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MORPHOLOGICAL PLASTICITY OF POSTSYNAPTIC NEURONES IN REACTIVE SYNAPTOGENESIS

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Summary

Partial deafferentation of certain brain regions (septal nuclei, hippocampus, etc.) in adult animals results (1) in the disappearance of degenerating axon terminals and (2) in the short-term persistence of vacant postsynaptic sites. These postsynaptic sites have been shown to be re-supplied by sprouted axon terminals of intact axons. This paper will demonstrate that, in brain regions (e.g. cerebellar cortex, lateral geniculate nucleus) where axonal sprouting of local elements or of persisting afferent axons is negligible or absent, synaptic reorganization involves the active participation of postsynaptic dendritic and somatic elements of surviving local nerve cells. Synaptic regeneration can be demonstrated by morphological means both in developing and in adult central nervous system. The dendrites may show two types of response to deafferentation: (1) the formation of presynaptic specializations along their otherwise 'classical' postsynaptic membrane (the axonization of dendrites) resulting in the formation of new, dendrodendritic synapses, and (2) the 'adaptive' (structural) reduction in size ('atrophy') of the denervated nerve cell dendritic arborization, leading to a relative increase in density of the surviving (though non-sprouting) afferent axon terminals. In both cases a partial functional recovery can be demonstrated.

Introduction

It is generally accepted that certain neurones in the central nervous system (CNS) of adult animals maintain their potential to form new synaptic junctions in response to lesions or other stimuli. It has been demonstrated that partial denervation of septal nuclei (Raisman, 1969; Raisman and Field, 1973), hippocampus (Matthews *et al.* 1976; Frotscher *et al.* 1981; Steward and Vinsant, 1983; Hoff, 1986; Steward *et al.* 1988), red nucleus (Tsukahara, 1981; Murakami *et al.* 1982) and other CNS regions (Murray *et al.* 1979; Zimmer *et al.* 1982; Bromberg *et al.* 1987; Ichikawa, 1987*a*,*b*) was followed by reoccupation of the partially denervated nerve cell by newly formed (collateral) axonal branches of persisting afferent or local fibres, resulting in the formation of 'new' synaptic contacts. This process has been defined (Matthews *et al.* 1976) as 'reactive' synaptogenesis, implying that it is

Key words: synaptogenesis, dendrites, cerebellum, thalamus.

a reaction to stimuli such as lesions but is not part of the normal developmental process. The emphasis in this type of reactive synaptogenesis is on the active role of axonal processes in finding and 'resaturating' the available vacant postsynaptic sites. Previously, ultrastructural studies of reinnervation in the CNS as well as in autonomic ganglia (Raisman and Field, 1973) have suggested that the target neurones have a more or less fixed number of postsynaptic sites, and that no new postsynaptic sites are formed during reactive synaptogenesis. More recently, however, indirect evidence (Matthews *et al.* 1976; Hillman and Chen, 1981; Somogyi *et al.* 1982) and direct observations (Purves and Lichtman, 1987) have suggested that mature mammalian neurones maintain a potential to produce new postsynaptic receptor surfaces for new synaptic contacts. They are not, therefore, merely passive participants in reactive synaptogenesis, but are actively involved. The aim of this paper is to present further evidence for the dynamic role of postsynaptic elements during synaptogenesis in certain regions of the adult nervous system. In brain regions such as the cerebellar cortex and the thalamic nuclei, where the neuronal basis of axonal-type reactive synaptogenesis involving the sprouting of local or extrinsic axons is negligible or lacking, synaptic reorganization following partial (Hamori and Silakov, 1980; Somogyi *et al.* 1984, 1987) or total (Hamori and Somogyi, 1982) deafferentation occurs *via* the active participation of postsynaptic dendritic processes or even of postsynaptic perikaria. Two types of dendritic reactive synaptogenesis will be described. In the first, the formation of presynaptic specializations along their otherwise 'classical' postsynaptic membrane (Hamori and Silakov, 1980; Hamori and Somogyi, 1982; Somogyi *et al.* 1984; Kalil and Behan, 1987) results in the genesis of new, dendrodendritic or even somato-dendritic synapses. In the second, the 'adaptive' structural reduction in size of the denervated nerve cell dendritic arborization leads to a relative increase in density of the surviving (though nonsprouting) afferent axon terminals (Somogyi *et al.* 1987).

