Demonstration of retinal afferents in the RCS rat, with reference to the retinohypothalamic projection and suprachiasmatic nucleus

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Abstract. In the Royal College of Surgeons (RCS) rat, characterized by inherited retinal dystrophy, retinal projections to the brain were studied using anterograde neuronal transport of cholera toxin B subunit upon injection into one eye. The respective immunoreactivity was found predominantly contralateral to the injection site in the lateral geniculate nucleus, superior colliculus, nucleus of the optic tract, medial terminal nucleus of the accessory optic tract, and bilateral hypothalamic suprachiasmatic nuclei. Although terminal density was somewhat reduced in dystrophic rats, the projection patterns in these animals appeared similar to those seen in their congenic controls and were comparable to the visual pathways described for the rat previously. In dystrophic rats, the number of cell bodies exhibiting immunoreactivity to vasoactive intestinal polypeptide, viz. a population of suprachiasmatic neurons receiving major retinohypothalamic input, was reduced by one-third, and some differences were observed in the termination pattern of the geniculohypothalamic tract, as revealed by immunoreactivity to neuropeptide Y in the suprachiasmatic nucleus.

Key words: Hypothalamus – Vasoactive intestinal polypeptide – Neuropeptide Y – Geniculohypothalamic tract – Lateral geniculate nucleus – Superior colliculus – Nucleus of the optic tract – Rat (Royal College of Surgeons)

Introduction

The Royal College of Surgeons (RCS) rat strain serves as an animal model in pathomorphological studies of hereditary retinal dystrophies, such as Retinitis pigmentosa in humans. The rat is characterized as having an autosomal recessive mutation of the retinal dystrophy gene (rdy/rdy; Mullen and LaVail 1976) resulting in the gradual destruction of the retinal photoreceptor cell layer. While development seems normal for the first two postnatal weeks, progressive degeneration of the photoreceptor cells starts thereafter (Bourne et al. 1938; Dowling and Sidman 1962). Retinal pigment epithelial cells of the RCS rat exhibit defective phagocytosis of shed outer segments (Mullen and LaVail 1976; Edwards and Szamier 1977; Goldman and O’Brien 1978; Tamai and O’Brien 1979). The outer segment debris accumulates in the subretinal space reaching a maximal thickness at postnatal days 27–35 (Dowling and Sidman 1962; LaVail et al. 1972). In addition, lysosomal membranes of the retinal pigment epithelium of the RCS rat are less stable compared with those of the normal retina (El-Hinfawi et al. 1994). It is assumed that these alterations result in a diffusion barrier and/or a neurotoxic effect (Dowling and Sidman 1962) causing destruction of almost all photoreceptor cells in the outer nuclear layer by the age of 2–3 months, leading to blindness (Bok and Hall 1971; LaVail et al. 1974). In addition, abnormalities in the interphotoreceptor matrix may be involved in the degeneration process (LaVail et al. 1981; Porrello et al. 1986).

Although a considerable number of studies describe the retinal morphology in RCS rats, no information is available concerning the distribution of retino-afferent projections in this rat strain. We have therefore used the anterograde neuronal transport of cholera toxin B subunit (CTB) upon injection into the eye to trace retinal projections to the brain. In addition to the investigation of primary visual projections, we have focused on the retinohypothalamic tract (RHT), which connects the hypothalamus to the retina (Hendrickson et al. 1972; Moore and Lenn 1972). The RHT is known to mediate visual information for the entrainment of circadian rhythms generated in the hypothalamic suprachiasmatic nucleus (SCN; cf. Rusak and Zucker 1979; Moore 1983). We
Fig. 1. Retinal afferents terminating in the dorsal (DLGN) and ventral lateral geniculate nucleus (VLGN) and intergeniculate leaflet (IGL; arrow) as demonstrated by anterograde axonal transport of cholera toxin B upon injection into one eye, and seen in corresponding sections through the mid-portion of the contralateral LGN in (A) a rat exhibiting retinal dystrophy (DYS) and (B) a control animal (CTL). Bar: 100 μm (A,B)

have also studied the innervation of the SCN by neuropeptide Y (NPY) fibers which are believed to provide a secondary visual input stemming from the lateral geniculate nucleus (LGN; Albers et al. 1984). Since these fibers terminate on perikarya containing vasoactive intestinal polypeptide (VIP; Tanaka et al. 1993), we have also compared the distribution of VIP in control and dystrophic animals.