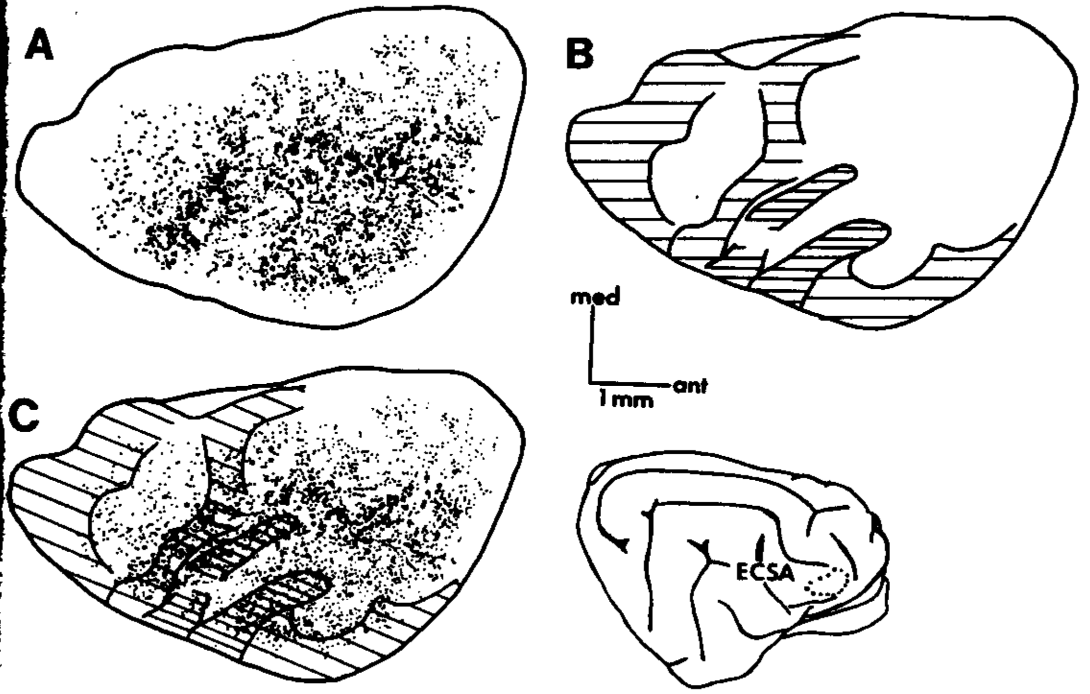

Figure 10. Tangential distributions of callosal neurons and of axon terminations in SII of the cat, labeled by an HRP injection in the contralateral homologous area. Reconstruction from three, superposed, tangential sections through layers III and IV (TMB reacted, 80 μm thick) of the region surrounded by dots in the brain inset. (A) Dots correspond to labeled neurons, large dots to heavily labeled ones. (B) Hatched "bands" correspond to regions containing labeled terminations; the density of anterograde labeling was particularly high in correspondence of the heavy hatching. (C) Superposition of A and B. From Hartenstein *et al.* (1980).

callosal termination in the same region (see Cipolloni and Peters, 1979, and Vaughan, 1983, for auditory cortex of the rat; Jones *et al.*, 1979, and Killackey *et al.*, 1983a, for somatosensory cortex of the monkey).

Beyond these semantic difficulties, the important question is whether the discontinuous distribution of callosal terminations correlates to other aspects of neocortical organization. Ipsilateral corticocortical connections also have the tendency to terminate in "columns" or "bands" (e.g., Jones *et al.*, 1975; Goldman and Nauta, 1977; Wong-Riley, 1979; Rockland and Pandya, 1979; see also Jones, this volume). In somatosensory and motor areas of the monkey, "bands" of callosal and ipsilateral corticocortical terminations partially interdigitate (Jones

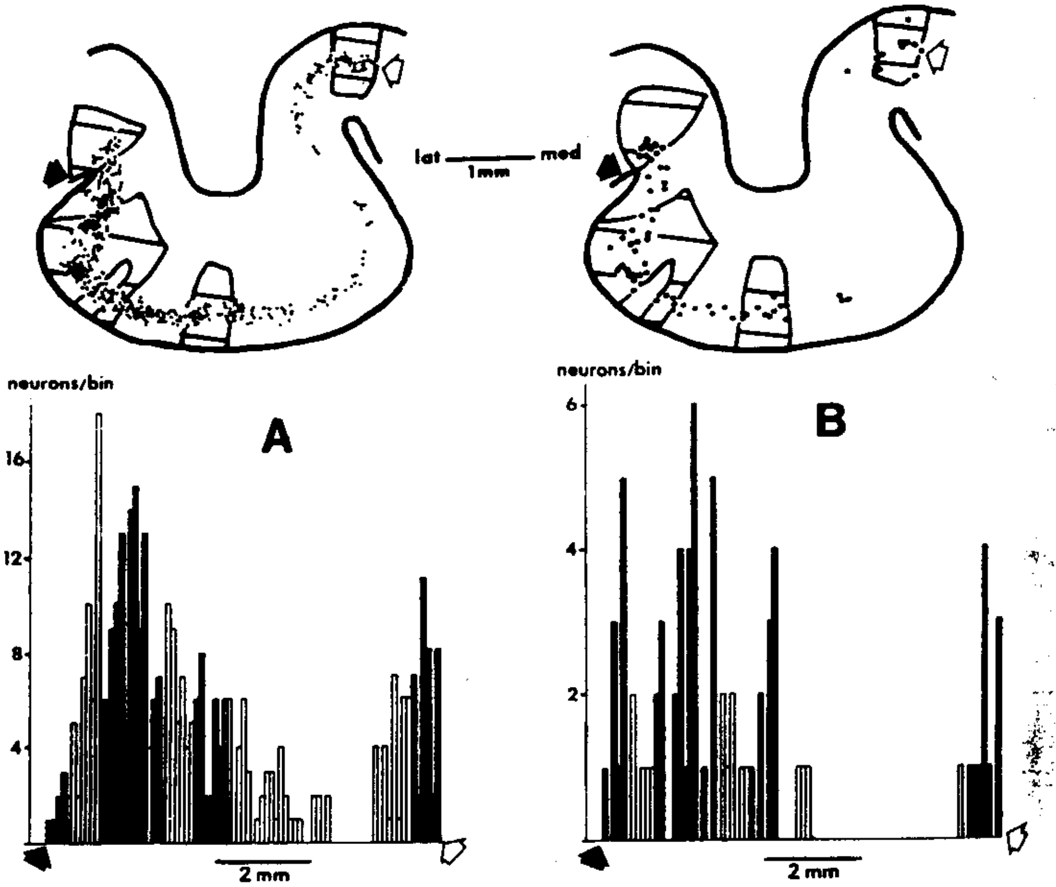

Figure 11. Relationship between callosal neurons (dots) and "columns" of callosal terminations (hatching) in SII of the cat, labeled by HRP injections in the contralateral homologous area. A and B represent the same coronal section (80 μm thick; TMB) but in A all the labeled neurons are shown, while B shows only those which were intensely labeled. The histograms were obtained by projecting the neurons onto a line running 400 μm deep and parallel to the pial surface and then counting the neurons over small segments of this line. The locations corresponding to the beginning and the end of the line are indicated by solid and open arrows, respectively. A higher proportion of labeled neurons is found within the columns (solid columns in the histogram) than between the "columns" and this is particularly striking when only the strongly labeled neurons are considered. Counts from several sections from this brain showed that 80% of the strongly labeled neurons were found within the "columns" while only 60% of all the labeled neurons were in this position. From Hartenstein *et al.* (1980).

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et al., 1979). Interdigitation is also found in frontal cortex of the monkey, between callosal and parietofrontal axons (Goldman-Rakic and Schwartz, 1982). It must be stressed that in both systems, the interdigitation is not perfect, i.e., some callosal and ipsilateral corticocortical "bands" overlap, or else the space between "bands" of one system is not, or is only partially, filled by terminations of the other system (see Figs. 14 and 15 in Jones *et al.*, 1979; Fig. 3 in Goldman-Rakic and Schwartz, 1982; Fig. 29 in Jones, this volume). Extensive overlap (rather than interdigitation) of callosal and ipsilateral association terminations has been observed in visual cortex of the monkey (Zeki, 1978; Van Essen *et al.*, 1982).

In somatosensory cortex of the rat, callosal "columns" interdigitate with the similarly discretely organized thalamocortical terminations (Wise and Jones, 1976; Akers and Killackey, 1978). Furthermore, the thalamic and callosal recipient zones are cytoarchitectonically different, i.e., the former are "granular" and the latter "agranular."

On the contrary, in visual cortex of the hedgehog (Gould and Ebner, 1978), in visual (Cusick and Lund, 1981), auditory (Vaughan, 1983), and cingulate (Vogt *et al.*, 1981) cortices of the rat, and in auditory cortex of the monkey (Pandya and Rosene, 1983), thalamic and callosal terminations both overlap and interdigitate in the tangential plane. In the studies mentioned above, as well as in visual (Lund *et al.*, 1981), somatosensory and motor (Sloper and Powell, 1979) cortex of the monkey, incomplete radial segregation of callosal and thalamic terminals has also been observed.

In auditory cortex of the cat, the "bands" of callosal terminations run roughly perpendicular to the isofrequency lines and correspond to aural dominance "bands," where neurons respond preferentially to the ipsilateral ear and/or responses from the two ears summate. These "bands" alternate with others, free of callosal terminals, where the contralateral ear is dominant and/or binaural responses are smaller than monaural responses (Imig and Brugge, 1978).

Probably the "bands" of callosal terminations in SII of the cat are related to representations of the ipsilateral body (Hartenstein *et al.*, 1980). In SII, callosal afferents impinge on neurons with bilateral receptive fields while neurons driven exclusively by contralateral receptive fields are not activated by the corpus callosum (Innocenti *et al.*, 1972; Robinson, 1973). Callosal afferents carry, almost exclusively, information from the side of the body ipsilateral to the site of termination of their axons (Innocenti *et al.*, 1973; Lepore *et al.*, 1983b), and the callosal input strongly contributes to the ipsilateral responses in SII (Innocenti *et al.*, 1973).

While, as discussed above, the notion of a "columnar" distribution of callosal terminals requires some qualification, it is far less clear to what an extent callosal neurons are also organized according to a similar, tangentially discontinuous, pattern. Clusters of callosal neurons have been described in somatosensory cortex of the rat (Wise and Jones, 1976; Ivy *et al.*, 1979) and monkey (Jones *et al.*, 1975, 1979): they can, in some experiments, be seen in suprasylvian cortex (Keller and Innocenti, 1981; Segraves and Rosenquist, 1982b) but not in the other visual areas of the cat. In SI of the macaque monkey, Jones *et al.* (1975, 1979) have found that the clusters of callosal neurons match the "columns" of callosal terminals. However, in the same region, in the macaque and the owl monkey, Killackey *et al.* (1983a) have emphasized the absence of clusters of callosal neurons or of "columns" of callosal terminals. Callosal neurons have a nearly continuous distribution in auditory cortex of the cat, but become more numerous in correspondence with the termination "columns" (Imig and Brugge, 1978; Imig *et al.*, 1982; but see Kelly and Wong, 1981, for a different interpretation). We have found a more widespread distribution of callosal neurons than of callosal terminals in SII of the cat (Hartenstein *et al.*, 1980; Figs. 10, 11) and a similar distribution exists in parietal cortex of the monkey (Caminiti and Sbriccoli, 1983, 1985). Interestingly, through, we found a better match between callosal neurons and terminals when we considered only the most strongly labeled callosal neurons (Figs. 10, 11). Finally, the discontinuous and locally "columnar" distribution of callosal terminals in visual cortex of the monkey is matched, with some exceptions, by a similar, although considerably more blurred, distribution of callosal neurons (Van Essen *et al.*, 1982).

In conclusion, the discrete organization of callosal terminations in most areas is not matched by an equally precise, discrete distribution of callosal neurons. This seems to imply that callosal connections are organized in a fine-grained convergent manner, a view which is strengthened by the clear-cut convergence–divergence exhibited by callosal connections during development (Innocenti and Clarke, 1984b).

There are some indications that, in rodents, callosal connections originating from supragranular and infragranular layers prefer to terminate, respectively, superficially and deep in the cortex (Jacobson and Trojanowski, 1974; Yorke and Caviness, 1975; Ribak, 1977; Vogt *et al.*, 1981). However, callosal axons which form their main terminal arbor in supragranular layers can give rise to a few collaterals in the deep layers (Hartenstein and Innocenti, 1981; Fig. 5).

5.4. Some Electrophysiological Correlates of Callosal Connections: Callosal Connections at the Cellular Level

The close correspondence between the distribution of callosal neurons and terminals has generated the hypothesis that callosal axons may originate and terminate on the same neurons (Wise and Jones, 1976; Jones *et al.*, 1979). Callosal axons have indeed been found to form synapses on callosal neurons in the primary motor representation of the vibrissae in the mouse (Porter *et al.*, 1983) but were not found in somatosensory cortex of the monkey (Hendry and Jones, 1983).

Three, not mutually exclusive models of the cellular organization of callosal connections are conceivable. I will call them the reciprocal, the homologous, and the heterologous models (Fig. 12). Which of these models may actually be the case is of paramount importance to the understanding of information processing between the hemispheres.

Presently, only the anatomical results of Porter *et al.* (1983) support either the reciprocal or the homologous model. Most electrophysiological results support the heterologous model.

In particular, inhibitory responses (Hossmann, 1969) are elicited disynaptically across the corpus callosum (Toyama *et al.*, 1969, 1974; Innocenti *et al.*, 1972) in different areas of the cat. In agreement with the observation that callosal

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axons terminate exclusively with asymmetrical, hence probably excitatory, synapses (see Section 4), it was proposed that they generate inhibitory responses by synapsing with local inhibitory interneurons (Toyama *et al.*, 1969; Innocenti *et al.*, 1972; Toyama and Matsunami, 1976; Innocenti, 1980). It has also been proposed that in visual cortex of the cat such interneurons may be stellate cells with smooth dendrites (Innocenti, 1980). Indeed, it was recently found that the layer III–IV "basket cell," a neuron type forming symmetrical, hence probably inhibitory synapses with pyramidal cells, can be monosynaptically activated by transcallosal stimulation (Somogyi *et al.*, 1983). Inhibitory neurons, however, are probably not the only target of callosal axons. Callosal transection modifies responses of neurons in the superior colliculus probably because it interrupts a calloso-cortico-collicular pathway (Antonini *et al.*, 1979). In fact, neurons projecting from visual cortex to superior colliculus are excited by electrical stimulation of the callosal pathway (Toyama *et al.*, 1974; Singer *et al.*, 1975).

The reciprocal and homologous models are incompatible with the finding that, at least in the 17/18 region of the cat (Toyama *et al.*, 1974; Harvey, 1980; Innocenti, 1980) and of the rabbit (Swadlow, 1974), very few, if any, callosal neurons, identified by antidromic invasion, can also be transsynaptically activated by electrical stimulation of the callosal pathway. Furthermore, these neurons might be activated by the antidromically invaded local collaterals of callosal axons rather than by callosal afferents (Feeney and Orem, 1971; Innocenti, 1980). The transsynaptic, excitatory responses of callosal neurons to callosal stimulation observed *in vitro* in cingulate cortex of the rat (Vogt and Gorman, 1982) could also be explained in this way. Obviously, similar objections can be extended to many of the studies where excitatory transsynaptic responses were obtained by electrical stimulation of cerebral cortex or of the callosum itself; for example, the early findings of transcallosal activation of the pyramidal tract (Asanuma and Okamoto, 1959), or the recent report of transcallosal activation of corticothalamic neurons (Diadori *et al.*, 1983).

Two other arguments support the heterologous model. First, neurons transsynaptically activated through the corpus callosum are found through all cortical

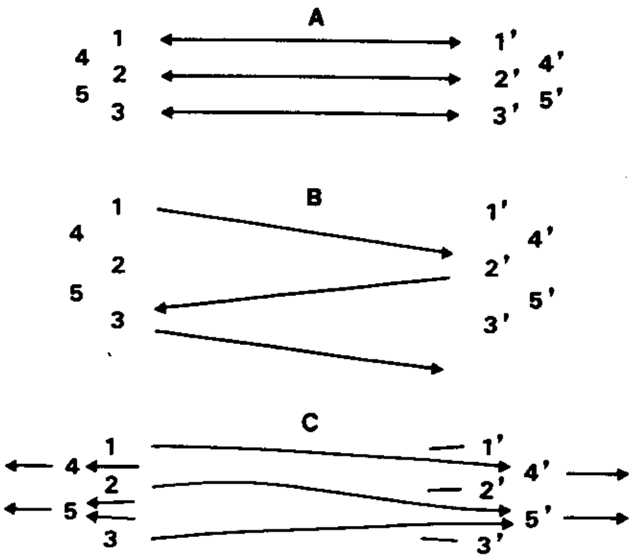

Figure 12. Three models of callosal connectivity. Neurons in the two hemispheres are represented by two groups of numbers; 1–3 and 1'–3' are callosal neurons; 4 and 5, and 4' and 5' do not project into the corpus callosum. (A) The reciprocal model: callosal neurons are reciprocally interconnected; (B) the homologous model: callosal neurons are interconnected, but not reciprocally; (C) the heterologous model: callosal neurons project to the noncallosal neurons. Connections between the two hemispheres are probably symmetrical, but in B only half of the connections are drawn, and in C one set of connections is denoted by interrupted arrows.

layers (Harvey, 1980; Innocenti, 1980), consistent with the laminar distribution of callosal afferents and differently from callosal neurons. Second, in the cat, both somatosensory and visual callosal neurons have much smaller receptive fields than the neurons activated transsynaptically through the corpus callosum (Innocenti *et al.*, 1972; Robinson, 1973; Harvey, 1980; Innocenti, 1980); furthermore, in visual cortex, the latter neurons have, as a rule, "complex" receptive fields while some callosal neurons have "simple" receptive fields (Hubel and Wiesel, 1967; Shatz, 1977a; Innocenti, 1980; Lepore and Guillemot, 1982). In the rabbit, neurons transsynaptically activated through the corpus callosum, unlike callosal neurons, can be activated by diffuse illumination (Swadlow, 1974).