Deafferentation-induced development of presynaptic dendrites in cerebellar cortex

In normal, intact cerebellar cortices, all nerve cells are classical neurones (Eccles *et al.* 1967; Palay and Chan-Palay, 1974); the somata and dendrites are invariably postsynaptic, and the axons are exclusively presynaptic. Under abnormal conditions, as in organotypic cerebellar cultures (Kim, 1974) or in cerebellar mutant mice (Sotelo, 1975), however, granule cells were shown to accumulate synaptic vesicles in their somata or in their dendrites. Similarly, following neonatal X-irradiation, Golgi neurones were shown to develop presynaptic sites in their somata and dendrites (Sotelo, 1977).

In another experimental study (Hamori and Somogyi, 1982) it was shown that mossy fibre deafferentation of the granular layer alone results in the synaptic reorganization of cerebellar glomeruli, with the formation of presynaptic sites in

the dendrites and somata of granule cells and of numerous (although not all) Golgi nerve cells.

The main synaptic afferents to the granular layer are the mossy fibres. The majority of these are excitatory and utilise glutamate as a transmitter, although some nucleocortical mossy endings have been shown to be GABAergic (Hamori and Takacs, 1989). The mossy terminal in the cerebellar glomerulus is contacted synaptically by 200–300 small postsynaptic dendritic digits of the granule cells (Jakab and Hamori, 1988). In addition, in many glomeruli large 'hairy' dendritic processes of the Golgi neurones also receive synaptic contacts from the centrally located mossy terminal (Eccles *et al.* 1967). Both types of dendrite receive synaptic contacts at the periphery of the glomerulus from small axonal profiles of the Golgi cells (Eccles *et al.* 1967).

Fifteen to thirty days after surgical deafferentation of the cerebellar cortex the small Golgi nerve cells (but not the large ones) developed presynaptic sites both on their somata and on their thick intraglomerular dendritic processes (Hamori and Somogyi, 1982). Interestingly, the Golgi neurones that developed presynaptic dendrites were, without exception, glycine-containing, whereas those that did not exhibit presynaptic dendrites, usually large Golgi cells, stained only for GABA (R. L. Jakab and J. Hamori, unpublished observations). In any case, the newly developed presynaptic sites faced the dendritic digits of the granule cells; the dendro-dendritic synapses were, occasionally, reciprocal.

Granule cells also frequently developed presynaptic sites, both in their dendrites and in their somata, after mossy fibre deafferentation. Quantitative analysis of synaptic numbers in mossy-deafferented glomeruli has shown that the resulting presynaptic dendritic synapses by granule cells are numerous within the glomeruli. Nearly 50 such synaptic contacts can be found in each deafferented glomerulus. These are mainly dendro-dendritic and are probably excitatory (Table 1; R. L. Jakab and J. Hamori, in preparation).

Of special interest was the finding that, following mossy fibre degeneration, the total number of synaptic junctions in the reorganised synaptic glomeruli did not change significantly (Table 1). The only important alteration was in the proportion

Table 1. *Number of synaptic junctions in control and mossy-fibre-deafferented cerebellar glomeruli*

	Number of synapses			
	Mossy	Golgi axon	Dendro-dendritic	Total number
Control	145±23	87±33	0	232
Deafferented	0	201±59	47±9	248

Average of five simple glomeruli in each group.
Dendro-dendritic synapses represent granule-to-granule dendritic contact only, since dendrites of Golgi cells were absent in the simple glomeruli investigated.

