We further investigated the defect in degradation by determining the activity of six hydrolytic lysosomal enzymes in fibroblasts from the affected and normal cats (*12*) (Table 1). The activities of five of these enzymes from the affected cat's cells were significantly increased ($P < .02$). The arylsulfatase B activity, however, was significantly lower than that of the controls, averaging 10 percent of the activity observed in normal cells ($P < .01$). Initial determinations have shown that the following enzymes are active in the affected cat: α-L-iduronidase and heparan sulfatase, measured in cultured fibroblasts, and iduronate sulfatase, measured in serum (*13*).

The proposita is the offspring of a mother-son mating. Her pedigree suggests an autosomal recessive mode of inheritance. There were two offspring from a previous mating of the same parents with facial features similar to that of the proposita and these also reportedly experienced progressive difficulty with locomotion. One of these animals died at approximately 1 year of age of undetermined causes and we have been unable to locate the other. The parents, however, are both clinically normal and exhibit normal urinary GAG excretion.

The above results are essentially the same as those in human patients with Maroteaux-Lamy syndrome (*14*). The clinical features of the syndrome closely parallel those of the affected cat, while the patterns of excretion of urinary GAG and the deficiency in arylsulfatase B activity are identical. We therefore suggest that the cat represents a naturally occurring animal model of this syndrome. We are attempting to establish a breeding colony of affected animals for further study of the disease and to make this model available to other investigators.

Note added in proof: Since this manuscript was submitted, we have identified four additional individuals from two different families of Siamese cats with clinical features similar to and biochemical abnormalities identical with those of the affected cat described in this report.

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15. Supported by NIH Genetics Center grant GM20138.

11 January 1977; revised 16 June 1977

Postnatal Development of the Human Lateral Geniculate Nucleus: Relationship to a Critical Period for the Visual System

Abstract. *The cross-sectional areas of 31,800 dorsal lateral geniculate nucleus cells were measured in 53 human brains ranging in age from newborn to 40 years. Geniculate cells increase in size rapidly during the first 6 to 12 months of postnatal life, with cells in the parvocellular layers developing faster than cells in the magnocellular layers. At least 2 years are required before all cells have reached their adult size.*

It is generally accepted that there are periods during the development of an organism when it is particularly sensitive to outside influences (*1*). For instance, on the basis of changes in the ocular dominance of cortical cells and in overall visual capabilities, a sensitive or critical period in the development of the visual system has been defined for both the cat (*2*) and the monkey (*3*). In addition, clinical reports and psychophysical studies have suggested that a similar period exists during the development of the human visual system (*4*) sometime during the first 2 years of life; however, the period of susceptibility may continue to some extent until the child is 4 or 5 years old. Although an increasing amount of clinical and psychophysical information about the development of the human visual system is being made available, almost nothing is known about the postnatal growth of human central visual system structures, for example, the dorsal lateral geniculate nucleus (LGN). Such information could be important since other data suggest a close relationship between the time during which the visual system is growing and the time during which it is most susceptible to outside influences (*1*). If such a relationship does exist, it should be possible to define the critical period in the development of the human visual system by first defining the period during which growth occurs. I have found that there are two partially overlapping periods of postnatal cell growth in the human LGN. For cells in the parvocellular layers of the geniculate, there is a period of rapid growth that ends about 6 months after birth. However, cells in the magnocellular layers continue to grow rapidly until one full year after birth and do not reach adult size until the end of the second year. Such a time course of development resembles previous clinical and psychophysical estimates of the critical period in the human.

Brain tissue was obtained from 53 humans ranging in age at the time of their death from newborn to 40 years. All

brain tissue was collected during normal autopsy procedures at two local hospitals. Only brains showing no gross pathology or past history of neurological abnormality were included in the analyses. Upon receipt, all brain tissue was place in 10 percent buffered formalin for at least 2 weeks. Blocks of tissue containing one LGN were then dehydrated in a series of alcohols, embedded in celloidin, sectioned frontally at 40 μm, and stained with cresyl violet. Geniculate cells showing a well-defined nucleolus were drawn at a magnification of $\times 1000$ (oil) with the help of a camera lucida (Zeiss). Cells were sampled from a corresponding part of the binocular segment of each geniculate (that part of the geniculate that receives input from the binocular part of the visual field). The details of this procedure have been described for cell measurements in the cat LGN (*5*). The cross-sectional area of each cell outline was later determined with the use of a graphics calculator (Numonics Corporation, North Wales, Pennsylvania). The slides from which the cells were drawn were coded so that no information was available concerning the age of the tissue. One hundred cells were measured in each of the four parvocellular and two magnocellular laminae of every LGN studied (Fig. 1).