6. Function of Callosal Connections

The role of callosal connections in behavior and some of the underlying electrophysiological events have been excellently reviewed (Bremer *et al.*, 1956; Berlucchi, 1972, 1981; Doty and Negrao, 1973; Gazzaniga and Ledoux, 1978; Sperry, 1982; Elberger, 1982; Berlucchi and Antonini, 1986), and need no reiteration here. Briefly, interruption of the corpus callosum in man and animals has demonstrated that this structure integrates sensory and motor performances of the two hemispheres. These integrative functions have an electrophysiological correlate in neurons whose response properties depend on callosal input. Such neurons have, thus far, been best documented in the visual and somatosensory areas (see below).

The question I want to consider here is whether a single theoretical construct can accommodate the structural and functional aspects of callosal organization in different areas and species.

The leading view of the morphofunctional organization of callosal connections is, what I will call, modifying the terminology of Blakemore *et al.* (1983): the hypothesis of peripherally homeomorphic integration. This hypothesis, which disposed of the so-called Fleschig rule (see Berlucchi, 1972), derives from studies on the visual system (Choudhury *et al.*, 1965; Hubel and Wiesel, 1967; Berlucchi *et al.*, 1967), and was later extended to the somatosensory system (Jones and Powell, 1968). I will divide the hypothesis into three independent elements: (1) callosal connections integrate the hemirepresentations of the periphery in the two hemispheres; (2) the integration conforms to rules of homeomorphism between the peripheries and their central representations. Thus, callosal connections reestablish continuity along the lines which split the peripheries into two halves, each connected exclusively, or preferentially, with a different hemisphere. This aspect of callosal organization is usually known as the "midline rule." (3) The callosal input provides cortical neurons with information they do not (or do not fully) receive from the thalamus.

All elements of the hypothesis apply perfectly well to the findings that visual and primary somatosensory (and probably motor) (Section 5.2) callosal connections run exclusively (or preferentially) between regions representing the "midlines" of the respective peripheries. Furthermore, neurons in the primary visual areas of the cat (Berlucchi and Rizzolatti, 1968; Lepore and Guillemot, 1982), as well as in higher-order areas of cat (Antonini *et al.*, 1983) and monkey (Gross *et al.*, 1977), have bilateral receptive fields whose ipsilateral halves depend on the callosal input.

At first glance, the hypothesis of peripherally homeomorphic integration seems to emphasize the reconstruction, by callosal connections, of the spatial continuum of the periphery, while disregarding other functions of callosal connections. However, the hypothesis implicitly predicts that the input from the callosum may be responsible not only for a portion of a neuron's receptive field, but also for other response properties of neurons. In fact: "[Callosal fibers] might be expected to serve the same functions as intracortical fibers linking cells with receptive fields clustered in other, more outlying parts of the visual fields" (Hubel and Wiesel, 1967). Callosal connections play a role in coarse stereopsis (Blakemore, 1969), and this suggests that they should also be, to some extent, responsible for the binocularity of cortical neurons. The binocularity of cortical neurons does indeed depend on callosal input in areas 17 and 18a of the albino rat (Diao *et al.*, 1983) and in lateral suprasylvian visual areas of the Siamese cat (Marzi *et al.*, 1980, 1982; Zeki and Fries, 1980). In the same areas of normal cats, however, binocularity is not modified by callosal transection (Marzi *et al.*, 1980, 1982, Zeki and Fries, 1980). And the direct (Payne *et al.*, 1980; Blakemore *et al.*, 1983) evidence for a callosum-dependent binocularity of neurons in the 17/18 region of the cat, although indirectly supported by the results of Dreher and Cottee (1975) and Lepore *et al.* (1983a), is highly controversial (Elberger and Smith, 1983; Berlucchi and Antonini, 1986).

The second element of the hypothesis of peripherally homeomorphic integration seems, however, too restrictive. It is unclear whether the "midline rule" can be extended to the auditory callosal connections because auditory cortex seems organized according to frequency of sound and side of the receptor organs, rather than in terms of auditory space. Furthermore, the organization of several areas, most typically the "associative" areas, probably does not have a direct counterpart in the spatial organization of the periphery. But, more important, the periphery is not represented in a homeomorphic manner everywhere in the cortex, since in certain areas neurons can have discontinuous or multimodal receptive fields (e.g., Rizzolatti *et al.*, 1981a,b; see also below). There is no reason why callosal connections should, in these areas, conform to rules of peripheral homeomorphism and, in fact, they do not. One of these areas is the complex of somesthetic representations traditionally called SII where discontinuous receptive fields, often symmetrical on the two body halves, were found in cats and monkeys (Whitsel *et al.*, 1969; Robinson, 1973; Clemo and Stein, 1983). The callosal connections of these areas in the cat clearly violate the "midline rule."* On the other hand, callosal connections obey organizing principles which are not obviously or directly imposed on an area by the spatial

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* The distal extremities seem to violate the principle of homeomorphism between the periphery and their central representations by virtue of (1) their callosal connections and (2) the fact that many of the discontinuous receptive fields found in various areas include the distal part of the extremities. These violations may be imposed by the great motility of the extremities (Caminiti *et al.*, 1979) and may provide the conditions for a stimulus equivalence across somatosensory periphery translations analogously to what seems to occur in the visual system (see below).

properties of the periphery it represents. For example, in the visual areas of the cat, callosal afferents match their targets not only for position, but also for orientation and direction specificity of the receptive fields (Berlucchi and Rizzolatti, 1968; Lepore and Guillemot, 1982; Antonini *et al.*, 1983).

A way to circumvent the difficulties raised by the second element of the hypothesis of peripherally homeomorphic integration may come from trying to understand the organization of callosal connections within the broader framework of corticocortical connectivity, as prompted by Hubel and Wiesel's statement quoted above. There seem to be profound similarities in the anatomical and functional organization of callosal connections and of the intrahemispheric corticocortical connections (see, e.g., Gross and Mishkin, 1977; Innocenti, 1980; Van Essen *et al.*, 1982). And one would expect that both types of connections should similarly obey, or violate, the strict peripheral homeomorphism.

The functional similarity of callosal and intrahemispheric connections has been emphasized by the following statement of Gross and Mishkin (1977) "... interhemispheric transfer of visual habits is a special case of stimulus equivalence across retinal translation ..." This statement was based on the observation that, in inferotemporal cortex of the monkey, neurons which receive callosal afferents have large receptive fields and, although extraordinarily selective for certain aspects of stimulus organization, are equally responsive to the stimulus throughout their receptive fields. These neurons receive the ipsilateral half of their receptive fields from visual areas in the other hemisphere via the corpus callosum, and the contralateral half of their receptive fields from the convergence of intrahemispheric corticocortical afferents (Gross *et al.*, 1977; Gross and Mishkin, 1977).

The "complex" receptive fields of neurons within areas 17 and 18 of the cat, although much smaller than those found in inferotemporal cortex of the monkey, seem similarly capable of detecting a stimulus irrespective of its precise position (Hubel and Wiesel, 1962). Neurons with this type of receptive field have long been suspected to be the target of intracortical projections, and they are also the main target of callosal afferents (Innocenti, 1980; Lepore and Guillemot, 1982), as Hubel and Wiesel (1967) predicted. In the somatosensory areas of the cat, neurons receiving callosal input also have large, usually bilateral receptive fields (Innocenti *et al.*, 1972), and the responses to the ipsilateral part of the receptive field largely depend on the callosal input (Innocenti *et al.*, 1973). The same type of cell also receives association afferents from ipsilateral SI (Manzoni *et al.*, 1979).

While, in the examples mentioned above, callosal connections seem to be involved in generalizing stimulus detection across the sensory midlines, this may not be their only function. Callosally mediated inhibition has been demonstrated in VIV of the macaque (Moran *et al.*, 1983). This mechanism may be similar to the "surround inhibition" generated by intrahemispheric connections, possibly in order to improve stimulus detection (Mountcastle and Powell, 1959).

In conclusion, the aspects of callosal organization discussed in this section justify the metaphore used in the Introduction by pointing to a general integrative role for interhemispheric connections. Inter- and intrahemispheric connections probably perform similar tasks and obey similar organizing principles, but these may be different in different areas, depending upon the rules according

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to which the various areas are organized. One way to identify these principles may be to study what dictates the organization of callosal connections in development.

7. The Development of Callosal Connections

The macroscopic development of the corpus callosum in early embryogenesis has been a classic theme of neuroembryology (see, e.g., Zuckerkandl, 1909; Hewitt, 1962; Auroux, 1964; Rakic and Yakovlev, 1968; for other references see also Silver *et al.*, 1982). Attention has also been focused on myelination of the corpus callosum (Grafstein, 1964; Yakovlev and Lecours, 1967; Fleischhauer and Wartenberg, 1967; Seggie and Berry, 1972; Looney and Elberger, 1983) and on some electrophysiological aspects of callosal development (Ulett *et al.*, 1944; Meyerson, 1968; Shofer and Purpura, 1972; Seggie and Berry, 1972). During the last few years, though, attention has shifted to the development of callosal connections as a model for studying the mechanisms underlying the development of interneuronal connections (as opposed to connections with the sensory or motor periphery) in mammals and, in particular, of neocortical connections.

As outlined in the preceding sections, the callosal connections constitute a complex network whose organization is only partially known. These are not the qualities one usually requires in an experimental model. Nevertheless, while the study of "simple" models of neuronal connections is undoubtedly unveiling elegant developmental mechanisms, the crucial question for understanding the development of the mammalian brain is to what extent the complexity of a neuronal network imposes different developmental mechanisms from those which underlie the development of simpler neuronal connections. Alternatively, the development of a "complex" network may exaggerate mechanisms already expressed in "simpler" systems; these mechanisms thus become easier to study.

Needless to say, the work on the development of callosal connections has thus far generated more questions than it has answered. In some cases, however, at least some of the possible answers to these questions can be ruled out.

7.1. What Causes Cortical Neurons to Send an Axon through the Corpus Callosum?

Thus far, callosal neurons have been identified by retrograde tracers only at relatively late stages of development, i.e., usually during the first few postnatal days when their axons have already reached the white matter of the contralateral hemisphere.

At these stages, callosal neurons are found at roughly the same restricted radial positions as in the adult (Innocenti *et al.*, 1977; Innocenti and Caminiti, 1980; Chow *et al.*, 1981; Ivy and Killackey, 1981; Feng and Brugge, 1983). However, the relative contribution of the different layers of a given area to the corpus callosum is not necessarily the same as in the adult (Innocenti *et al.*, 1977; Ivy and Killackey, 1981). Young callosal neurons have immature dendritic trees (Jacobson and Trojanowski, 1975; Innocenti *et al.*, 1977; Ivy and Killackey, 1981); they are also smaller than in the adult and furthermore, at least in the cat, the important size difference between callosal and noncallosal neurons, which is characteristic of the adult, has not yet been expressed (Innocenti and Caminiti, 1980). Nevertheless, the same types of neurons which send an axon across the corpus callosum in the adult do so in newborn kittens (Innocenti *et al.*, 1977; Innocenti and Caminiti, 1980).

One important question is which neurons are the first to send an axon through the corpus callosum, because these early axons may function as a guide for later growing ones. In parietal cortex of the rat, the first callosal neurons become labeled after contralateral injections on postnatal day (pd) 2–3; these

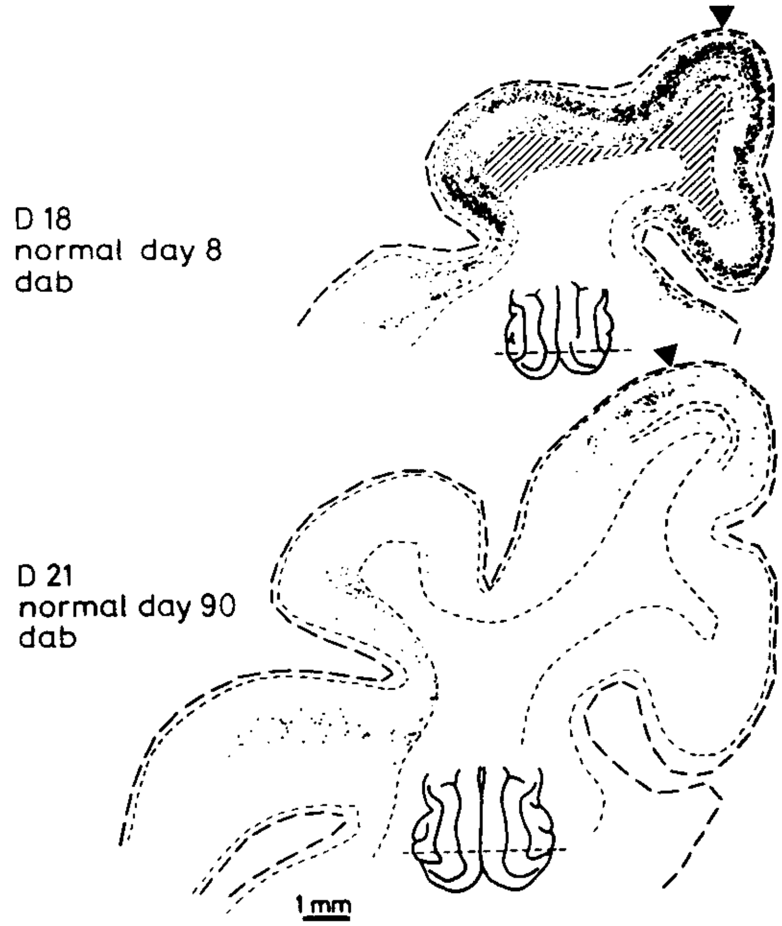

Figure 13. Computer-microscope charts showing the distribution of callosal neurons (dots) labeled by homotopic HRP injections in two normal kittens (D18 and D21), respectively 8 and 90 days old at the time of injection. Thin dashed lines mark the bottoms of layers I, IV, V, and VI. Triangles point to the borders between areas 17 and 18. The hatched portion of the white matter in D18 contains a high density of neurons. The sections were 80 μm thick, at the levels indicated in the brain insets. From Innocenti and Frost (1979).

neurons are in two separated laminae which were identified as layers III and V (Jacobson and Trojanowski, 1975; Wise and Jones, 1976). A later study has, instead, suggested that these laminae are layers Va and Vc–VIa (Ivy and Killackey, 1981). Because these early labeled callosal neurons lie in the cortical subplate, this interpretation is consistent with the notion that the subplate is the forerunner of layers V and VI (Rice, 1975; Rice and Van der Loos, 1977).

Unlike the radial distribution, the tangential distribution of callosal neurons is profoundly different in newborn and adult animals. The wide regions devoid of callosal efferents, which are characteristic of primary visual and somatosensory cortices in adult cats, contain callosal neurons in newborn kittens (Innocenti *et al.*, 1977; Innocenti and Caminiti, 1980; Figs. 13, 14). Indeed, in all other areas and/or species studied, callosal neurons are, at birth, distributed continuously through the cortex instead of discontinuously as in the adult (Wise and Jones, 1976; Ivy *et al.*, 1979; Ivy and Killackey, 1981; Feng and Brugge, 1983), or they are at least more widely distributed than in the adult (Rao, 1979; Chow *et al.*, 1981).

The transitory callosal projections are eliminated in the early postnatal period. In both rats and cats, the main part of the elimination immediately precedes the myelination of the corpus callosum and it is simultaneous with a quick phase of cortical synaptogenesis (see Fig. 15). There is probably more than a casual correlation between these three events, which may allow the prediction of the period of more active elimination of callosal connections in man (Innocenti, 1981a; Fig. 15).

The property of some retrograde fluorescent tracers of remaining in the neurons for a long period of time was used to determine that the loss of callosal

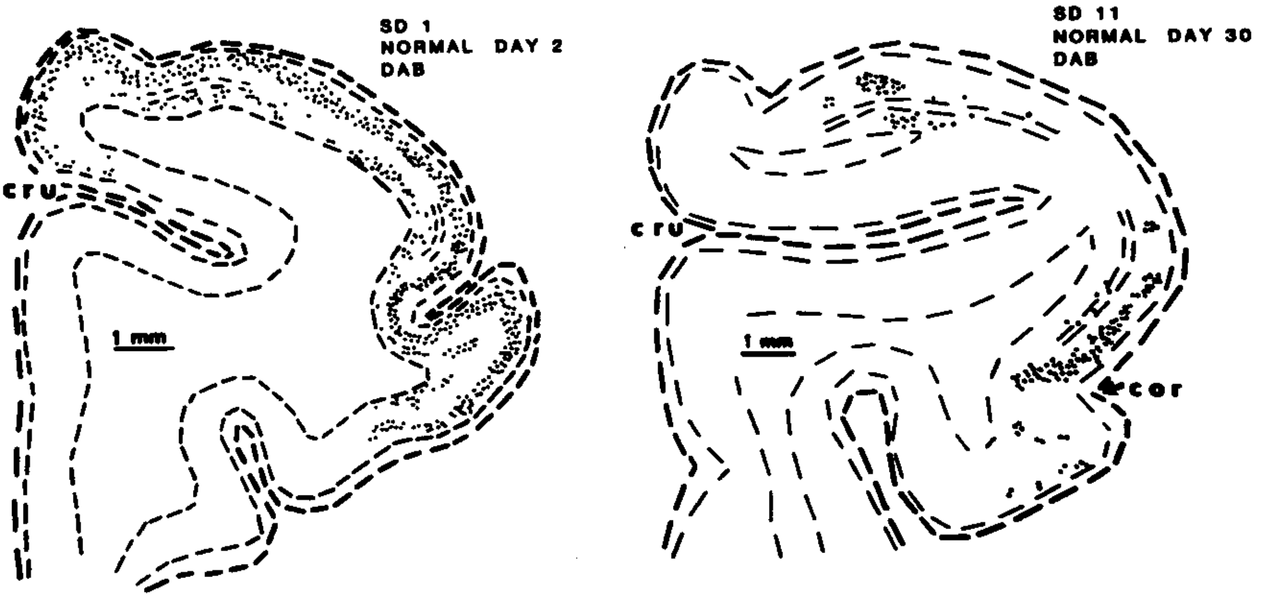

Figure 14. Computer-microscope charts showing the distribution of callosal neurons (dots) labeled by a large HRP injection centered on contralateral SII in two normal kittens (SD 1 and SD 11), respectively 2 and 30 days old at the time of injection. Thin dashed lines mark the bottoms of layers I, IV, V, and VI. The sections were 80 μm thick, reacted with DAB. cru, Cruciate sulcus; cor, coronal sulcus. From Innocenti and Caminiti (1980).