Table 2. *Number of granule cell dendrites and digits in control and mossy-fibre-deafferented simple glomeruli*

	Dendrites	Digits
Control	53	208
Deafferented	52	216

of excitatory and inhibitory synaptic junctions. In the normal glomeruli, excitatory synaptic junctions (represented exclusively by mossy terminals) made up the majority of the 232 individual junctions (Table 1); in the reorganised glomeruli, the inhibitory junctions of Golgi axons became the dominant synaptic type, while dendro-dendritic (excitatory) junctions between granule cells represented only one-fifth of all synaptic junctions. The number of postsynaptic dendrites within the mossy-fibre-deprived glomerulus did not change during the first month after deafferentation (Table 2), suggesting that the number of synapses that belonged to the postsynaptic nerve cells remained unchanged, irrespective of the excitatory or inhibitory nature of the new presynaptic elements. A similar observation has been made by Hillman and Chen (1981) in experiments leading to a reduction of the presynaptic parallel fibre/Purkinje cell ratio in the cerebellar cortex. These authors have suggested that there is a constancy in total synaptic area determined intrinsically by the recipient nerve cell. This might also be the case in sympathetic ganglia, where Field and Raisman (1985) have demonstrated that, under normal conditions, postsynaptic ganglion cells have a very limited potential to increase their synaptic surface, even in the presence of an excess of presynaptic partners.

Deafferentation- and/or axotomy-induced development of presynaptic dendrites in lateral geniculate nucleus of cat

'Axonization', the development of presynaptic sites in partially deafferented relay cell dendrites, has been observed in a specific thalamic nucleus, the lateral geniculate nucleus (LGN) of cats (Hamori and Silakov, 1980; Hamori, 1982; Somogyi *et al.* 1984; Kalil and Behan, 1987). Following chronic disconnection from the cortex (the main source of afferentation to the LGN), it has been found that those geniculo-cortical relay neurones surviving axotomy (about 15 % of the total number of relay cells in the intact LGN: Madarasz *et al.* 1983) developed presynaptic sites on the surface of their dendritic processes (Fig. 1). The new presynaptic dendrites formed synaptic contacts with other relay neurones or with local, GABAergic interneurones. Recent electrophysiological data suggest that, following damage to the visual cortex in adult cats (Tumosa *et al.* 1989), surviving geniculo-cortical relay neurones exhibit abnormally large receptive-field centres. It is suggested that the newly formed dendro-dendritic excitatory synapses between surviving cells, mostly Y-cells, are the morphological basis for this electrophysiological observation.

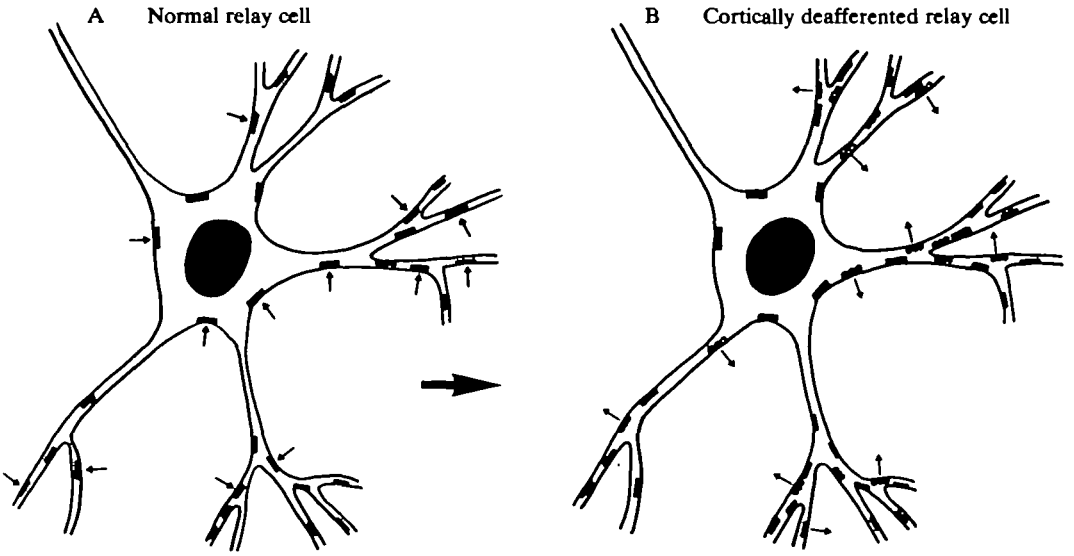

Fig. 1. Induction of presynaptic sites in geniculo-cortical relay cells following chronic cortical deafferentation. Perikarya and dendrites of relay neurones in the control LGN possess exclusively postsynaptic sites (A). In addition to postsynaptic sites, cortically deafferented neurones also develop presynaptic sites (B) (indicated by synaptic vesicles), mostly in their dendrites. Arrows indicate direction of impulse transmission.