As in other animals (*6*), the average size of geniculate cells obtained from similarly aged humans varies considerably. Most of this variability is between, not within, subjects. A consistent relationship exists between the cells in the different laminae of a given subject. For example, in comparisons the mean cross-sectional areas for cells in each lamina for all 19 brains obtained from humans 2 years of age and older, lamina 1 cells were significantly larger than lamina 2 cells (t-test, $P < .01$) and lamina 6 cells were significantly smaller than the other parvocellular layer cells (t-test, $P < .01$). No differences existed be-

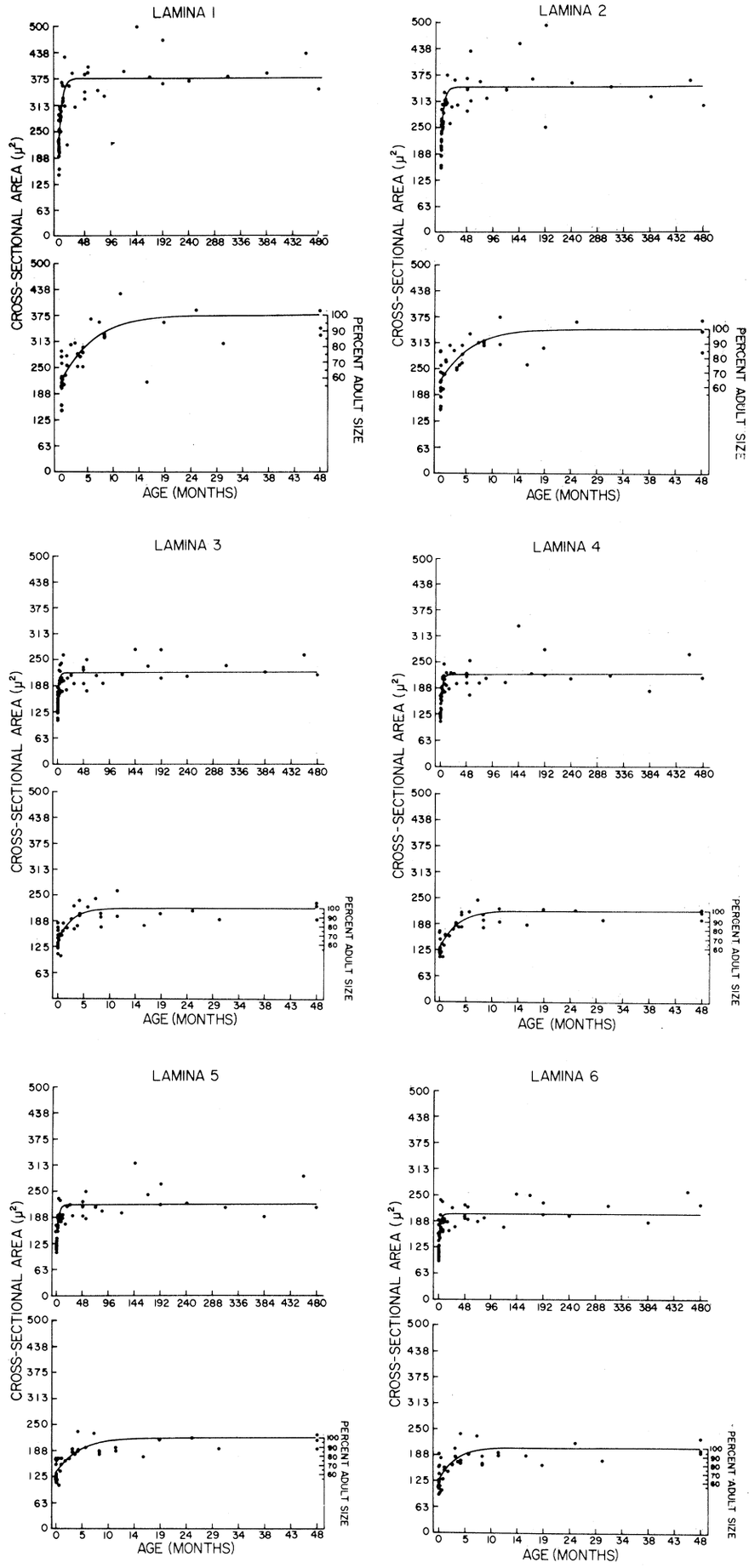

Fig. 1. Changes in cross-sectional area of human LGN cells as a function of age. One pair of graphs is shown for each of the two magnocellular laminae (1 and 2) and four parvocellular laminae (3, 4, 5, and 6). For each lamina, the top graph shows all of the data collected from humans ranging in age from newborn (0 months) to 40 years (480 months). The bottom graphs show, in more detail, the same data covering only the first 48 months of life, that segment of the curve in each of the top graphs that depicts the rapid changes in cell cross-sectional area. The correlations between the curves and the data points were .83, .76, .80, .80, .79, and .78 for laminae 1 through 6, respectively. For all graphs, each data point represents the mean of 100 cell measurements.

tween the mean cross-sectional areas of lamina 3, 4, and 5 cells. Similar comparisons could not be made between subjects of different ages since the material at any given age is limited. Therefore, in an attempt to show an average change in cell size during development, a Gompertz growth curve was fitted to the data according to a least-squares criterion.

Comparisons between the bottom graphs (Fig. 1) show that, in all cases, geniculate cell growth in the human is nearing completion by the end of the second year. The time required to reach adult size, however, is different for cells in the magnocellular and parvocellular layers of the geniculate. While the larger layer 1 and layer 2 cells require at least 24 months to complete their growth, the smaller parvocellular layer cells reach adult size near the end of the first year. For both groups of cells, rapid growth occurs during the first few months of life. For the smaller cells the rapid growth ends at 6 months. For the magnocellular layer cells, however, this period continues for as long as 12 months.