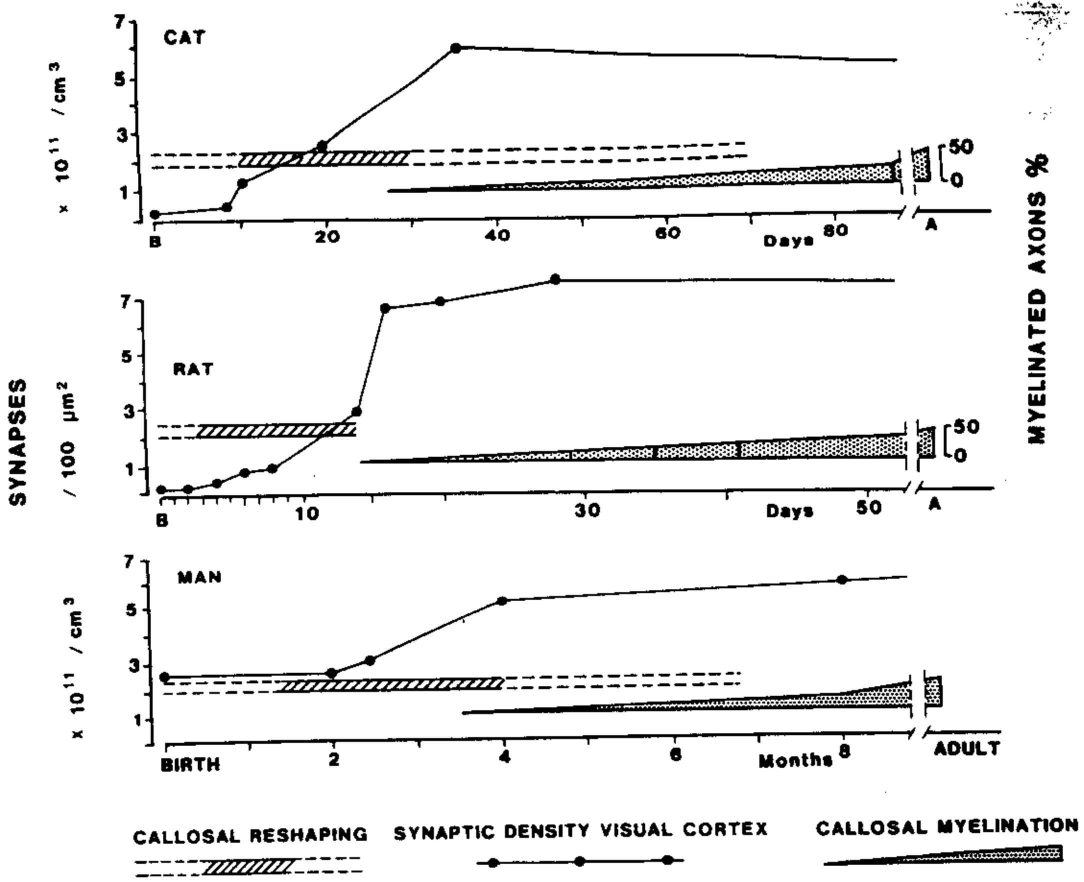

Figure 15. Time relationship between callosal reshaping, changes in synaptic density in visual area 17, and myelination of the corpus callosum. The data on myelination are from Grafstein (1963), Fleischhauer and Wartenberg (1967), Yakovlev and Lecours (1967), and Seggie and Berry (1972). Preliminary data by Looney and Elberger (1983) indicate that myelination of the corpus callosum in the cat may begin a few days earlier than indicated here. The data on synaptic density are from Cragg (1975), Huttenlocher *et al.* (1982), and Blue and Parnavelas (1983). The slopes of the synaptic density diagrams to the right of the last plotted points were determined according to experimental points falling off the scale. The period of the most intense loss of juvenile callosal connections in cat (Innocenti and Caminiti, 1980) and rat (Ivy and Killackey, 1981) is marked by a hatched bar; in cat visual cortex, this period is followed by a less massive elimination whose end was not precisely timed (dashed lines); in both rat and cat, some elimination may actually have begun earlier than thus far detected (dashed lines). The period of callosal reshaping indicated for man is hypothetical and is based on the assumption that it bears similar relationship to callosal myelination and fast synaptogenesis as in the two other species.

afferents from specific portions of cortex consists of elimination of axons without (or with negligible) neuronal death. Neurons labeled in the medial bank of area 17 by neonatal injections of Fast Blue in the contralateral hemisphere are still visible several weeks after this part of the cortex has lost access to the corpus callosum (Innocenti, 1981a; Fig. 16). Similar experiments and results have led to identical conclusions for the elimination of callosal axons from parietal cortex of the rat (O'Leary *et al.*, 1981; Ivy and Killackey, 1982).

Thus, it appears that some cortical neurons send a transitory axon through

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the corpus callosum and that they will then eliminate this axon and form permanent connections within the ipsilateral hemisphere, probably in cortical areas (see Ivy and Killackey, 1982). It is so far unclear whether these neurons send, from the beginning, an axon collateral to the area where they will form their permanent connections or whether they will grow a new axon following elimination of the callosal one. The transitory callosal axons may be phagocytosed by macrophages (Innocenti *et al.*, 1983a,b).

Neocortical neurons seem to decide at an early stage whether to send an axon through the corpus callosum or to the ipsilateral hemisphere. Retrograde transport studies using simultaneous injections of different retrograde tracers in the two hemispheres of newborn cats and fetal monkeys have so far indicated that in any given area, different neurons project inter- or intrahemispherically (Schwartz and Goldman-Rakic, 1982; Innocenti and Clarke, 1983) although, as in adults, a few neurons send bifurcating axons to both hemispheres. Most importantly, different neurons project to corresponding areas in the two hemispheres or to different areas in the contralateral hemisphere (Innocenti and Clarke, 1983), which suggests that the factors which induce an axon to cross the corpus callosum may be different from those determining its choice of an area.

The findings discussed above suggest that what causes some axons to grow through the corpus callosum must be a common character of a set of cortical neurons or, most probably, a factor from the neuronal "milieu" acting selectively on a set of neurons with a common character. This factor, or character, acts independently of whatever will determine which neurons form permanent callosal connections, although it is obviously a necessary condition for the latter event to occur.

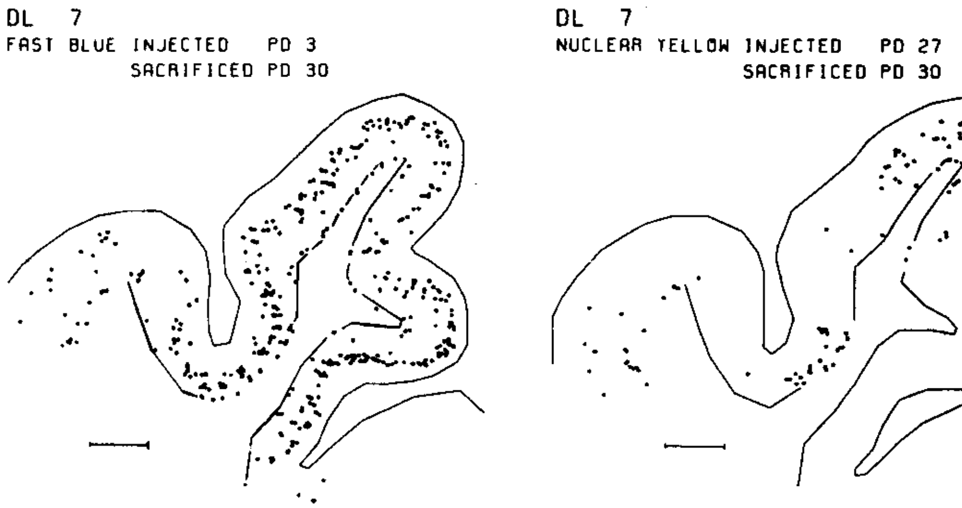

Figure 16. Elimination of callosal axons in the course of normal development. Computer charts of the distribution of labeled neurons in the lateral gyrus (areas 17, 18, 19) of a 30-day-old kitten by a Fast Blue injection on postnatal day 3 and by a Nuclear Yellow injection on postnatal day 27; both injections were placed in the contralateral areas 17 and 18. Note that neurons labeled by the first injection have a widespread distribution while neurons labeled by the second injection have a restricted distribution, indicating that many of the neurons labeled by the first injection have eliminated their callosally directed axon. Modified from Innocenti (1981a).

What could such a factor or character be? As mentioned above, both transitory and permanent callosal neurons occupy a specific and, in general, superficial radial location in the cortex. This probably means that callosal neurons are generated over a restricted, and late, period of gestation (Angevine and Sidman, 1961; Rakic, 1974). The fact that in rats prenatal X-ray irradiation, which destroys selectively supragranular layers, also eliminates the callosal projection from the otherwise nearly intact infragranular layers, may suggest (but other interpretations are possible) that late generation is an important characteristic of the callosal neurons, including those in the deep layers (Jensen and Altman, 1982). That a neuron's choice of the callosal pathway may depend on its time of generation, rather than its radial position, is more strongly suggested by the finding that in reeler mice the callosal neurons are radially malpositioned, but their date of birth is probably similar to that of callosal neurons in normal mice (Caviness and Yorke, 1976; Caviness, 1982). Interestingly, the receptive field properties of the callosal neurons in reeler mice are also similar to those in normal mice (Simmons and Pearlman, 1983), which suggests that callosal neurons in the reeler may also receive normal afferents.

An answer to the question of which factor induces a cortical neuron to send an axon into the corpus callosum, may come from studying the interaction of growing callosal axons with elements along the pathway between the hemispheres. Interest in this aspect of callosal development arose as a consequence of the attention given to the possible role of glial elements in directing axonal growth (Singer *et al.*, 1979). A bridge of glial elements (a "sling") seems to form, rostral to the *lamina terminalis*, before callosal axons cross the midline (Silver *et al.*, 1982). The hypothesis that the formation of a cellular bridge at the midline precedes and conditions that of the corpus callosum is not new (for references see Auroux, 1964). However, this hypothesis is now supported by the following observations: (1) surgical interruption of the "sling" leads to callosal agenesis in mice (Silver *et al.*, 1982) and hamsters (Lent, 1983); (2) the sling does not form in the acallosal mutant mouse (BALB/cCF; Wahlsten, 1974) or in the opossum (Silver *et al.*, 1982); and (3) a glia-covered scaffold, placed between the hemispheres after the sling has been sectioned, allows at least some callosal axons to cross the midline (Silver and Ogawa, 1983).

The question arising is, in my opinion, whether the "sling" directs callosal axons across the midline in the manner that induces axons, possibly specifically certain axons, to cross and maybe even profoundly influences their future trajectory. Alternatively, the sling may just be a permissive pathway condition. The electron microscopic (Valentino and Jones, 1982) and immunohistochemical (Valentino *et al.*, 1983) visualizations of astrocytic processes seem to support the second interpretation. The astrocytic processes seem to lack the orderly orientation which would be expected if they were to direct the trajectory of growing callosal axons.

7.2. What Directs Callosal Axons to a Given Area?

Retrograde transport studies using simultaneous injections of different retrograde tracers, in different visual areas of the same hemisphere, have indicated

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that in newborn kittens, different callosal neurons project to different areas (Innocenti and Clarke, 1983, 1984b) although, as in adults (Segraves and Innocenti, 1982), a few neurons send bifurcating axons to more than one area. This early differentiation of the cortical output to the callosum is found also in those parts of visual areas which will normally lose access to the corpus callosum (Innocenti and Clarke, 1983). Thus, neurons which have sent an axon to the corpus callosum, seem also to choose, early and specifically, a certain target area. It should be emphasized that the interpretation that *different* factors determine (1) which brain side and (2) which areas a neuron will project to, rests on the observation that, in newborn animals, different neurons project from a given area to corresponding areas in the two hemispheres, and on the assumption that these areas are identical in all respects but for their laterality in the brain.

Do these results imply that the pattern of area-to-area connections, typical of the adult, is established from the beginning even though parts of the connections between certain areas will be eliminated?

Indications that this may not be the case came from an electron microscopic study (Fig. 17) where we estimated the loss of callosal axons in development. The postnatal loss of callosal axons in the cat is at least 70% (Koppel and Innocenti, 1983; Fig. 18). While this loss is probably a low estimate of the real one (for discussion see Koppel and Innocenti, 1983), it seems much too large to be accounted for simply by the creation of acallosal portions of neocortex. Since the retrograde transport studies mentioned above speak against an excessive,

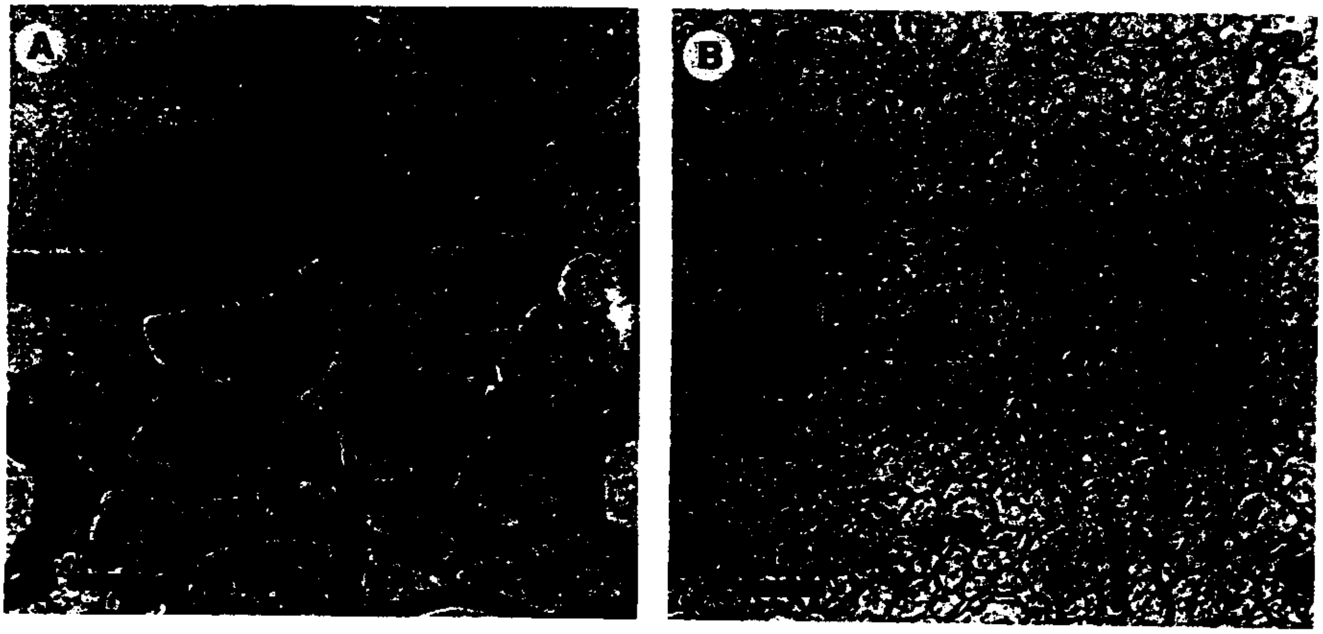

Figure 17. Electron micrographs of parasagittal sections of the cat corpus callosum (rostrum). (A) Adult animal, showing myelinated and unmyelinated axons; (B) newborn animal, showing large numbers of small axons interspersed with a few larger axons. Glial processes are clearly distinguishable from axons, both on account of their profiles (which are irregular, tortuous, and often extensive) and their cytoplasm: astrocytes (arrows) contain clear cytoplasm and prominent glycogen granules. Sections (50–100 nm) mounted on Pioloform-coated slot grids and stained with lead citrate. Bars = 0.5 μm. From Koppel and Innocenti (1983).

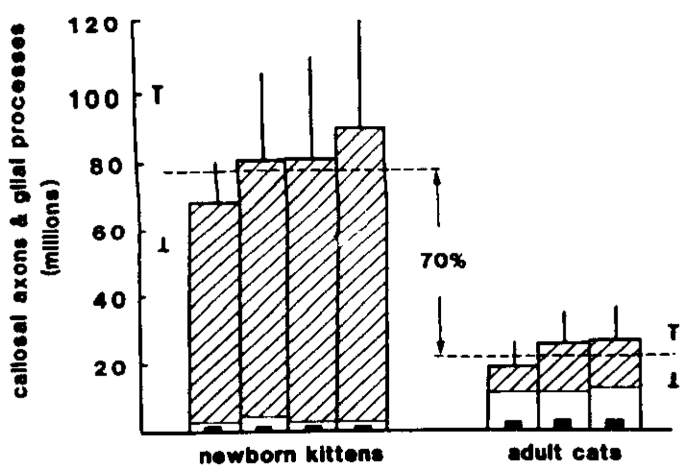

Figure 18. Histogram showing total numbers of elements per corpus callosum at birth and at maturity. The bars, indicating total axon numbers (with the standard deviations represented by vertical lines), have been subdivided; in the newborn animal the large (diameter > 0.5 μm) and small axons are represented by open and hatched sectors, respectively, while in the adult the same conventions denote unmyelinated and myelinated axons. The solid rectangles represent numbers of glial processes. Mean numbers of axons for each age group are indicated by the dashed horizontal lines and their standard deviations by the two pairs of "T's" on the left and right of the histogram. From Koppel and Innocenti (1983).