Adaptive atrophy of dendrites following visual deafferentation of lateral geniculate nucleus

Chronic visual deprivation of the developing subcortical 'relay' station, the LGN, has been shown to result in a shrinkage of the transneuronally affected geniculo-cortical neuronal perikarya in rats, cats and monkeys. Neurones in the visually deprived LGN lamina become 20–60% smaller following monocular eyelid closure (Garey and Blakemore, 1977; LeVay and Ferster, 1977; Hitchcock and Hickey, 1982; Tigges *et al.* 1984) or after neonatal enucleation (Robertson *et al.* 1989). Other studies have demonstrated a shrinkage of the deafferented LGN lamina in the adult monkey (Matthews *et al.* 1976; LeVay, 1971) as well as in adult cats (Cook *et al.* 1951; Guillery, 1973; Eysel and Wolfhard, 1984). Apart from the loss of retinogeniculate fibres and terminals, the main morphological event in this transneuronal atrophy in adult animals is probably the shrinkage of neuronal somata. No cell death was found in the visually deafferented lamina up to 163 days after enucleation (Eysel and Wolfhard, 1984). Recently it was found that, not only relay cell perikarya, but also their dendritic arborizations, react to chronic deprivation by specific morphological alterations.

This type of active response of dendrites has been described in the LGN of cats (Somogyi *et al.* 1987) following chronic visual (retinal) deafferentation. Their study was designed to establish the morphological background of the electrophysiologically observed functional plasticity in the LGN of adult cats after total or

partial retinal lesions (Eysel, 1979, 1982; Eysel and Wolfhard, 1984). In a previous study, Eysel (1979) reported that, after visual deafferentation, the maintained activity of the deafferented relay cells was initially depressed, but recovered significantly after 10 weeks. A total absence of reactive sprouting of retinal axons in adult LGN, which would otherwise provide a possible explanation for the observed functional plasticity following partial retinal lesions, has been established beyond doubt by several authors (Baisden *et al.* 1980; Eysel, 1982; Guillery, 1972; Stelzner and Keating, 1977). Other possible mechanisms for the recovery of excitability of retinally deafferented geniculo-cortical relay cells should, therefore, be taken into account. These include: (1) the disinhibition due to selective transneuronal degeneration of GABAergic interneurones, (2) axonal sprouting of cortical fibres and (3) dendritic elongation of relay neurones. The second possibility seemed to be particularly attractive since the regained, and even increased, excitatory drive in visually deafferented LGN cells following retinal lesions could also be elicited by electrical stimulation of the visual cortex (Eysel, 1979). Indeed, the cortically elicited response in the deafferented LGN was even enhanced compared with the control. Contrary to expectations, however, investigations disproved all three of these possibilities (Somogyi *et al.* 1987). It was shown that the regained excitability of relay neurones could not be caused by disinhibition, since quantitative immunocytochemistry revealed that the proportion of GABA-positive and GABA-negative cells, as well as the synaptic density of GABA axons in the LGN, were unchanged even 9 months after retinal deafferentation. The second possibility, that the enhanced excitability of LGN neurones could be the result of sprouting of corticothalamic axons, was also disproved, since quantitative electron microscopic analysis showed that the number of cortical terminals in the retinally deafferented LGN did not change either. Similarly, the third possibility, that elongation of relay cell dendrites led to the re-establishment of functional connections, could not be substantiated; on the contrary, the main and meaningful alteration was a significant numerical decrease of postynaptic dendrites of both X and Y cells. According to our recent, unpublished data (G. Legrady and J. Hamori, in preparation) this shrinkage of the dendritic arborization is due almost exclusively to a significant shortening of dendritic segments between two branching points, while the number of branches remains at the control level. Because of the shrinkage of the dendritic trees, however, the density of cortical synaptic input to LGN cells becomes elevated by almost 60%. This naturally means that there is a substantial relocation of the cortical terminals along the shrunken dendritic arborization (Fig. 2). It is suggested (Somogyi *et al.* 1987) that the regained excitability of geniculocortical neurones is at least partly a consequence of this adaptive reduction in size of the dendritic arborization of the retinally denervated neurones. This results in a relative increase in density of the excitatory cortical input per neurone (Fig. 2). It is relevant to mention here that, in the cortical pyramidal cells of ageing rodents, dogs, monkeys and also man (Leuba, 1983; Geinisman, 1979; Machado-Salas *et al.* 1977; Mervis, 1978; Uemera, 1980; Scheibel *et al.* 1975), a marked physiological

