DEVELOPMENT OF THE VISUAL CORTEX DEPRIVED PRENATALLY OF RETINAL CUES

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INTRODUCTION

The mammalian visual system provides a unique model to analyze some of the factors influencing the development of laminated regions of the brain, especially the visual cortex. This review is focused on the development of the human and nonhuman primate primary visual (striate) cortex under normal and abnormal conditions. Principles of development revealed in this model are contrasted with observations in the visual cortex of other mammals and other sensory cortices, to try to identify rules applicable to the specification of the cerebral cortex in general.

DEVELOPMENT OF THE VISUAL CORTEX IN ANOPHTHALMIC ANIMALS AND HUMANS

Much information has been gathered during the last five decades about the development of the visual cortex in both human anophthalmia and experimental models of this condition. Some of the salient findings are reviewed here, in an attempt to summarize some of the emerging principles of development of the striate cortex deprived of the retinal cues in utero.

The visual cortex of anophthalmic rodents

Chase and Chase (1941) described a mutant strain of mice in which 90% of the individuals are eyeless. This trait is primarily due to a failure of the optic vesicle to develop into a normal optic cup about the 10th day of gestation (E10). In normal C57 mice, optic nerve fibers begin to grow out by E13 and reach the diencephalon by E14. According to Chase (1945), the adult ZRDCT congenitally anophthalmic mice (ZRDCT-An) exhibit: (a) a dorsal lateral geniculate body (dLGN) less than half the size of that in the normal; (b) the ventral nucleus of the lateral geniculate body is also small, but over half the size in controls, and (c) the stratum griseum superficiale and stratum opticum of the superior colliculus is markedly reduced in thickness. Except for the visual cortex, these reductions in size are not much greater than those found by Tsang (1937) in rats blinded at birth. Many of the changes observed in adult ZRDCT-An specimens develop postnatally, since both the geniculate nucleus and the superior colliculus appear normal at E18.
Kaiserman-Abramof et al. (1980) found that although the dLGN of ZRDCT-An undergoes a reduction of its neuronal population to 76% of normal, its projection to area 17 exhibits an essentially normal topographic pattern. An interesting additional finding from the latter investigators is that the projection to area 17 from the nucleus lateralis posterior (LP) of the thalamus is considerably greater in congenitally anophthalmic than in normal-eyed mice, which suggests compensatory innervation from LP, perhaps partially substituting reduced dLGN afferents.

The visual cortex of ZRDCT-An, also called "eyeless" (ey; Sidman, Green & Appel, 1965), appears undifferentiated on embryonic day 18 (E18). Layers II/III reportedly become distinct at E19, and layer IV is clearly identifiable at birth. When compared to controls, five to six-month-old eyeless mice were found to have thinner layers II-IV, with a less distinct separation between layers III and IV. Layer V was found to be thicker and layer VI thinner than in controls (Chase, 1945). Unfortunately, precise quantitative determinations of these changes in the visual cortex are not available. This important void of information includes the surface area of the striate cortex, as well as any information about possible associated changes in peristriate cortices.

Interesting additional findings in ZRDCT-An include the formation of cranial nerves III-VI, which are present at birth but disappear or become reduced in the neonatal period and their nuclei become small by six months of age. The only exception is the ophthalmic division of the Vth nerve, which is small at birth but does not change appreciably afterwards.

The visual cortex in human anophthalmia

Anophthalmia in humans has long attracted the attention of clinicians, primarily from the perspective of understanding the mechanisms responsible for the formation of the eye. Relatively little is known, by contrast, about the cortical changes associated with the congenital absence of eyes in humans.

True anophthalmos is a rare clinical entity, the diagnosis of which rests on a careful histological examination of the orbital contents. Such analysis reveals that most cases of presumed anophthalmos are instead the more common condition of microphthalmia in which - contrary to anophthalmia - remnants of the eye, which are sometimes microscopic, can be found embedded among the tissues occupying the orbit (Pritkin, 1980). Given that the scope of this review is limited to instances of complete absence of retinal input to the cerebral cortex, I will address only the pathological findings of true anophthalmia. It should be recognized, nevertheless, that even the restricted category of true anophthalmia comprises a heterogeneous group of conditions. In fact, Mann (1957) subdivided this category into three conditions: (a) primary anophthalmos due to failure of development restricted to the optic vesicles, (b) secondary anophthalmos due to a more generalized maldevelopment of the forebrain, and (c) degenerative (also called consecutive) anophthalmos due to complete regression or involution of the optic vesicles. It should be emphasized that, although by definition there is complete absence of neuroectodermal derivatives in the orbits in all three of these conditions, in practice this can be quite difficult to prove conclusively. For example, cases of extreme microphthalmos can easily be misdiagnosed, and, even when there is no detectable residual eye tissue in the orbits, it is often impossible to establish whether this was primarily due to agenesis or involution. These difficulties are important to keep in mind, since they can