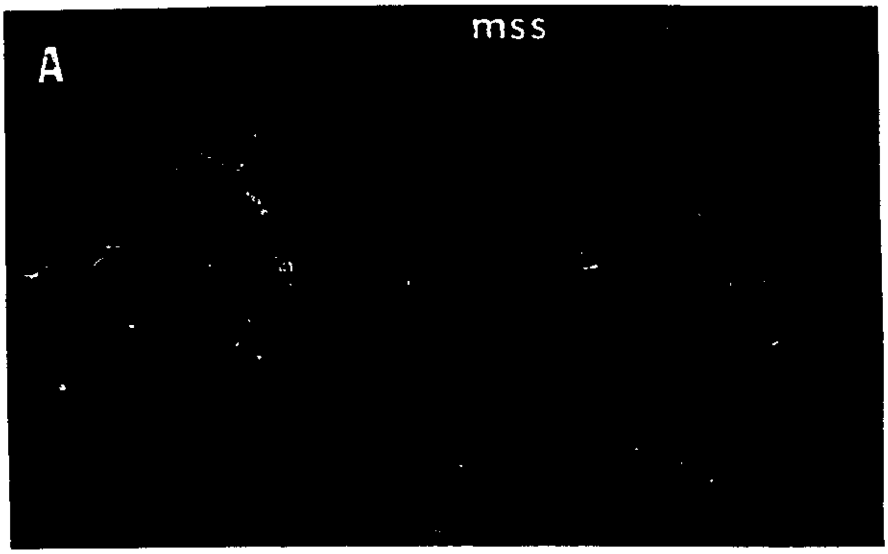

Figure 19. Lateral view photographs of two kitten brains showing the distribution of neurons retrogradely labeled by Fast Blue (solid dots) or Diamidino Yellow (open dots). A and B are from the same animal (DL 39; injected on day 2½, sacrificed on day 9½). A is the hemisphere ipsilateral and B the hemisphere contralateral to a Fast Blue injection in the caudal part of areas 17/18 (the center of injection was 6.6 mm rostral from the occipital pole); C is from another animal (DL 74; injected on day 2, sacrificed on day 9) and shows the hemisphere contralateral to two injections (of different dyes) spaced rostrocaudally in areas 17/18. The centers of the Diamidino Yellow and Fast Blue injections are, respectively, 4.8 and 8.4 mm rostral from the occipital pole. In each photograph, arrows mark rostral and caudal limits of the reconstructed region. Dots are arrayed parallel to the plane of sectioning; their density along an array gives a rough indication of the density of labeled neurons. In A and B, the distance between arrays corresponds to that between the sections examined; in C, symbols for Fast Blue- and Diamidino Yellow-labeled neurons from the same section are staggered. ls, Lateral sulcus; mss, middle suprasylvian sulcus; pes, posterior ectosylvian sulcus; aes, anterior ectosylvian sulcus. The cortex dorsal and rostral to pes contains the AI and AII auditory areas. Calibration is in millimeters (small divisions). From Innocenti and Clarke (1984a).

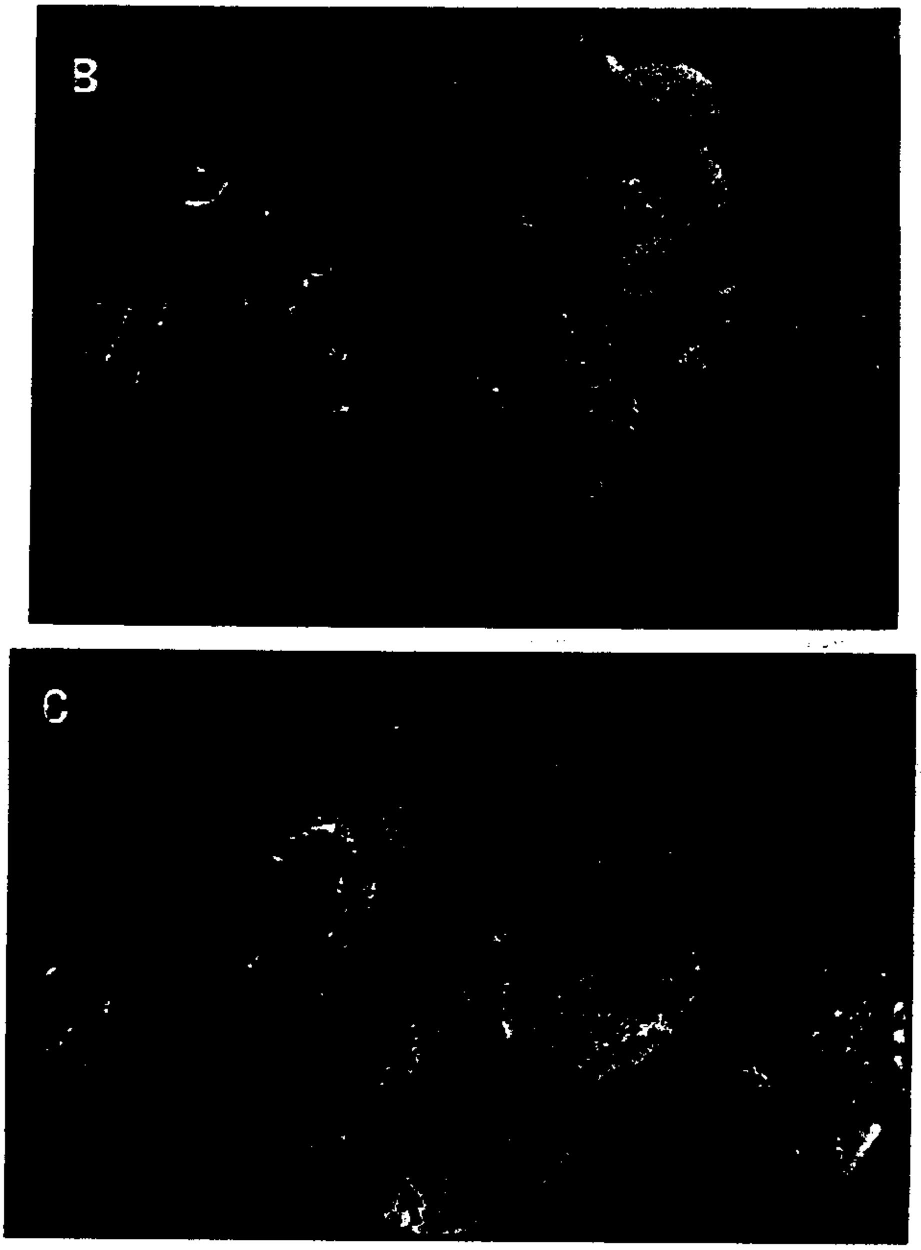

Figure 19. (*continued*)

transitory, collateralization of callosal axons, an explanation for the magnitude of callosal axon loss may be that, in addition to connecting portions of cortex destined to become acallosal, transitory axons may also connect "wrong" areas.

Unequivocal support for this interpretation came from the discovery of transitory callosal projections from primary and secondary auditory areas to the visual areas 17 and 18 (Innocenti and Clarke, 1984a,b; Fig. 19). Auditory areas in the two hemispheres are callosally connected in the adult, although their juvenile callosal connections undergo a partial postnatal elimination (Feng and Brugge, 1983). However, the auditory areas in normal adult cats do not project to contralateral visual cortices. Elimination of the transitory auditory-to-visual projection takes place mainly during the first postnatal month, apparently through axon elimination rather than neuronal death.

Auditory areas also send a transitory projection to ispilateral visual areas, which strongly suggests that similar developmental mechanisms underlie the formation of callosal and ipsilateral corticocortical connections (Innocenti and Clarke, 1984a; Fig. 19).

Again, one can postulate that neurons going to a given ipsilateral or contralateral areas may share an unknown character or respond similarly to a factor in their "milieu." In auditory cortex, neurons projecting to ipsilateral areas 17/18, contralateral areas 17/18, and contralateral auditory areas occupy, in this order, increasingly deeper cortical locations (Innocenti and Clarke, 1984a). Thus, not only the choice of the brain side but also that of area may be related to a neuron's birthdate.

7.3. Factors Involved in the Elimination/Stabilization of Juvenile Callosal Connections

In newborn kittens, the diffuse distribution of callosal neurons contrasts with the presence of terminating callosal axons in restricted portions of the gray matter (Fig. 20). The tangential distribution of these projections establishes, in the visual areas, an overall pattern very similar to that of the adult (Innocenti, 1981a; Innocenti and Clarke, 1984b). In addition, many callosal axons have not entered the gray matter to any great extent, if at all. These axons are more widely distributed than those which enter the gray matter and reach cortical regions, such as medial area 17, destined to become acallosal (Innocenti, 1981a; Innocenti and Clarke, 1984b).

A similar picture (widespread distribution of callosal neurons, restricted intracortical termination of callosal axons, and presence of transitory axons in the deepest portions of the gray matter) has been reported for auditory cortex of the newborn kitten (Feng and Brugge, 1983). In visual cortex of the rabbit, on the contrary, a diffuse distribution of terminating axons in the cortex seems to parallel that of callosal neurons (Chow *et al.*, 1981).

In somatosensory cortex of the rat, callosal axons grow into the gray matter postnatally (on day 4–11) and selectively, in the "columnar" pattern typical of the adult, while the callosal neurons are diffusely distributed (Wise and Jones, 1976; Ivy *et al.*, 1979). Finally, a similar restricted "columnar" growth of callosal

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axons into the cortex occurs between embryonic days E123 and E155 (Goldman and Nauta, 1977; Goldman-Rakic, 1981) in prefrontal cortex of the monkey.

In the cat, the great majority of the axons which have entered the gray matter come from regions which will maintain their projection into the corpus callosum. On the contrary, most of the axons which are confined to the bottom of the gray matter come from regions destined to become acallosal (Innocenti and Clarke, 1983, 1984b; Fig. 21).

Therefore, it appears that the incoming callosal axons may undergo a process of selection near their target and that this may be a crucial mechanism, although not necessarily the final one (see below), deciding of their fate. The selection seems to occur while callosal axons wait in the white matter (Wise and Jones, 1976). Therefore, it may not involve contact between callosal axons and their targets. This interpretation must be qualified since (1) small processes of transitory axons entering the gray matter may have thus far escaped light microscopic visualization and (2) transitory callosal axons may contact the dendrites of layer VI neurons or neurons in the white matter.

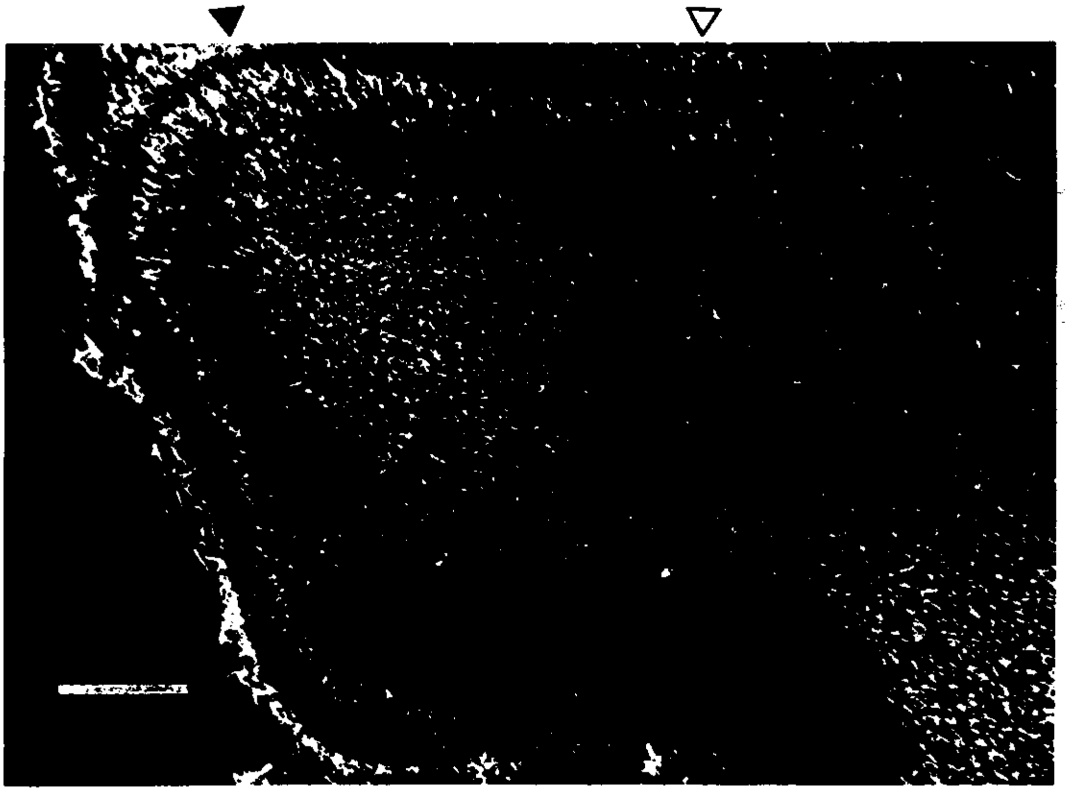

Figure 20. Polarized light photomicrograph showing distribution of anterogradely labeled callosal neurons in the lateral gyrus of a kitten injected with WGA-HRP in the homotopic contralateral region on pd 1 and sacrificed on pd 2. Callosal axons have a widespread distribution in the white matter but they enter the cortex selectively at the 17/18 border (solid triangle) and in a small part of area 19 (open triangle). The continuous band of neuronal labeling corresponds to layer III. Bar 500 µm.

Which factor(s) may be responsible for the maturation of callosal connections has so far been explored by two experimental approaches: manipulation of the sensory experience and early lesions of the nervous system.

Strabismus induced by early (on pd 0–36) section of the extraocular eye muscles (Innocenti and Frost, 1978, 1979; Berman and Payne, 1983) or 1 month of binocular eyelid suture (Innocenti *et al.*, 1985; Fig. 22) enlarges the efferent callosal zone in area 17, apparently by stabilizing transitory callosal projections. The same result is obtained by short periods of visual experience followed by binocular deprivation (Innocenti *et al.*, 1985; Fig. 22) and by monocular deprivation (Innocenti and Frost, 1979). Strabismus also increases the width of the callosal terminal territory near the 17/18 border (Lund *et al.*, 1978) although inconstantly (Berman and Payne, 1983). The claim that unilateral strabismus induces unilateral enlargement (contralateral to the deviated eye) of the callosal terminal territory (Lund and Mitchell, 1979b) was not confirmed in a recent study (Berman and Payne, 1983).

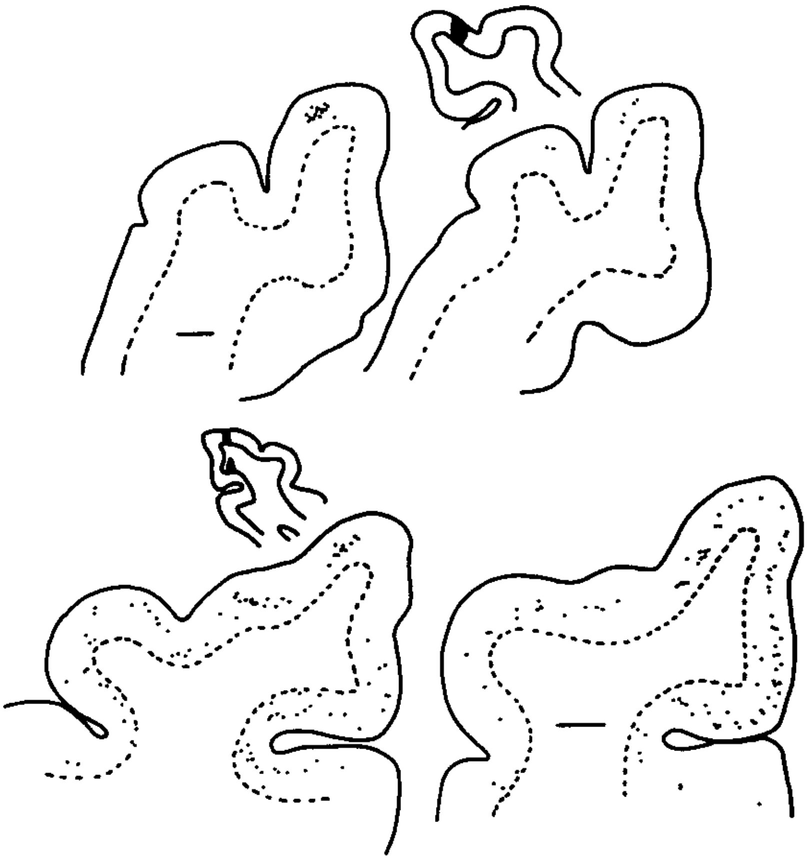

Figure 21. Origin of the callosal axons which enter the gray matter and of those which do not. (Top) Distribution of retrogradely labeled neurons after a small Fast Blue injection centered near the 17/18 border (inset) in a kitten injected on pd 3 and sacrificed on pd 8. (Bottom) Distribution of retrogradely labeled neurons after a small Fast Blue injection extending into the white matter underneath area 17 (inset) in a kitten injected on day 1 and sacrificed on day 6. Bars = 1 mm. The bottom part is redrawn from Innocenti and Clarke (1983) but mirror reversed in order to facilitate the comparison with the upper part of the figure.