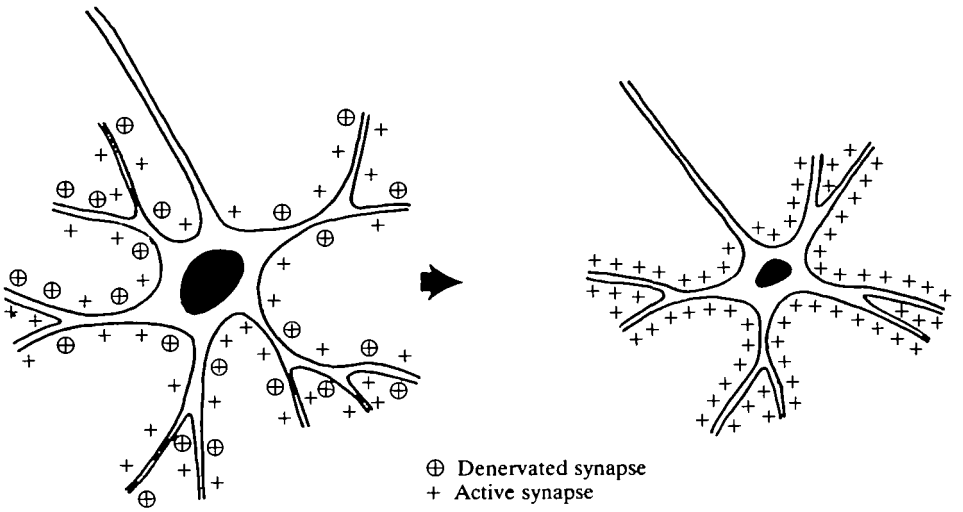

Fig. 2. Dendritic processes of geniculo-cortical neurones become shorter following retinal deafferentation (denervated synapse) of the LGN, resulting in an increase in the density of cortical terminals to the shrunken nerve cell.

loss of presynaptic neurones is accompanied by a similar atrophy, with a 30–40 % decrease in dendritic branches and á 50 % decrease in dendritic spines.

Concluding remarks

In addition to classical axonal reactive synaptogenesis, a new type, the dendritic type of reactive synaptogenesis, has been recognized and described. By definition, there is an active participation of postsynaptic dendrites (or even somata) in the induced synaptogenesis that follows deafferentation in the adult nervous system. Two regions where this 'dormant' morphogenetic potential of certain neurones has been investigated in detail are the cerebellar cortex and the LGN. In both regions, the reactive development of presynaptic sites in otherwise exclusively postsynaptic dendritic processes (granule cells and small Golgi neurones, in the cerebellar cortex and relay neurones in the LGN) has been described. The new synaptic formations were dendro-dendritic, dendro-somatic, somato-dendritic or even somato-somatic (Hamori and Somogyi, 1982). The other major type of dendritic reaction to deafferentation was observed in the LGN, where there was an adaptive reduction in size (functional atrophy) of relay cell dendrites. In this case, since dendritic atrophy caused by visual deafferentation was accompanied neither by axonal sprouting nor by axonal loss of the main surviving (cortical) afferents, the net result was the synaptic reorganization of cortical endings onto the shortened relay cell dendrites and, as a consequence, an increased density of this type of excitatory input along the dendrites of relay neurones.

The main factor in eliciting either of these active dendritic structural alterations appears to be the partial (in the LGN) or total (in the cerebellar cortex)

deafferentation of the particular region. The absence of significant axonal sprouting for reactive synaptogenesis in both regions is, at least partly, compensated for either by axonization or by the shrinkage of postsynaptic dendrites. Although a functional study of the synaptically reorganised cerebellar glomeruli is still lacking, electrophysiological investigations of the chronically decorticated LGN (Tumosa *et al.* 1989) also demonstrate a certain functional recovery within the nucleus, though with more diffuse and abnormally large receptive field centres than in the control LGN. This suggests, that the newly formed dendro-dendritic synaptic links between neighbouring relay neurones are functionally valid. The synaptic reorganization of cortical input to the shrunken dendritic arborizations of retinally deafferented relay neurones in the LGN (Somogyi *et al.* 1987) provides another example of the active participation of postsynaptic elements in functional recovery (Eysel and Wolfhard, 1984) of nerve cells previously handicapped by partial deafferentation.

References

BAISDEN, R. H., POLLEY, E. H., GOODMAN, D. C. AND WOLF, E. D. (1980). Absence of sprouting by retinogeniculate axons after chronic focal lesions in the adult cat retina. *Neurosci. Lett.* **17**, 33–38.

BROMBERG, M. B., PAMEL, G., STEPHENSON, B. S., YOUNG, A. B. AND PENNEY, J. B. (1987). Evidence for reactive synaptogenesis in the ventrolateral thalamus and red nucleus of the rat: changes in high affinity glutamate uptake and numbers of corticofugal fiber terminals. *Expl Brain Res.* **69**, 53–59.

COOK, W. H., WALKER, J. H. AND BARRY, M. L. (1951). A cytological study of transneuronal atrophy in the cat and the rabbit. *J. comp. Neurol.* **94**, 267–292.

ECCLES, J. C., ITO, M. AND SZENTAGOTHAI, J. (1967). *The Cerebellum as a Neuronal Machine.* Berlin, Heidelberg, New York: Springer-Verlag.

EYSEL, U. T. (1979). Maintained activity, excitation and inhibition of lateral geniculate neurons after monocular deafferentation in the adult cat. *Brain Res.* **166**, 259–271.

EYSEL, U. T. (1982). Functional reconnections without new axonal growth in a partially denervated visual relay nucleus. *Nature.* **299**, 442–444.

EYSEL, U. T. AND WOLFHARD, U. (1984). The effects of partial retinal lesions on activity and size of cells in the dorsal lateral geniculate nucleus. *J. comp. Neurol.* **299**, 301–309.

FIELD, P. M. AND RAISMAN, G. (1985). The density of reinnervation of adult rat superior cervical sympathetic ganglionic neurons is limited by the number of available postsynaptic sites. *Brain Res.* **360**, 398–402.

FROTSCHER, M., NITSCH, C. AND HASSLER, R. (1981). Synaptic reorganization in the rabbit hippocampus after lesion of commissural afferents. *Anat. Embryol.* **163**, 15–30.

GAREY, L. J. AND BLAKEMORE, C. (1977). The effects of monocular deprivation on different neuronal classes in the lateral geniculate nucleus of the cat. *Expl Brain Res.* **28**, 259–278.

GEINISMAN, Y. (1979). Loss of axosomatic synapses in the dentate gyrus of aged rats. *Brain Res.* **168**, 485–492.

GUILLERY, R. W. (1972). Experiments to determine whether retinogeniculate axons can form translaminar collateral sprouts in the dorsal lateral geniculate nucleus of the cat. *J. comp. Neurol.* **146**, 407–420.

GUILLERY, R. W. (1973). Quantitative studies of transneuronal atrophy in the dorsal lateral geniculate nucleus of cats and kittens. *J. comp. Neurol.* **49**, 423–438.

HAMORI, J. (1982). "De novo" formation of synapses by experimentally induced presynaptic dendrites in adult mammalian brain. *Acta biol. Acad. Sci. hung.* **33**, 173–187.

HAMORI, J. AND SILAKOV, V. L. (1980). Plasticity of relay neurons in dorsal lateral geniculate nucleus of the adult cat: morphological evidence. *Neuroscience* **5**, 2073–2077.

HAMORI, J. AND SOMOGYI, J. (1982). Presynaptic dendrites and perikarya in de-afferented cerebellar cortex. *Proc. natn. Acad. Sci. U.S.A.* **79**, 5093–5096.