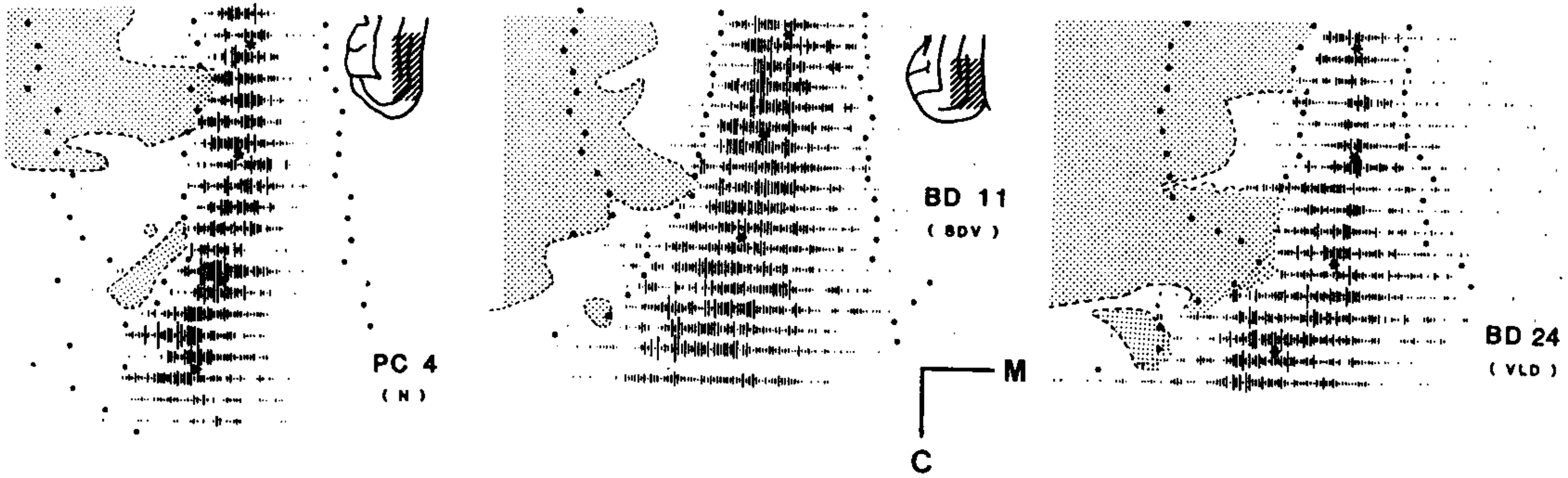

Figure 22. Computer reconstructions of a part of the callosal zone (layers II–IV) in one normal adult cat (PC 4; N), in one cat which was deprived of vision by bilateral eyelid suture until pd 37 (BD 11; SDV) and then normally reared until pd 147; and in one cat which had 10 days of normal vision, followed by 99 days of binocular deprivation by eyelid suture (BD 24; VLD). At the end of the rearing period, BD 11 had developed divergent strabismus. The reconstructions are flattened views of the lateral and postlateral gyri (hatched areas in corresponding insets of dorsal views of brains traced from photographs). Dotted lines represent, from lateral to medial, the fundi of the lateral, postlateral, and suprasplenial sulci. The asterisks mark the boundary between areas 17 (medially) and 18 (laterally). The neurons in layers II–IV of each section were projected onto a line running parallel to the pial surface and 400 μm deep; the line was divided into bins of 100 μm and the number of neurons in each bin was represented by one segment whose length is proportional to the number of neurons in the bin (shortest segments = 1 neuron). Each row of line segments represents one section. Stippling indicates regions of areas 18 and 19 that are continuous with the reconstructed parts of the callosal zone, and within which there is a very high density of labeled callosal neurons. Scale lines = 2 mm; M, medial; C, caudal. From Innocenti *et al.* (1985).

47.

Continuous binocular deprivation by bilateral eyelid suture during 3 or more months following natural eye opening decreases by about 50%, and irreversibly, the number of callosal neurons which can be labeled in areas 17/18 (Innocenti and Frost, 1979, 1980; Innocenti *et al.*, 1985; Fig. 23) and the density of callosal terminal labeling in the same area (Innocenti *et al.*, 1985). Ten days of normal vision following natural eye opening is sufficient to prevent this effect of binocular deprivation (Innocenti *et al.*, 1985). Dark rearing decreases the density of callosal terminations at the 17/18 border as visualized by anterograde degeneration (Lund and Mitchell, 1979a).

The experience-dependent effects thus far observed in visual cortex of the cat can be explained by assuming that vision plays an active role in the stabilization and elimination of part of the transitory callosal projections. It seems reasonable to assume that vision should affect axons which have already entered the cortex although it cannot be excluded that the growth into the cortex may also be vision dependent. In animals with normal visual experience, the initial (first postnatal month) effect of vision is to stabilize callosal connections originating from a wider region than in the normal adult, but much narrower than in the neonate. During the second and possibly third postnatal month, this initial projection is progressively restricted. The condition necessary for this restriction to occur seems to be normal binocular vision (for further discussion on the effects of vision, see Innocenti *et al.*, 1985). The mechanism underlying normal and experience-dependent maturation of callosal connections may be competition for terminal space between callosal axons and other axons. In monocularly deprived,

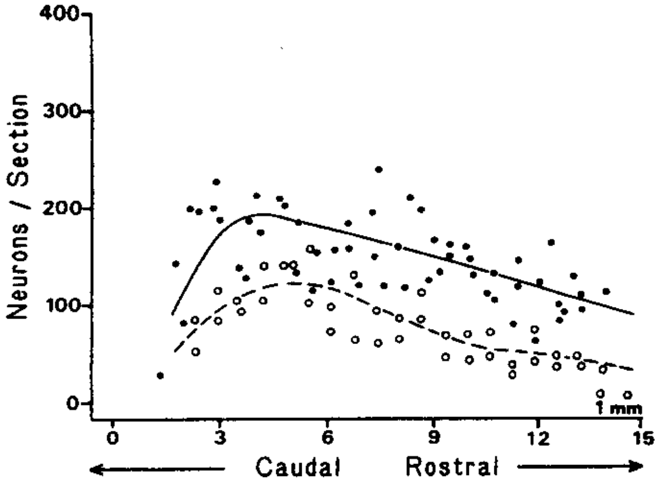

Figure 23. Effects of binocular deprivation on the development of visual callosal connections. Each dot represents the number of HRP-labeled callosal neurons in layers II–IV of areas 17 and 18 of the cat, in one coronal section at a given distance from the occipital pole of the hemisphere. Solid dots are counts from three normal adult animals, open dots are counts from two animals deprived of vision by binocular eyelid suture maintained during their entire postnatal life (respectively 173 and 253 days). Continuous and dashed lines fit (by eye) the two sets of data. The sections were 80 μm thick reacted with TMB. From Innocenti (1981b).

split-chiasm kittens, callosal axons seem, in fact, to compete with thalamocortical axons or at least with neurons driven by them, as proven by the modifications of ocular dominance in visual cortex (Cynader *et al.*, 1981).

One fascinating aspect of the relationship between normal binocular vision and callosal maturation is that kittens whose corpus callosum was sectioned during the first postnatal month fail to acquire normal eye alignment (Elberger, 1979, 1982; Elberger and Hirsch, 1982). Callosal transection performed before pd 19 also decreases the binocularity of neurons in area 17, while callosal transection performed later does not (Elberger and Smith, 1983). The last finding is, however, in conflict with the loss of binocularity observed by others after callosal transection in adults (Payne *et al.*, 1980; Blakemore *et al.*, 1983).

Elberger's findings and ours tend to suggest that eye alignment and callosal connections may influence each other in development; the maturation of intertectal commissures seems similarly linked to that of eye alignment in *Xenopus* (Keating, 1977). However, it cannot yet be excluded that the modifications in eye alignment observed after early callosotomy may be due to a hypothetical rewiring induced by the lesion rather than to the lack of callosal connections in development.

Neonatal monocular enucleation in rats and hamsters widens the distribution of callosal neurons (Rhoades and Dellacroce, 1980b; Rothblat and Hayes, 1982) and of terminals (Rhoades and Dellacroce, 1980b; Cusick and Lund, 1982) at the area 17/18a border ipsilaterally to the remaining eye. Distributions of callosal neurons and terminals contralaterally to the remaining eye are unchanged. Monocular enucleation also widens the callosal zone in cats, but in this species the effects are observed in both hemispheres (Innocenti and Frost, 1979, and unpublished). Binocular enucleation widens slightly the distribution of callosal neurons in cats (Innocenti and Frost, 1980), although it decreases their number, and it also enlarges the callosal terminal territory in both hemispheres in rats (Cusick and Lund, 1982). Neonatal unilateral optic tract lesion decreases, but thalamic lesion increases, the width of the callosal terminal territory at the 17/18a border in rats (Cusick and Lund, 1982).

At the moment, it seems impossible to explain all of the effects of eye enucleation by a single mechanism, although the loss of binocular vision could be the cause for the enlarged callosal zone, at least in the monocularly enucleated cats. Furthermore, important species differences begin to emerge, mainly in the monocular enucleation experiments. These differences may be due to the dissimilarities in the organization of the visual pathways in rodents and cats and/or to the different maturation of the brain in the two species at the time of enucleation. Finally, in rodents, mainly modifications of the terminal territories have been studied and the enlargement of the callosal terminal territories may not be due to stabilization of transitory callosal connections but to sprouting of the normal connections.

Taken together, these results agree with those of selective visual rearing in proving that the transitory callosal projections can provide the potential for the juvenile plasticity of callosal connections. It also appears certain that factors independent of visual experience can play a role in focusing both the callosal efferent zone and the callosal terminal territory to near the 17/18 border. These factors may depend on the topographical organization of the visual pathways, which at birth, in both rodents and cats, may have already determined the future development of the callosal connections. Consistently with this interpretation, the most profound departure from the normal topographical distribution of callosal neurons and terminals is found in the Siamese cat (Shatz, 1977b) and the anophthalmic mouse (Rhoades *et al.*, 1983), i.e., in two conditions in which profound modifications in the organization of the visual pathways occur during embryonic life. Unfortunately, in neither case can the possibility of a more direct action of the genetic mutation on callosal development be ruled out.

Only a few studies have investigated the plasticity of callosal connections in sensory systems other than the visual. Preliminary results indicate that unilateral or bilateral cochlear destruction in newborn cats does not prevent callosal neurons from assuming their discontinuous "columnar" distribution (Brugge *et al.*, 1983). Unlike visual cortex, in somatosensory cortex of the rat callosal connections are apparently not modified by neonatal thalamic lesions (Wise and Jones, 1978). In the same study, those authors also failed to observe modifications of the thalamocortical input following neonatal callosotomy. On the contrary, Vaughan and Foundas (1982) reported sprouting of thalamic terminals into the callosal territory, in auditory cortex of the rat following callosotomy at 30 days.

In the cat, neonatal lesioning of SI stabilizes some of the transitory callosal projections from the remaining SI to the SII area on the lesioned side (Caminiti and Innocenti, 1981). These effects are not modified by the lesioning of contralateral SII, which is by itself ineffective. These experiments in the cat were aimed at testing the possibility that the fate of transitory callosal projections may be determined by competition between different sets of callosal axons or between callosal axons and ipsilateral corticocortical axons. The results seem to support the second alternative. However, the possibility that the modification of callosal connections may be secondary to modifications of thalamocortical connections to SII, induced by the ipsilateral lesion of SI, cannot be ruled out.

In frontal cortex of the monkey early unilateral lesions of the dorsal bank of the sulcus principalis are followed by growth of callosal axons from regions homotopic to the lesion into more dorsal regions (Goldman-Rakic, 1981). The mechanisms of this effect are unknown.

8. Conclusions

While waiting for our knowledge of the normal organization and development of callosal connections to become more complete, we can go back to the "creationistic" metaphor in the Introduction and ask which minimal, theoretical conditions should interhemispheric connections fulfill in order to establish, between the two hemispheres, the structural continuity necessary to unify brain function.

1. Most areas, irrespective of whether they contain simple or complex maps either of the sensory or motor peripheries, or of higher-order "associative" functions, seem to be essentially mosaics. They are mosaics because of the discrete input they receive (perhaps the best example of this is the barrel field; Woolsey

and Van der Loos, 1970) and because of their discrete ("columnar") internal organization (see Jones, this volume; White, this volume). Thus, if horizontal connections within an area are necessary for the integrated functioning of the mosaic, some identical connections must exist between homologous areas in the two hemispheres.

2. For the integrated functioning of different areas, connections between heterologous areas in the two hemispheres, similar to those between the corresponding areas in the same hemisphere, must also exist. This does not necessarily imply that an area must be callosally connected to all of those to which it is associationally connected. It is easy to conceive conditions in which callosal connections between two areas may be unnecessary, or else redundant, with their association connections.

In reality, both types of interhemispheric connections do exist. They bear with intracortical or association connections some of the structural and functional similarities that the theoretical considerations above would predict. The fact that some transitory callosal neurons end up forming ipsilateral connections serves to stress the similarity between the two systems.

3. Inter- and intrahemispheric connections must obey a major constraint, i.e., the peripherotopic or functionotopic* organization of the receiving cortex. This organization differs, for different peripheries and for different areas connected with the same periphery. This explains the failure to understand the organization of all callosal connections on the grounds of a unique organizing principle such as, for example, the selective connectivity of the sensory midlines. Still, this principle remains essential to understand callosal connections in a certain number of visual and somatosensory areas, i.e., in those areas where the sensory periphery is represented with high resolution and according to simple homeomorphic principles.

The necessity of corticocortical connections to obey local peripherotopic or functionotopic organizational constraints is probably at the roots of the ephemerality of an impressive number of corticocortical connections in development. The organization of callosal connections and other corticocortical projections (Innocenti *et al.*, 1985), at the time they grow toward their targets, obeys different organizing principles from those which will later be imposed by the receiving cortex at the expenses of massive axonal elimination.

Thus, exuberancy and plasticity of corticocortical connections are necessarily closely related events in development. That is why the stabilization or elimination of juvenile connections can be modulated by environmental manipulations, as well as by genetic extravagancies.

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* An example of what I mean for obedience to functionotopic constraints is that visual callosal afferents match their target neurons for orientation (and directionality) of the receptive fields (Berlucchi and Rizzolatti, 1968; Lepore and Guillemot, 1982: Antonini *et al.*, 1983), and orientation specificity is orderly represented across the cortex.

9. References

Akers, R. M., and Killackey, H. P., 1978, Organization of cortico-cortical connections in the parietal cortex of the rat, *J. Comp. Neurol.* **181**:513–538.

Angevine, J. B., and Sidman, R. L., 1961, Autoradiographic study of cell migration during histogenesis of cerebral cortex in the mouse, *Nature* **192**:766–768.

Antonini, A., Berlucchi, G., Marzi, C. A., and Sprague, J. M., 1979, Importance of corpus callosum for visual receptive fields of single neurons in cat superior colliculus, *J. Neurophysiol.* **42**:137–152.

Antonini, A., Berlucchi, G., and Lepore, F., 1983, Physiological organization of callosal connections of a visual lateral suprasylvian cortical area in the cat, *J. Neurophysiol.* **49**:902–921.

Asanuma, H., and Okamoto, K., 1959, Unitary study on evoked activity of callosal neurons and its effect on pyramidal tract cell activity on cats, *Jpn. J. Physiol.* **9**:473–483.

Auroux, M., 1964, Étude des commissures télencéphaliques du foetus de rat normal, *Arch. Anat. Histol. Embryol. Norm. Exp.* **47**:503–522.

Bailey, P., Garol, H. W., and McCulloch, W. S., 1941, Cortical origin and distribution of corpus callosum and anterior commissure in chimpanzee (*Pan satyrus*), *J. Neurophysiol.* **4**:564–571.

Beckstead, R. M., 1979, An autoradiographic examination of cortico-cortical and subcortical projections of the mediodorsal-projection (prefrontal) cortex in the rat, *J. Comp. Neurol.* **184**:43–62.

Berlucchi, G., 1972, Anatomical and physiological aspects of visual functions of corpus callosum, *Brain Res.* **37**:371–392.

Berlucchi, G., 1981, Recent advances in the analysis of the neural substrates of interhemispheric communication, in: *Brain Mechanisms and Perceptual Awareness* (O. Pompeiano and C. Ajmone Marsan, eds.), Raven Press, New York, pp. 133–152.

Berlucchi, G., and Antonini, A., 1986, the role of the corpus callosum in the representation of the visual field in cortical areas, in: *Brain Circuits and Functions of the Mind: Essays in honour of R. W. Sperry* (C. Trevarthen, ed), Cambridge University Press, London (in press).

Berlucchi, G., and Rizzolatti, G., 1968, Binocularly driven neurons in visual cortex of split-chiasm cats, *Science* **159**:308–310.

Berlucchi, G., Gazzaniga, M. S., and Rizzolatti, G., 1967, Microelectrode analysis of transfer of visual information by the corpus callosum, *Arch. Ital. Biol.* **105**:583–596.

Berman, N., and Payne, B. R., 1982, Contralateral corticofugal projections from the lateral, suprasylvian and ectosylvian gyri in the cat, *Exp. Brain Res.* **47**:234–238.

Berman, N. E., and Payne, B. R., 1983, Alterations in connections of the corpus callosum following convergent and divergent strabismus, *Brain Res.* **274**:201–212.

Bishop, G. H., and Smith, J. M., 1964, The sizes of nerve fibers supplying cerebral cortex, *Exp. Neurol.* **9**:483–501.

Blakemore, C., 1969, Binocular depth perception and the optic chiasm, *Vision Res.* **10**:43–47.

Blakemore, C., Diao, Y., Pu, M., Wang, Y., and Xiao, Y., 1983, Possible functions of the interhemispheric connexions between visual cortical areas in the cat, *J. Physiol.* (*London*) **337**:331–349.

Blue, M. E., and Parnavelas, J. G., 1983, The formation and maturation of synapses in the visual cortex of the rat. II. Quantitative analysis, *J. Neurocytol.* **12**:697–712.

Bremer, F., Brihaye, J., and André-Balisaux, G., 1956, Physiologie et pathologie du corps calleux, *Schweiz. Arch. Neurol. Psychiatr.* **78**:31–87.

Brugge, J. F., Feng, J. Z., Reale, R. A., and Chan, J. C. K., 1983, Topographic distribution of primary auditory cortical field (AI) callosal neurons in cats reared with unilateral or bilateral cochlear destruction, *Soc. Neurosci. Abstr.* **9**:377.