HAMORI, J. AND TAKACS, J. (1989). Two types of GABA-containing axon terminals in cerebellar glomeruli of cat: an immunogold-EM study. *Expl Brain Res.* **74**, 471–479.

HILLMAN, D. E. AND CHEN, S. (1981). Vulnerability of cerebellar development in malnutrition. II. Intrinsic determination of total synaptic area on Purkinje cell spines. *Neuroscience* **6**, 1263–1275.

HITCHCOCK, P. F. AND HICKEY, T. L. (1982). Cell size changes in the lateral geniculate nucleus of normal and monocularly deprived cats treated with 6-hydroxydopamine and/or norepinephrine. *J. Neurosci.* **2**, 681–686.

HOFF, S. F. (1986). Lesion-induced transneuronal plasticity in the adult rat hippocampus. *Neuroscience* **19**, 1227–1233.

ICHIKAWA, M. (1987*a*). Synaptic reorganization in the medial amygdaloid nucleus after lesion of the accessory olfactory bulb of adult rat. I. Quantitative and electron microscopic study of the recovery of synaptic density. *Brain Res.* **420**, 243–252.

ICHIKAWA, M. (1987*b*). Synaptic reorganization in the medial amygdaloid nucleus after lesion of the accessory olfactory bulb of adult rat. II. New synapse formation in the medial amygdaloid nucleus by fibers from the bed nucleus of the stria terminalis. *Brain Res.* **420**, 253–258.

JAKAB, R. L. AND HAMORI, J. (1988). Quantitative morphology and synaptology of cerebellar glomeruli in the rat. *Anat. Embryol.* **179**, 81–88.

KALIL, R. E. AND BEHAN, M. (1987). Synaptic reorganization in the dorsal lateral geniculate nucleus following damage to visual cortex in newborn or adult cats. *J. comp. Neurol.* **257**, 216–236.

KIM, S. U. (1974). Granule cell with somatodendritic synapse in organotypic cultures of mouse cerebellum. *Expl Neurol.* **45**, 659–662.

LEUBA, G. (1983). Aging of dendrites in the cerebral cortex of the mouse. *Neuropath. appl. Neurobiol.* **9**, 467–475.

LEVAY, S. (1971). On the neurons and synapses of the lateral geniculate nucleus of the monkey, and the effects of eye enucleation. *Z. Zellforsch. mikrosk. Anat.* **113**, 396–419.

LEVAY, S. AND FERSTER, D. (1977). Relay cell classes in the lateral geniculate nucleus of the cat and the effects of visual deprivation. *J. comp. Neurol.* **172**, 563–584.

MACHADO-SALAS, J., SCHEIBEL, M. E. AND SCHEIBEL, A. B. (1977). Morphologic changes in the hypothalamus of the old mouse. *Expl Neurol.* **57**, 102–111.

MADARASZ, M., SOMOGYI, J., SILAKOV, V. L. AND HAMORI, J. (1983). Residual neurons in the lateral geniculate nucleus of adult cats following chronic disconnection from the cortex. *Expl Brain Res.* **52**, 363–374.

MATTHEWS, D. A., COTMAN, C. AND LYNCH, G. (1976). An electron microscopic study of lesion-induced synaptogenesis in the dentate gyrus of the adult rat. II. Reappearance of morphologically normal synaptic contacts. *Brain Res.* **115**, 23–41.

MERVIS, R. (1978). Structural alterations in neurons of aged canine neocortex: a Golgi study. *Expl Neurol.* **62**, 417–432.

MURAKAMI, F., KATSUMARU, H., SAITO, K. AND TSUKAHARA, N. (1982). A quantitative study of synaptic reorganization in red nucleus neurons after lesion of the nucleus interpositus of the cat: an electron microscopic study involving intracellular injection of horseradish peroxidase. *Brain Res.* **242**, 41–53.

MURRAY, M., ZIMMER, J. AND RAISMAN, G. (1979). Quantitative electron microscopic evidence for reinnervation in the adult rat interpeduncular nucleus after lesions of the fasciculus retroflexus. *J. comp. Neurol.* **187**, 447–468.

PALAY, S. L. AND CHAN-PALAY, V. (1974). *Cerebellar Cortex, Cytology and Organization.* Berlin, Heidelberg, New York: Springer-Verlag.