Burton, H., Mitchell, G., and Brent, D., 1982, Second somatic sensory area in the cerebral cortex of cats: Somatotopic organization and cytoarchitecture, *J. Comp. Neurol.* **210**:109–135.

Caminiti, R., and Innocenti, G. M., 1981, The postnatal development of somatosensory callosal connections after partial lesions of somatosensory areas, *Exp. Brain Res.* **42**:53–62.

Caminiti, R., and Sbriccoli, A., 1983, Callosal connections of the superior parietal lobule in the monkey, *Soc. Neurosci. Abstr.* **9**:493.

Caminiti, R., and Sbriccoli, A., 1985, The callosal system of the superior parietal lobule in the monkey, *J. Comp. Neurol.* **237**:85–99.

Caminiti, R., Innocenti, G. M., and Manzoni, T., 1979, The anatomical substrate of callosal messages from SI and SII in the cat, *Exp. Brain Res.* **35**:295–314.

Carman, J. B., Cowan, W. M., Powell, T. P. S., and Webster, K. E., 1965, A bilateral cortico-striate projection, *J. Neurol. Neurosurg. Psychiatry* **28**:71–77.

Catsman-Berrevoets, C. E., Lemon, R. N., Verburgh, C. A., Bentivoglio, M., and Kuypers, H. G. J. M., 1980, Absence of callosal collaterals derived from rat corticospinal neurons: A study using fluorescent retrograde tracing and electrophysiological techniques, *Exp. Brain Res.* **39**:433–440.

Cavada, C., and Reinoso-Suárez, F., 1981, Interhemispheric cortico-cortical connections to the prefrontal cortex in the cat, *Neurosci. Lett.* **24**:211–214.

Cavada, C., and Reinoso-Suárez, F., 1983, Afferent connections of area 20 in the cat studied by means of the retrograde axonal transport of horseradish peroxidase, *Brain Res.* **270**:319–324.

Caviness, V. S., 1982, Neocortical histogenesis in normal and reeler mice: A developmental study based upon [^{3}H]thymidine autoradiography, *Dev. Brain Res.* **4**:**293–302**.

Caviness, V. S., and Yorke, C. H., 1976, Interhemispheric neocortical connections of the corpus callosum in the reeler mutant mouse: A study based on anterograde and retrograde methods, *J. Comp. Neurol.* **170**:449–460.

Choudhury, B. P., Whitteridge, D., and Wilson, M. E., 1965, The function of the callosal connections of the visual cortex, *Q. J. Exp. Physiol.* **50**:214–219.

Chow, K. L., Baumbach, H. D., and Lawson, R., 1981, Callosal projections of the striate cortex in the neonatal rabbit, *Exp. Brain Res.* **42**:122–126.

Cipolloni, P. B., and Peters, A., 1979, The bilaminar and banded distribution of the callosal terminals in the posterior neocortex of the rat, *Brain Res.* **176**:33–47.

Cipolloni, P. B., and Peters, A., 1983, The termination of callosal fibres in the auditory cortex of the rat: A combined Golgi–electron microscope and degeneration study, *J. Neurocytol.* **12**:713–726.

Clare, M. H., Landau, W. M., and Bishop, G. H., 1961, The cortical response to direct stimulation of the corpus callosum in the cat, *Electroencephalogr. Clin. Neurophysiol.* **13**:21–33.

Clarke, P. G. H., Martin, K. A. C., Ramachandran, V. W., Rao, V. M., and Whitteridge, D., 1979, Development and plasticity of neuronal connections in the lamb visual system, in: *Developmental Neurobiology of Vision* (R. D. Freeman, ed.), Plenum Press, New York, pp. 403–410.

Clemo, H. R., and Stein, B. E., 1983, Organization of a fourth somatosensory area of cortex in cat, *J. Neurophysiol.* **50**:910–925.

Code, R. A., and Winer, J. A., 1983, Heterogeneous origin of commissural neurons in cat primary auditory cortex (AI), *Soc. Neurosci. Abstr.* **9**:953.

Cragg, B. G., 1975, The development of synapses in the visual system of the cat, *J. Comp. Neurol.* **160**:147–166.

Cumming, W. J. K., 1969, The fibre-content of the corpus callosum of the albino rat, *J. Anat.* **104**:187.

Curtis, H. J., 1940, Intercortical connections of corpus callosum as indicated by evoked potentials, *J. Neurophysiol.* **3**:407–413.

Curtis, H. J., and Bard, P., 1939, Intercortical connections of the corpus callosum as indicated by evoked potentials, *Am. J. Physiol.* **126**:473.

Cusick, C. G., and Lund, R. D., 1981, The distribution of the callosal projection to the occipital visual cortex in rats and mice, *Brain Res.* **214**:239–259.

Cusick, C. G., and Lund, R. D., 1982, Modification of visual callosal projections in rats, *J. Comp. Neurol.* **212**:385–398.

Cusick, C. G., Gould, H. J., and Kaas, J. H., 1983, Callosal connections of visual cortex in owl monkeys, marmosets, and galagos, *Soc. Neurosci. Abstr.* **9**:1220.

Cynader, M., Leporé, F., and Guillemot, J.-P., 1981, Inter-hemispheric competition during postnatal development, *Nature* **290**:139–140.

De Lacoste, M. C., and Woodward, D. J., 1983, Neocortical commissural size and sex differences in primate brain, *Soc. Neurosci. Abstr.* **9**:493.

De Lacoste-Utamsing, C., and Holloway, R. L., 1982, Sexual dimorphism in the human corpus callosum, *Science* **216**:1431–1432.

Diadori, P., Landry, P., and Dykes, R. W., 1983, Responses of corticothalamic cells to callosal and thalamic stimulation in cat somatosensory cortex, *Soc. Neurosci. Abstr.* **9**:250.

Diamond, I. T., Jones, E. G., and Powell, T. P. S., 1968, Interhemispheric fiber connections of the auditory cortex of the cat, *Brain Res.* **11**:177–193.

Diao, Y.-C., Wang, Y.-K., and Pu, M.-L., 1983, Binocular responses of cortical cells and the callosal projection in the albino rat, *Exp. Brain Res.* **49**:410–418.

Doty, R. W., and Negrao, N., 1973, Forebrain commissures and vision, in: *Handbook of Sensory Physiology*, Volume VII/3 (R. Jung, ed.) Springer-Verlag, Berlin, pp. 543–582.

Dreher, B., and Cottee, L. J., 1975, Visual receptive-field properties of cells in area 18 of cat's cerebral cortex before and after acute lesions in area 17, *J. Neurophysiol.* **38:**735–750.

Dürsteler, M. R., Blakemore, C., and Garey, L. J., 1979, Projections to the visual cortex in the golden hamster, *J. Comp. Neurol.* **183:**185–204.

Ebner, F. F., and Myers, R. E., 1962, Commissural connections in the neocortex of monkey, *Excerpta Med.* **48:**1096.

Ebner, F. F., and Myers, R. E., 1965, Distribution of corpus callosum and anterior commissure in cat and racoon, *J. Comp. Neurol.* **124:**353–366.

Elberger, A. J., 1979, The role of the corpus callosum in the development of interocular alignment and the organization of the visual field in the cat, *Exp. Brain Res.* **36:**71–85.

Elberger, A. J., 1982, The functional role of the corpus callosum in the developing visual system: A review, *Prog. Neurobiol.* **18:**15–79.

Elberger, A. J., and Hirsch, H. V. B., 1982, Divergent strabismus following neonatal callosal section is due to a failure of convergence, *Brain Res.* **239:**275–278.

Elberger, A. J., and Smith, E. L., 1983, Corpus callosum and development of striate binocularity: Complete critical period within three postnatal weeks, *Soc. Neurosci. Abstr.* **9:**912.

Fadiga, E., Innocenti, G. M., Manzoni, T., and Spidalieri, G., 1972, Peripheral and transcallosal reactivity of neurones sampled from the face subdivision of the SI cortical area, *Arch. Ital. Biol.* **110:**444–475.

Feeney, D. M., and Orem, J. M., 1971, Influence of antidromic callosal volleys on single units in visual cortex, *Exp. Neurol.* **33:**310–321.

Feng, J. Z., and Brugge, J. F., 1983, Postnatal development of auditory callosal connections in the kitten, *J. Comp. Neurol.* **214:**416–426.

Fisken, R. A., Garey, L. J., and Powell, T. P. S., 1975, The intrinsic, association and commissural connections of area 17 of the visual cortex, *Philos. Trans. R. Soc. London Ser. B* **272:**487–536.

Fitzpatrick, K. A., and Imig, T. J., 1980, Auditory cortico-cortical connections in the owl monkey, *J. Comp. Neurol.* **192:**589–610.

Fleischhauer, K., and Wartenberg, H., 1967, Elektronenmikroskopische Untersuchungen über das Wachstum der Nervenfasern and über das Auftreten von Markscheiden im Corpus callosum der Katze, *Z. Zellforsch. Mikrosk. Anat.* **83:**568–581.

Garcia-Rill, E., Nieto, A., Adinolfi, A., Hull, C. D., and Buchwald, N. A., 1979, Projections to the neostriatum from the cat precruciate cortex: Anatomy and physiology, *Brain Res.* **170:**393–407.

Garey, L. J., Jones, E. G., and Powell, T. P. S., 1968, Interrelationships of striate and extrastriate cortex with the primary relay sites of the visual pathway, *J. Neurol. Neurosurg. Psychiatry* **31:**135–157.

Garol, H. W., 1942, Cortical origin and distribution of corpus callosum and anterior commissure in the cat, III, *J. Neuropathol.* **1:**422–429.

Gazzaniga, M. S., and Ledoux, J. E., 1978, *The Integrated Mind*, Plenum Press, New York.

Gilbert, C. D., and Wiesel, T. N., 1979, Morphology and intracortical projections of functionally characterised neurones in the cat visual cortex, *Nature* **280:**120–125.

Glickstein, M., and Whitteridge, D., 1976, Degeneration of layer III pyramidal cells in area 18 following destruction of callosal input, *Brain Res.* **104:**148–151.

Goldman, P. S., and Nauta, W. J. H., 1977, Columnar distribution of cortico-cortical fibers in the frontal association, limbic, and motor cortex of the developing rhesus monkey, *Brain Res.* **122:**393–413.

Goldman-Rakic, P. S., 1981, Development and plasticity of primate frontal association cortex, in: *The Organization of the Cerebral Cortex* (F. O. Schmitt, ed.), MIT Press, Cambridge, Mass., pp. 69–97.

Goldman-Rakic, P. S., and Schwartz, M. L., 1982, Interdigitation of contralateral and ipsilateral columnar projections to frontal association cortex in primates, *Science* **216:**755–757.

Gould, H. J., and Ebner, F. F., 1978, Connections of the visual cortex in the hedgehog (*Paraechinus hypomelas*). II. Corticocortical projections, *J. Comp. Neurol.* **177:**473–502.

Gould, H. J., and Kaas, J. H., 1981, The distribution of commissural terminations in somatosensory areas I and II of the grey squirrel, *J. Comp. Neurol.* **196:**489–504.

Gould, H. J., Cusick, C. G., Pons, T. P., and Kaas, J. H., 1983, The relation of callosal connections to microstimulation maps of precentral motor cortex in owl monkeys, *Soc. Neurosci. Abstr.* **9:**309.

Grafstein, B., 1963, Postnatal development of the transcallosal evoked response in the cerebral cortex of the cat, *J. Neurophysiol.* **26**:79–99.

Grafstein, B., 1964, Postnatal development of the corpus callosum in the cat: Myelination of a fibre tract in the central nervous system, in: *Neurological and Electroencephalographic Correlative Studies in Infancy* (P. Kellaway and I. Petersen, eds.), Grune & Stratton, New York, pp. 52–67.

Graziosi, M. E., Tucci, E., Barbaresi, P., Ugolini, G., and Manzoni, T., 1982, Cortico-cortical neurones of somesthetic area SI as studied in the cat with fluorescent retrograde double-labelling, *Neurosci. Lett.* **31**:105–110.

Gross, C. G., and Mishkin, M., 1977, The neural basis of stimulus equivalence across retinal translation, in: *Lateralization in the Nervous System* (S. Harnard, R. W. Doty, L. Goldstein, J. Jaynes, and G. Krauthamer, eds.), Academic Press, New York, pp. 109–122.

Gross, C. G., Bender, D. B., and Mishkin, M., 1977, Contributions of the corpus callosum and the anterior commissure to visual activation of inferior temporal neurons, *Brain Res.* **131**:227–239.

Hartenstein, V., and Innocenti, G. M., 1981, The arborization of single callosal axons in the mouse cerebral cortex, *Neurosci. Lett.* **23**:19–24.

Hartenstein, V., Innocenti, G. M., and Caminiti, R., 1980, An anatomical basis for the representation of the ipsilateral periphery in the second somatosensory area (S2) of the cat, *Neurosci. Lett. Suppl.* **5**:484.

Harvey, A. R., 1980, A physiological analysis of subcortical and commissural projections of areas 17 and 18 of the cat, *J. Physiol.* (*London*) **302**:507–534.

Heath, C. J., and Jones, E. G., 1970, Connexions of area 19 and the lateral suprasylvian area of the visual cortex of the cat, *Brain Res.* **19**:302–305.

Hedreen, J. C., and Yin, T. C. T., 1981, Homotopic and heterotopic callosal afferents of caudal inferior parietal lobule in *Macaca mulatta*, *J. Comp. Neurol.* **197**:605–621.

Heimer, L., Ebner, F. F., and Nauta, W. J. H., 1967, A note on the termination of commissural fibers in the neocortex, *Brain Res.* **5**:171–177.

Hendry, S. H. C., and Jones, E. G., 1980, Electron microscopic demonstration of thalamic axon terminations on identified commissural neurons in monkey somatic sensory cortex, *Brain Res.* **196**:253–257.

Hendry, S. H. C., and Jones, E. G., 1983, Thalamic inputs to identified commissural neurons in the monkey somatic sensory cortex, *J. Neurocytol.* **12**:299–316.

Herron, P., and Miller, J., 1983, The interrelation of callosal and corticospinal neurons in the sensorimotor region of the rat, *Soc. Neurosci. Abstr.* **9**:493.

Hewitt, W., 1962, The development of the human corpus callosum, *J. Anat.* **96**:355–358.

Hornung, J. P., and Garey, L. J., 1980, A direct pathway from thalamus to visual callosal neurons in cat, *Exp. Brain Rex.* **38**:121–123.

Hornung, J. P., and Garey, L. J., 1981, Ultrastructure of visual callosal neurons in cat identified by retrograde axonal transport of horseradish peroxidase, *J. Neurocytol.* **10**:297–314.

Hossmann, K. A., 1969, Untersuchungen über transcallosale Potentiale an der akuten Corpus Callosum-Katze, *Dtsch. Z. Nervenheilkd.* **195**:79–102.

Hubel, D. H., and Wiesel, T. N., 1962, Receptive fields, binocular interaction and functional architecture in the cat's visual cortex, *J. Physiol.* (*London*) **160**:106–154.

Hubel, D.H., and Wiesel, T.N., 1965, Receptive fields and functional architecture in two nonstriate visual areas (18 and 19) of the cat, *J. Neurophysiol.* **28**:229–289.

Hubel, D. H., and Wiesel, T. N., 1967, Cortical and callosal connections concerned with the vertical meridian of visual fields in the cat, *J. Neurophysiol.* **30**:1561–1573.

Hughes, A., and Wilson, M. E., 1969, Callosal terminations along the boundary between visual areas I and II in the rabbit, *Brain Res.* **12**:19–25.

Huttenlocher, P. R., de Courten, C., Garey, L. J., and Van der Loos, H., 1982, Synaptogenesis in human visual cortex—Evidence for synapse elimination during normal development, *Neurosci. Lett.* **33**:247–252.

Imig, T. J., and Brugge, J. F., 1978, Sources and terminations of callosal axons related to binaural and frequency maps in primary auditory cortex of the cat, *J. Comp. Neurol.* **182**:637–660.

Imig, T. J., and Reale, R. A., 1980, Patterns of cortico-cortical connections related to tonotopic maps in cat auditory cortex, *J. Comp. Neurol.* **192**:293–332.

Imig, T. J., Morel, A., and Kauer, C. D., 1982, Covariation of distributions of callosal cell bodies and callosal axon terminals in layer III of cat primary auditory cortex, *Brain Res.* **251**:157–159.

Innocenti, G. M., 1979, Adult and neonatal characteristics of the callosal zone at the boundary between areas 17 and 18 in the cat, in: *Structure and Function of the Cerebral Commissures* (I. S. Russel, M. W. Van Hof, and G. Berlucchi, eds.), Macmillan, London, pp. 244–258.

Innocenti, G. M., 1980, The primary visual pathway through the corpus callosum: Morphological and functional aspects in the cat, *Arch. Ital. Biol.* **118**:124–188.

Innocenti, G. M., 1981a, Growth and reshaping of axons in the establishment of visual callosal connections, *Science* **212**:824–827.

Innocenti, G. M., 1981b, The development of interhemispheric connections, *Trends Neurosci.* **4**:142–144.

Innocenti, G. M., and Caminiti, R., 1980, Postnatal shaping of callosal connections from sensory areas, *Exp. Brain Res.* **38**:381–394.

Innocenti, G. M., and Clarke, S., 1983, Multiple sets of visual cortical neurons projecting transitorily through the corpus callosum, *Neurosci. Lett.* **41**:27–32.

Innocenti, G. M., and Clarke, S., 1984a, Bilateral transitory projection to visual areas from auditory cortex in kittens, *Dev. Brain Res.* **14**:143–148.

Innocenti, G. M., and Clarke, S., 1984b, The organization of immature callosal connections, *J. Comp. Neurol.* **230**:287–309.

Innocenti, G. M., and Fiore, L., 1976, Morphological correlates of visual field transformation in the corpus callosum, *Neurosci. Lett.* **2**:245–252.

Innocenti, G. M., and Frost, D. O., 1978, Visual experience and the development of the efferent system to the corpus callosum, *Soc. Neurosci. Abstr.* **4**:475.

Innocenti, G. M., and Frost, D. O., 1979, Effects of visual experience on the maturation of the efferent system to the corpus callosum, *Nature* **280**:231–234.

Innocenti, G. M., and Frost, D. O., 1980, The postnatal development of visual callosal connections in the absence of visual experience or of the eyes, *Exp. Brain Res.* **39**:365–375.

Innocenti, G. M., Manzoni, T., and Spidalieri, G., 1972, Peripheral and transcallosal reactivity of neurones within SI and SII cortical areas: Segmental divisions, *Arch. Ital. Biol.* **110**:415–443.

Innocenti, G. M., Manzoni, T., and Spidalieri, G., 1973, Relevance of the callosal transfer in defining the peripheral reactivity of somesthetic cortical neurones, *Arch. Ital. Biol.* **111**:187–221.

Innocenti, G. M., Manzoni, T., and Spidalieri, G., 1974, Patterns of the somesthetic messages transferred through the corpus callosum, *Exp. Brain Res.* **19**:447–466.

Innocenti, G. M., Fiore, L., and Caminiti, R., 1977, Exuberant projection into the corpus callosum from the visual cortex of newborn cats, *Neurosci. Lett.* **4**:237–242.

Innocenti, G. M., Koppel, H., and Clarke, S., 1983a, Transitory macrophages in the white matter of the developing visual cortex. I. Light and electron microscopic characteristics and distribution, *Dev. Brain Res.* **11**:39–53.

Innocenti, G. M., Clarke, S., and Koppel, H., 1983b, Transitory macrophages in the white matter of the developing visual cortex. II. Development and relations with axonal pathways, *Dev. Brain Res.* **11**:55–66.

Innocenti, G. M., Frost, D. O., and Illes, J., 1985, Maturation of visual callosal connections in visually deprived kittens: A challenging critical period, *J. Neurosci.* **5**:255–267.

Ivy, G. O., and Killackey, H. P., 1981, The ontogeny of the distribution of callosal projection neurons in the rat parietal cortex, *J. Comp. Neurol.* **195**:367–389.

Ivy, G. O., and Killackey, H. P., 1982, Ontogenetic changes in the projections of neocortical neurons, *J. Neurosci.* **2**:735–743.

Ivy, G. O., Akers, R. M., and Killackey, H. P., 1979, Differential distribution of callosal projection neurons in the neonatal and adult rat, *Brain Res.* **173**:532–537.

Jacobson, S., and Marcus, E. M., 1970, The laminar distribution of fibers of the corpus callosum: A comparative study in the rat, cat, rhesus monkey and chimpanzee, *Brain Res.* 517–520.

Jacobson, S., and Trojanowski, J. Q., 1974, The cells of origin of the corpus callosum in rat, cat and rhesus monkey, *Brain Res.* **74**:149–155.

Jacobson, S., and Trojanowski, J. Q., 1975, The appearance of dendrites of callosal and corticothalamic neurons in somatosensory cortex of immature rats demonstrated by horseradish peroxidase, *Adv. Neurol.* **12**:319–333.

Jacobson, S., and Trojanowski, J. Q., 1977, Prefrontal granular cortex of the rhesus monkey. II. Interhemispheric cortical afferents, *Brain Res.* **132**:235–246.

Jenny, A. B., 1979, Commissural projections of the cortical hand motor area in monkeys, *J. Comp. Neurol.* **188**:137–146.

Jensen, K. F., and Altman, J., 1982, The contribution of late-generated neurons to the callosal projection in the rat: A study with prenatal x-irradiation, *J. Comp. Neurol.* **209:**113–122.

Jones, E. G., and Hendry, S. H. C., 1980, Distribution of callosal fibers around the hand representations in monkey somatic sensory cortex, *Neurosci. Lett.* **19:**167–172.

Jones, E. G., and Powell, T. P. S., 1968, The commissural connexions of the somatic sensory cortex in the cat, *J. Anat.* **103:**433–455.

Jones, E. G., and Powell, T. P. S., 1969, Connexions of the somatic sensory cortex of the rhesus monkey. II. Contralateral cortical connexions, *Brain* **92:**717–730.

Jones, E. G., and Powell, T. P. S., 1970, An electron microscopic study of the laminar pattern and mode of termination of afferent fibre pathways in the somatic sensory cortex of the cat, *Philos. Trans. R. Soc. London Ser. B* **257:**45–62.

Jones, E. G., and Wise, S. P., 1977, Size, laminar and columnar distribution of efferent cells in the sensory-motor cortex of monkeys, *J. Comp. Neurol.* **175:**391–438.

Jones, E. G., Burton, H., and Porter, R., 1975, Commissural and cortico-cortical "columns" in the somatic sensory cortex of primates, *Science* **190:**572–574.

Jones, E. G., Coulter, J. D., and Wise, S. P., 1979, Commissural columns in the sensory-motor cortex of monkeys, *J. Comp. Neurol.* **188:**113–136.

Jouandet, M. L., Lachat, J. -J., and Garey, L. J., 1985, Distribution of the neurons of origin of the great cerebral commissures in the cat, *Anat. Embryol.* **171:**105–120.

Kaas, J. H., Lin, C. S., and Wagor, E., 1977, Cortical projections of posterior parietal cortex in owl monkeys, *J. Comp. Neurol.* **171:**387–408.

Karol, E. A., and Pandya, D. N., 1971, The distribution of the corpus callosum in the rhesus monkey, *Brain* **94:**471–486.

Kawamura, K., 1973, Corticocortical fiber connections of the cat cerebrum. III. The occipital region, *Brain Res.* **51:**41–60.

Keating, M. J., 1977, Evidence for plasticity of intertectal neuronal connections in adult *Xenopus*, *Philos. Trans. B. Soc. London Ser. B* **278:**277–294.

Keller, G., and Innocenti, G. M., 1981, Callosal connections of suprasylvian visual areas in the cat, *Neuroscience* **6:**703–712.

Kelly, J. P., and Van Essen, D. C., 1974, Cell structure and function in the visual cortex of the cat, *J. Physiol. (London)* **238:**515–547.

Kelly, J. P., and Wong, D., 1981, Laminar connections of the cat's auditory cortex, *Brain Res.* **212:**1–15.

Killackey, H. P., Gould, H. J., Cusick, C. G., Pons, T. P., and Kaas, J. H., 1983a, The relation of corpus callosum connections to architectonic fields and body surface maps in sensorimotor cortex of New and Old World monkeys, *J. Comp. Neurol.* **219:**384–419.

Killackey, J., Olavarria, J., and Van Sluyters, R. C., 1983b, A vibrissae related pattern of callosal connections in the primary somatosensory cortex of the rat, *Soc. Neurosci. Abstr.* **9:**251.

Koppel, H., and Innocenti, G. M., 1983, Is there a genuine exuberancy of callosal projections in development? A quantitative electron microscopic study in the cat, *Neurosci. Lett.* **41:**33–40.

Künzle, H., 1975, Bilateral projections from precentral motor cortex to the putamen and other parts of the basal ganglia: An autoradiographic study in *Macaca fascicularis*, *Brain Res.* **88:**195–209.

Künzle, H., 1976, Alternating afferent zones of high and low axon terminal density within the macaque motor cortex, *Brain Res.* **106:**365–370.

Künzle, H., 1978, Cortico-cortical efferents of primary motor and somatosensory regions of the cerebral cortex in *Macaca fascicularis*, *Neuroscience* **3:**25–39.

Künzle, H., and Akert, K., 1977, Efferent connections of cortical area 8 (frontal eye field) in *Macaca fascicularis:* A reinvestigation using the autoradiographic technique, *J. Comp. Neurol.* **173:**147–163.

La Mantia, A.-S., and Rakic, P., 1984, The number, size, myelination, and regional variation of axons in the corpus callosum and anterior commissure of the developing rhesus monkey, *Neurosci. Abstr.* **10:**1081.

Laurberg, S., and Sørensen, K. E., 1981, Associational and commissural collaterals of neurons in the hippocampal formation (hilus fasciae dentate and subfield CA3), *Brain Res.* **212:**287–300.

Lent, R., 1983, Cortico-cortical connections reorganize in hamsters after neonatal transection of the callosal bridge, *Dev. Brain Res.* **11:**137–142.

Lepore, F., and Guillemot, J.-P., 1982, Visual receptive field properties of cells innervated through the corpus callosum in the cat, *Exp. Brain Res.* **46:**413–424.

Lepore, F., Samson, A., and Molotchnikoff, S., 1983a, Effects on binocular activation of cells in visual cortex of the cat following the transection of the optic tract, *Exp. Brain Res.* **50**:392–396.

Lepore, F., Prévost, L., Richer, L., and Guillemot, J. P., 1983b, Interhemispheric transfer of somesthetic information in the corpus callosum, *Soc. Neurosci. Abstr.* **9**:250.

Looney, G. A., and Elberger, A. J., 1983, Myelination of the visual fibers of the corpus callosum in cats. *Soc. Neurosci. Abstr.* **9**:1220.

Looney, G. A., and Elberger, A. J., 1983, Myelination of the visual fibers of the corpus callosum in cats. *Soc. Neurosci. Abstr.* **9**:**1220.**

Lund, J. S., and Boothe, R. G., 1975, Interlaminar connections and pyramidal neuron organisation in the visual cortex, area 17, of the macaque monkey, *J. Comp. Neurol.* **159**:305–334.

Lund, J. S., and Lund, R. D., 1970, The termination of callosal fibers in the paravisual cortex of the rat, *Brain Res.* **17**:25–45.

Lund, J. S., Lund, R. D., Hendrickson, A. E., Bunt, A. H., and Fuchs, A. F., 1975, The origin of efferent pathways from the primary visual cortex, area 17, of the macaque monkey as shown by retrograde transport of horseradish peroxidase, *J. Comp. Neurol.* **164**:287–304.

Lund, J. S., Hendrickson, A. E., Ogren, M. P., and Tobin, E. A., 1981, Anatomical organization of primate visual cortex area VII, *J. Comp. Neurol.* **202**:19–45.

Lund, R. D., and Mitchell, D. E., 1979a, The effects of dark-rearing on visual callosal connections of cats, *Brain Res.* **167**:172–175.

Lund, R. D., and Mitchell, D. E., 1979b, Asymmetry in the visual callosal connections of strabismic cats, *Brain Res.* **167**:176–179.

Lund, R. D., Mitchell, D. E., and Henry, G. H., 1978, Squint-induced modification of callosal connections in cats, *Brain Res.* **144**:169–172.

Luttenberg, J., 1974, Heterotopic contralateral projection of neocortical spheres of the cat brain, *Acta Univ. Carol. Med.* **20**:225–249.

Luttenberg, J., and Marsala, J., 1963, The topography of the commissural fibers in the corpus callosum of the cat's brain, *Cesk. Morfologie* **11**:166–176.

McCulloch, W. S., and Garol, H. W., 1941, Cortical origin and distribution of corpus callosum and anterior commissure in the monkey (*Macaca mulatta*), *J. Neurophysiol.* **4**:555–563.

Maciewicz, R. J., 1974, Afferents to the lateral suprasylvian gyrus of the cat traced with horseradish peroxidase, *Brain Res.* **78**:139–143.

McKenna, T. M., Whitsel, B. L., Dreyer, D. A., and Metz, C. B., 1981, Organization of cat anterior parietal cortex: Relations among cytoarchitecture, single neuron functional properties, and interhemispheric connectivity, *J. Neurophysiol.* **45**:667–697.

Manzoni, T., Caminiti, R., Spidalieri, G., and Morelli, E., 1979, Anatomical and functional aspects of the associative projections from somatic area SI to SII, *Exp. Brain Res.* **34**:453–470.

Manzoni, T., Barbaresi, P., Bellardinelli, E., and Caminiti, R., 1980, Callosal projections from the two body midlines, *Exp. Brain Res.* **39**:1–9.

Markowitsch, H. J., and Guldin, W. O., 1983, Heterotopic interhemispheric cortical connections in the rat, *Brain Res. Bull.* **10**:805–810.

Marzi, C. A., Antonini, A., Di Stefano, M., and Legg, C. R., 1980, Callosum-dependent binocular interactions in the lateral suprasylvian area of Siamese cats which lack binocular neurons in areas 17 and 18, *Brain Res.* **197**:230–235.

Marzi, C. A., Antonini, A., Di Stefano, M., and Legg, C. R., 1982, The contribution of the corpus callosum to receptive fields in the lateral suprasylvian visual areas of the cat, *Behav. Brain Res.* **4**:155–176.

Matsumura, M., and Kubota, K., 1979, Cortical projection to hand-arm motor area from postarcuate area in macaque monkeys: A histological study of retrograde transport of horseradish peroxidase, *Neurosci. Lett.* **11**:241–246.

Merzenich, M. M., Knight, P. L., and Roth, G. L., 1975, Representation of cochlea within primary auditory cortex in the cat, *J. Neurophysiol.* **38**:231–249.

Meyer, G., and Albus, K., 1981, Spiny stellates as cells of origin of association fibres from area 17 to area 18 in the cat's neocortex, *Brain Res.* **210**:335–341.

Meyerson, B. A., 1968, Ontogeny of interhemispheric functions: An electrophysiological study in pre- and postnatal sheep, *Acta Physiol. Scand. Suppl.* **312**:1–111.

Miller, R., 1975, Distribution and properties of commissural and other neurons in cat sensorimotor cortex, *J. Comp. Neurol.* **164**:361–374.

Minciacchi, D., Molinari, M., and Antonini, A., 1983, The commissural organization of the bilateral claustro-cortical projections, *Neurosci. Lett. Suppl.* **14:**S248.

Moran, J., Desimone, R., Schein, S. J., and Mishkin, M., 1983, Suppression from ipsilateral visual field in area V4 of the macaque, *Soc. Neurosci. Abstr.* **9:**957.

Mountcastle, V. B., and Powell, T. P. S., 1959, Neural mechanisms subserving cutaneous sensibility, with special reference to the role of afferent inhibition in sensory perception and discrimination, *Bull. Johns Hopkins Hosp.* **105:**201–232.

Myers, R. E., 1962, Commissural connections between occipital lobes of the monkey, *J. Comp. Neurol.* **118:**1–10.

Naito, H., Nakamura, K., Kurosaki, T., and Tamura, Y., 1970, Transcallosal excitatory postsynaptic potentials of fast and slow pyramidal tract cells in cat sensorimotor cortex, *Brain Res.* **19:**299–301.

Naito, H., Miyakawa, F., and Ito, N., 1971, Diameters of callosal fibers interconnecting cat sensorimotor cortex, *Brain Res.* **27:**369–372.

Newsome, W. T., and Allman, J. M., 1980, Interhemispheric connections of visual cortex in the owl monkey, *Aotus trivirgatus,* and the bushbaby, *Galago senegalensis, J. Comp. Neurol.* **194:**209–233.

O'Leary, D. D. M., Stanfield, B. B., and Cowan, W. M., 1981, Evidence that the early postnatal restriction of the cells of origin of the callosal projection is due to the elimination of axonal collaterals rather than to the death of neurons, *Dev. Brain Res.* **1:**607–617.

Pandya, D. N., and Rosene, D. L., 1983, Termination patterns of thalamic, callosal, and association afferents of the primary auditory area in the rhesus monkey, *Soc. Neurosci. Abstr.* **9:**954.

Pandya, D. N., and Vignolo, L. A., 1968, Interhemispheric neocortical projections of somatosensory areas I and II in the rhesus monkey, *Brain Res.* **7:**300–303.

Pandya, D. N., and Vignolo, L. A., 1969, Interhemispheric projections of the parietal lobe in the rhesus monkey, *Brain Res.* **15:**49–65.

Pandya, D. N., and Vignolo, L. A., 1971, Intra- and interhemispheric projections of the precentral, premotor arcuate areas in the rhesus monkey, *Brain Res.* **26:**217–233.

Pandya, D. N., Hallett, M., and Mukherjee, S. K., 1969, Intra- and interhemispheric connections of the neocortical auditory system in the rhesus monkey, *Brain Res.* **14:**49–65.

Pandya, D. N., Dye, P., and Butters, N., 1971a, Efferent cortico-cortical projections of the prefontal cortex in the rhesus monkey, *Brain Res.* **31:**35–46.

Pandya, D. N., Karol, E. A., and Heilbronn, D., 1971b, The topographical distribution of interhemispheric projections in the corpus callosum of the rhesus monkey, *Brain Res.* **32:**31–43.

Payne, B. R., Elberger, A. J., Berman, N., and Murphy, E. H., 1980, Binocularity in the cat visual cortex is reduced by sectioning the corpus callosum, *Science* **207:**1097–1099.

Pines, L. J., and Maiman, R. M., 1939, Cells of origin of fibers of corpus callosum: Experimental and pathologic observations, *Arch. Neurol. Psychiatry* **42:**1076–1082.

Porter, L. L., and White, E. L., 1983, Afferent and efferent pathways of the vibrissal region of primary motor cortex in the mouse, *J. Comp. Neurol.* **214:**279–289.

Porter, L. L., White, E. L., and Belford, G. R., 1983, Reciprocal synaptic relationships of MsI pyramidal neurons which project transcallosally in the mouse, *Soc. Neurosci. Abstr.* **9:**493.

Rakic, P., 1974, Neurons in rhesus monkey visual cortex: Systematic relation between time of origin and eventual disposition, *Science* **183:**425–427.

Rakic, P., and Yakovlev, P. I., 1968, Development of the corpus callosum and cavum septi in man, *J. Comp. Neurol.* **132:**45–72.

Ramón y Cajal, S., 1894, *Les Nouvelles Idées sur la Structure du Système Nerveux chez l'Homme et chez les Vertébrés,* Reinwald, Paris.

Ramón y Cajal, S., 1911, *Histologie du système Nerveux de l'Homme et des Vertébrés,* Volume II, Maloine, Paris, pp. 604–606.

Rao, V. M., 1979, Interhemispheric connections between primary visual areas in adult sheep and new-born lambs, *J. Physiol. (London)* **55:**89P.