PURVES, D. AND LICHTMAN, J. W. (1987). Synaptic sites on reinnervated nerve cells visualized at two different times in living mice. *J. Neurosci.* **7**, 1492–1497.

RAISMAN, G. (1969). Neuronal plasticity in the septal nuclei of the adult rat. *Brain Res.* **14**, 25–48.

RAISMAN, G. AND FIELD, P. (1973). A quantitative investigation of the development of collateral reinnervation after partial deafferentation of the septal nuclei. *Brain Res.* **50**, 341–364.

ROBERTSON, R. T., POON, H. K., DURAN, M. R. AND YU, J. (1989). Neonatal enucleations

reduce number, size, and acetylcholinesterase histochemical staining of neurons in the dorsal lateral geniculate nucleus of developing rats. *Devl Brain Res.* **47**, 209–225.

SCHEIBEL, M. E., LINDSAY, R. D., TOMIYASU, U. AND SCHEIBEL, A. B. (1975). Progressive dendritic changes in aging human cortex. *Expl Neurol.* **47**, 392–403.

SOMOGYI, J., EYSEL, U. AND HAMORI, J. (1987). A quantitative study of morphological reorganization following chronic optic deafferentation in the adult cat dorsal lateral geniculate nucleus. *J. comp. Neurol.* **255**, 341–350.

SOMOGYI, J., HAMORI, J. AND SILAKOV, V. L. (1982). Free postsynaptic sites in the lateral geniculate nucleus of adult cats following chronic decortication. *Cell Tissue Res.* **225**, 437–442.

SOMOGYI, J., HAMORI, J. AND SILAKOV, V. L. (1984). Synaptic reorganization in the lateral geniculate nucleus of the adult cat following chronic decortication. *Expl Brain Res.* **54**, 485–498.

SOTELO, C. (1975). Anatomical, physiological and biochemical studies of the cerebellum from mutant mice. II. Morphological study of cerebellar cortical neurons and circuits in the *weaver* mouse. *Brain Res.* **94**, 19–44.

SOTELO, C. (1977). Formation of presynaptic dendrites in the rat cerebellum following neonatal X-irradiation. *Neuroscience* **2**, 275–283.

STELZNER, D. J. AND KEATING, E. G. (1977). Lack of sprouting retinal axons in monkey LGN. *Brain Res.* **126**, 201–210.

STEWARD, O. AND VINSANT, S. L. (1983). The process of reinnervation in the dentate gyrus of the adult rat: a quantitative electron microscopic analysis of terminal proliferation and reactive synaptogenesis. *J. comp. Neurol.* **214**, 370–386.

STEWARD, O., VINSANT, S. L. AND DAVIS, L. (1988). The process of reinnervation in the dentate gyrus of adult rats: an ultrastructural study of changes in presynaptic terminals as a result of sprouting. *J. comp. Neurol.* **267**, 203–210.

TIGGES, M., HENDRICKSON, A. E. AND TIGGES, J. (1984). Anatomical consequences of long-term monocular eyelid closure on lateral geniculate nucleus and striate cortex in squirrel monkey. *J. comp. Neurol.* **227**, 1–13.

TSUKAHARA, N. (1981). Synaptic plasticity in the red nucleus. In *Regulatory Functions of the CNS Subsystems*, vol. 2 (ed. J. Szentagothai, J. Hamori and M. Palkovits), pp. 1–20. *Adv. Phys. Sci.* Oxford: Pergamon Press; Budapest: Akademiai Kiado.

TUMOSA, N., MCCALL, M. A., GUIDO, W. AND SPEAR, P. D. (1989). Responses of lateral geniculate neurons that survive long-term visual cortex damage in kittens and adult cats. *J. Neurosci.* **9**, 280–298.

UEMURA, E. (1980). Age-related changes in prefrontal cortex of *Macaca mulatta*: synaptic density. *Expl Neurol.* **69**, 164–172.

ZIMMER, J., LAWRENCE, J. AND RAISMAN, G. (1982). A quantitative electron microscopic study of synaptic reorganization in the rat medial habenular nucleus after transection of the stria medullaris. *Neuroscience* **7**, 1905–1928.