Ravizza, R. J., Straw, R. B., and Long, P. D., 1976, Laminar origin of efferent projections from auditory cortex in the golden Syrian hamster, *Brain Res.* **114:**497–500.

Reale, R. A., and Imig, T. J., 1980, Tonotopic organization in auditory cortex of the cat, *J. Comp. Neurol.* **192:**265–291.

Rhoades, R. W., and Dellacroce, D. D., 1980a, Visual callosal connections in the golden hamster, *Brain Res.* **190:**248–254.

Rhoades, R. W., and Dellacroce, D. D., 1980b, Neonatal enucleation induces an asymmetric pattern of visual callosal connections in hamsters, *Brain Res.* **202:**189–195.

Rhoades, R. W., Mooney, R. D., Yuen, G., and Fish, S. E., 1983, A comparison of visual connections in normal, neonatally blinded and congenitally anophthalmic mice, *Soc. Neurosci. Abstr.* **9:**910.

Ribak, E., 1977, A note on the laminar organization of rat visual cortical projections, *Exp. Brain Res.* **27:**413–418.

Rice, F. L., 1975, The development of the primary somatosensory cortex in the mouse: (1) A Nissl study of the ontogenesis of the barrels and the barrel field, (2) A quantitative autoradiographic study of the time of origin and pattern of migration of neuroblasts in area SI, Doctoral dissertation, Johns Hopkins University.

Rice, F. L., and Van der Loos, H., 1977, Development of the barrels and barrel field in the somatosensory cortex of the mouse, *J. Comp. Neurol.* **171:**545–560.

Rizzolatti, G., Scandolara, C., Matelli, M., and Gentilucci, M., 1981a, Afferent properties of periarcuate neurons in macaque monkeys. I. Somatosensory responses, *Behav. Brain Res.* **2:**125–146.

Rizzolatti, G., Scandolara, C., Matelli, M., and Gentilucci, M., 1981b, Afferent properties of periarcuate neurons in macaque monkeys. II. Visual responses, *Behav. Brain Res.* **2:**147–163.

Robinson, D. L., 1973, Electrophysiological analysis of interhemispheric relations in the second somatosensory cortex of the cat, *Exp. Brain Res.* **18:**131–144.

Rockland, K. S., and Pandya, D. N., 1979, Laminar origins and terminations of cortical connections of the occipital lobe in the rhesus monkey, *Brain Res.* **179:**3–20.

Rothblat, L. A., and Hayes, L. L., 1982, Age-related changes in the distribution of visual callosal neurons following monocular enucleation in the rat, *Brain Res.* **246:**146–149.

Sanides, D., 1978, The retinotopic distribution of visual callosal projections in the suprasylvian visual areas compared to the classical visual areas (17, 18, 19) in the cat, *Exp. Brain Res.* **33:**435–443.

Sanides, D., and Albus, K., 1980, The distribution of interhemispheric projections in area 18 of the cat: Coincidence with discontinuities of the representation of the visual field in the second visual area (V2), *Exp. Brain Res.* **38:**237–240.

Sanides, D., and Donate-Oliver, F., 1978, Identification and localisation of some relay cells in cat visual cortex, in: *Architectonics of the Cerebral Cortex* (M. A. B. Brazier and H. Petsche, eds.), Raven Press, New York, pp. 227–234.

Schwartz, M. L., and Goldman-Rakic, P. S., 1982, Single cortical neurones have axon collaterals to ipsilateral and contralateral cortex in fetal and adult primates, *Nature* **299:**154–155.

Seggie, J., and Berry, M., 1972, Ontogeny of interhemispheric evoked potentials in the rat: Significance of myelination of the corpus callosum, *Exp. Neurol.* **35:**215–232.

Segraves, M. A., and Innocenti, G. M., 1982, An examination of the projections of cat visual callosal neurons using double retrograde tracers, *Neurosci. Lett. Suppl.* **10:**S442.

Segraves, M. A., and Innocenti, G. M., 1985, A comparison of the distribution of ipsilaterally and contralaterally projecting corticocortical neurons in cat visual cortex using two fluorescent tracers, *J. Neurosci.* **5:**2107–2118.

Segraves, M. A., and Rosenquist, A. C., 1982a, The distribution of the cells of origin of callosal projections in cat visual cortex, *J. Neurosci.* **2:**1079–1089.

Segraves, M. A., and Rosenquist, A. C., 1982b, The afferent and efferent callosal connections of retinotopically defined areas in cat cortex, *J. Neurosci.* **2:**1090–1107.

Seltzer, B., and Pandya, D. N., 1983, The distribution of posterior parietal fibers in the corpus callosum of the rhesus monkey, *Exp. Brain Res.* **49:**147–150.

Shanks, M. F., Rockel, A. J., and Powell, T. P. S., 1975, The commissural fibre connections of the primary somatic sensory cortex, *Brain Res.* **98:**166–171.

Shatz, C., 1977a, Abnormal interhemispheric connections in the visual system of Boston Siamese cats: A physiological study, *J. Comp. Neurol.* **171:**229–246.

Shatz, C. J., 1977b, Anatomy of interhemispheric connections in the visual system of Boston Siamese and ordinary cats, *J. Comp. Neurol.* **173:**497–518.

Shofer, R. J., and Purpura, D. P., 1972, Spread of transcallosally evoked responses in immature association cortex, *Exp. Neurol.* **37:**431–445.

Sholl, D. A., 1955, The organization of the visual cortex in the cat, *J. Anat.* **89:**33–46.

Shoumura, K., 1972, Patterns of fiber degeneration in the lateral wall of the suprasylvian gyrus (Clare–Bishop area) following lesions in the visual cortex in cats. *Brain Res.* **43:**264–267.

Shoumura, K., 1974, An attempt to relate the origin and distribution of commissural fibers to the presence of large and medium pyramids in layer III in the cat's visual cortex, *Brain Res.* **67:**13–25.

60.

Shoumura, K., Ando, T., and Kato, K., 1975, Structural organization of 'callosal' OBg in human corpus callosum agenesis, *Brain Res.* **93:**241–252.

Sidtis, J. J., Volpe, B. T., Holtzman, J. D., Wilson, D. H., and Gazzaniga, M. S., 1981, Cognitive interaction after staged callosal section: Evidence for transfer of semantic activation, *Science* **212:**344–346.

Silver, J., and Ogawa, M. Y., 1983, Postnatally induced formation of the corpus callosum in acallosal mice on glia-coated cellulose bridges, *Science* **220:**1067–1069.

Silver, J., Lorenz, S. E., Wahlsten, D., and Coughlin, J., 1982, Axonal guidance during development of the great cerebral commissures: Descriptive and experimental studies, in vivo, on the role of preformed glial pathways, *J. Comp. Neurol.* **210:**10–29.

Simmons, P. A., and Pearlman, A. L., 1983, Receptive-field properties of transcallosal visual cortical neurons in the normal and reeler mouse, *J. Neurophysiol.* **50:**838–847.

Singer, M., Nordlander, R. H., and Egar, M., 1979, Axonal guidance during embryogenesis and regeneration in the spinal cord of the newt: The blueprint hypothesis of neuronal pathway patterning, *J. Comp. Neurol.* **185:**1–22.

Singer, W., Tretter, F., and Cynader, M., 1975, Organization of cat striate cortex: A correlation of receptive-field properties with afferent and efferent connections, *J. Neurophysiol.* **38:**1080–1098.

Sloper, J. J., and Powell, T. P. S., 1979, An experimental electron microscopic study of afferent connections to the primate motor and somatic sensory cortices, *Philos. Trans. R. Soc. London Ser. B* **285:**199–226.

Somogyi, P., Hodgson, A. J., and Smith, A. D., 1979, An approach to tracing neuron networks in the cerebral cortex and basal ganglia: Combination of Golgi staining, retrograde transport of horseradish peroxidase and anterograde degeneration of synaptic boutons in the same material, *Neuroscience* **4:**1805–1852.

Somogyi, P., Kisvárday, Z. F., Martin, K. A. C., and Whitteridge, D., 1983, Synaptic connections of morphologically identified and physiologically characterized large basket cells in the striate cortex of cat, *Neuroscience* **10:**261–294.

Spatz, W. B., and Tigges, J., 1972, Experimental-anatomical studies on the "middle temporal visual area (MT)" in primates. I. Efferent cortico-cortical connections in the marmoset *Callithrix jacchus*, *J. Comp. Neurol.* **146:**451–464.

Sperry, R., 1982, Some effects of disconnecting the cerebral hemispheres, *Science* **217:**1223–1226.

Squatrito, S., Battaglini, P. P., Galletti, C., and Riva Sanseverino, E., 1980, Projections from the visual cortex to the contralateral claustrum of the cat revealed by an anterograde axonal transport method, *Neurosci. Lett.* **19:**271–275.

Steele Russel, I., Van Hof, M. W., and Berlucchi, G., 1979, *Structure and Function of Cerebral Commissures*, Macmillan & Co., London.

Sunderland, S., 1940, The distribution of commissural fibres in the corpus callosum in the macaque monkey, *J. Neurol. Psychiatry* **3:**9–18.

Swadlow, H. A., 1974, Properties of antidromically activated callosal neurons and neurons responsive to callosal input in rabbit binocular cortex, *Exp. Neurol.* **43:**424–444.

Swadlow, H. A., 1977, Relationship of the corpus callosum to visual areas I and II of the awake rabbit, *Exp. Neurol.* **57:**516–531.

Swadlow, H. A., and Waxman, S. G., 1976, Variations in conduction velocity and excitability following single and multiple impulses of visual callosal axons in the rabbit, *Exp. Neurol.* **53:**128–150.

Swadlow, H. A., and Wayand, T. G., 1981, Efferent systems of the rabbit visual cortex: Laminar distribution of the cells of origin, axonal conduction velocities, and identification of axonal branches, *J. Comp. Neurol.* **203:**799–822.

Swadlow, H. A., Weyand, T. G., and Waxman, S. G., 1978, The cells of origin of the corpus callosum in rabbit visual cortex, *Brain Res.* **156:**129–134.

Swadlow, H. A., Geschwind, N., and Waxman, S. G., 1979, Commissural transmission in humans, *Science* **204:**530–531.

Swadlow, H. A., Waxman, S. G., and Geschwind, N., 1980, Small-diameter nonmyelinated axons in the primate corpus callosum, *Arch. Neurol.* **37:**114–115.

Teitelbaum, H., Sharpless, S. K., and Byck, R., 1968, Role of somatosensory cortex in interhemispheric transfer of tactile habits, *J. Comp. Physiol. Psychol.* **66:**623–632.

Tigges, J., Spatz, W. B., and Tigges, M., 1974, Efferent cortico-cortical fiber connections of area 18 in the squirrel monkey (*Saimiri*), *J. Comp. Neurol.* **158:**219–236.

Tomasch, J., 1954, Size, distribution and number of fibres in the human corpus callosum, *Anat. Rec.* **119:**119–135.

Towns, L. C., Giolli, R. A., and Haste, D. A., 1977, Corticocortical fiber connections of the rabbit visual cortex: A fiber degeneration study, *J. Comp. Neurol.* **173**:537–560.

Toyama, K., and Matsunami, K., 1976, Convergence of specific visual and commissural impulses upon inhibitory interneurones in cat's visual cortex, *Neuroscience* **1**:107–112.

Toyama, K., Tokashiki, S., and Matsunami, K., 1969, Synaptic action of commissural impulses upon association efferent cells in cat visual cortex, *Brain Res.* **14**:518–520.

Toyama, K., Matsunami, K., Ohno, T., and Tokashiki, S., 1974, An intracellular study of neuronal organization in the visual cortex, *Exp. Brain Res.* **21**:45–66.

Ulett, G., Dow, R. S., and Larsell, O., 1944, The inception of conductivity in the corpus callosum and the cortico-ponto-cerebellar pathway of young rabbits with reference to myelination, *J. Comp. Neurol.* **80**:1–10.

Valentino, K. L., and Jones, E. G., 1982, The early formation of the corpus callosum: A light and electron microscopic study in foetal and neonatal rats, *J. Neurocytol.* **11**:583–609.

Valentino, K. L., Jones, E. G., and Kane, S. A., 1983, Expression of GFAP immunoreactivity during development of long fiber tracts in the rat CNS, *Dev. Brain Res.* **9**:317–336.

Van der Loos, H., 1965, The "improperly" oriented pyramidal cell in the cerebral cortex and its possible bearing on problems of neuronal growth and cell orientation, *Bull. Johns Hopkins Hosp.* **117**:228–250.

Van Essen, D. C., and Zeki, S. M., 1978, The topographic organization of rhesus monkey prestriate cortex, *J. Physiol.* (*London*) **277**:193–226.

Van Essen, D. C., Newsome, W. T., and Bixby, J. L., 1982, The pattern of interhemispheric connections and its relationship to extrastriate visual areas in the macaque monkey, *J. Neurosci.* **2**:265–283.

Vaughan, D. W., 1983, Thalamic and callosal connections of the rat auditory cortex, *Brain Res.* **260**:181–189.

Vaughan, D. W., and Foundas, S., 1982, Synaptic proliferation in the auditory cortex of the young adult rat following callosal lesions, *J. Neurocytol.* **11**:29–51.

Vogt, B. A., and Gorman, A. L. F., 1982, Responses of cortical neurons to stimulation of corpus callosum in vitro, *J. Neurophysiol.* **48**:1257–1273.

Vogt, B. A., Rosene, D. L., and Peters, A., 1981, Synaptic termination of thalamic and callosal afferents in cingulate cortex of the rat, *J. Comp. Neurol.* **201**:265–283.

Wagor, E., Lin, C. S., and Kaas, J. H., 1975, Some cortical projections of the dorsomedial visual area (DM) of association cortex in the owl monkey, *Aotus trivirgatus*, *J. Comp. Neurol.* **163**:227–250.

Wahlsten, D., 1974, Heritable aspects of anomalous myelinated fibre tracts in the forebrain of the laboratory mouse, *Brain Res.* **68**:1–18.

Waxman, S. G., and Swadlow, H. A., 1976, Ultrastructure of visual axons in the rabbit, *Exp. Neurol.* **53**:115–127.

Weber, J. T., Rieck, R. W., and Gould, H. J., 1983, Interhemispheric and subcortical collaterals of single cortical neurons in the adult cat, *Brain Res.* **276**:333–338.

White, E. L., and DeAmicis, R. A., 1977, Afferent and efferent projections of the region in mouse SmI cortex which contains the posteromedial barrel subfield, *J. Comp. Neurol.* **175**:455–481.

Whitsel, B. L., Petrucelli, L. M., and Werner, G., 1969, Symmetry and connectivity in the map of the body surface in somatosensory area II of primates, *J. Neurophysiol.* **32**:170–183.

Wilson, M. E., 1968, Cortico-cortical connexions of the cat visual areas, *J. Anat.* **102**:375–386.

Winfield, D. A., Gatter, K. C., and Powell, T. P. S., 1975, Certain connections of the visual cortex of the monkey shown by the use of horseradish peroxidase, *Brain Res.* **92**:456–461.

Wise, S. P., 1975, The laminar organization of certain afferent and efferent fiber systems in the rat somatosensory cortex, *Brain Res.* **90**:139–142.

Wise, S. P., and Jones, E. G., 1976, The organization and postnatal development of the commissural projection of the rat somatic sensory cortex, *J. Comp. Neurol.* **168**:313–344.

Wise, S. P., and Jones, E. G., 1978, Developmental studies of thalamocortical and commissural connections in the rat somatic sensory cortex, *J. Comp. Neurol.* **178**:187–208.

Witelson, S. F., 1983, The corpus callosum is larger in left handers, *Soc. Neurosci. Abstr.* **9**:917.

Wong, D., and Kelly, J. P., 1981, Differentially projecting cells in individual layers of the auditory cortex: A double-labeling study, *Brain Res.* **230**:362–366.

Wong-Riley, M. T. T., 1974, Demonstration of geniculocortical and callosal projection neurons in the squirrel monkey by means of retrograde axonal transport of horseradish peroxidase, *Brain Res.* **79**:267–272.

Wong-Riley, M. T. T., 1979, Columnar cortico-cortical interconnections within the visual system of the squirrel and macaque monkeys, *Brain Res.* **162**:201–217.

Woolsey, T., and Van der Loos, H., 1970, The structural organization of layer IV in the somatosensory region (SI) of mouse cerebral cortex, *Brain Res.* **17**:205–242.

Yakovlev, P. I., and Lecours, A. -R., 1967, The myelogenetic cycles of regional maturation of the brain, in: *Regional Development of the Brain in Early Life* (A. Minkowski, ed.), Blackwell, Oxford, pp. 3–70.

Yorke, C. H., and Caviness, V. S., 1975, Interhemispheric neocortical connections of the corpus callosum in the normal mouse: A study based on anterograde and retrograde methods, *J. Comp. Neurol.* **164**:233–246.

Záborszky, L., and Wolff, J. R., 1982, Distribution patterns and individual variations of callosal connections in the albino rat, *Anat. Embryol.* **165**:213–232.

Zant, J. D., and Strick, P. L., 1978, The cells of origin of interhemispheric connections in the primate motor cortex, *Soc. Neurosci. Abstr.* **4**:308.

Zeki, S. M., 1970, Interhemispheric connections of prestriate cortex in monkey, *Brain Res.* **19**:63–75.

Zeki, S. M., 1978, The cortical projections of foveal striate cortex in the rhesus monkey, *J. Physiol. (London)* **277**:227–244.

Zeki, S., and Fries, W., 1980, A function of the corpus callosum in the Siamese cat, *Proc. R. Soc. London Ser. B* **207**:249–258.

Zeki, S. M., and Sandeman, D. R., 1976, Combined anatomical and electrophysiological studies on the boundary between the second and third visual areas of rhesus monkey cortex, *Proc. R. Soc. London Ser. B* **194**:555–562.

Zuckerkandl, E., 1909, Zur Entwicklung des Balkens, *Arb. Neurol. Inst. Univ. Wien* **17**:373–409.