The curves also show the percent of cell growth complete as a function of age. At birth all geniculate cells are, on average, 60 percent of their adult size (range across all laminae was 57 to 64 percent). During the first few months of life, all LGN cells appear to grow at about the same rate, at least in terms of area in square micrometers. However, since the adult size of the parvocellular layer cells is less than that for the magnocellular layer cells, this growth represents a greater percentage of increase in size for the former. For instance, by 6 months most cells in the parvocellular layer are approximately 95 percent of their adult size. Equivalent growth for the cells in the magnocellular layer is not reached until about the end of the first year. These curves again illustrate the difference in the time required for the large and small cells to complete all of their growth. Because of the variability in the data, it is impossible to be certain that cell growth in the geniculate is complete at a given time. It is possible that a very slow change in cell size continues well beyond 24 months for cells in the magnocellular layers. A similar statement could also be made for cells in the parvocellular layers. Nonetheless, all measurable changes in cell size take place during the first 24 months of life. In addition, even if slow changes in cell size do occur over long periods of time, the time required for development in the magnocellular and parvocellular layers differs markedly.

Although the relationship between periods of susceptibility and of rapid growth was first pointed out in teratology studies, it has since been extended to other aspects of development. These findings raise the question of whether the critical period during the development of the visual system also corresponds to a period of rapid growth in the visual system. Since most of the research on normal development has been done with the cat, one can relate the time course of normal development to that of the changes seen in visually deprived cats. Garey, Fisken, and Powell (*7*) have demonstrated a period of rapid cell growth in the cat LGN during the first 4 weeks of life. Other research suggests that growth occurs throughout the central visual pathway during this same period. Cragg (*8*) studied the development of synapses in the visual cortex and the LGN of the cat and found that synaptic development proceeded at about the same rate, with synapses in the geniculate developing approximately 2 days earlier than those in the visual cortex. In both areas there was a rapid increase in the number of synapses between 8 and 37 days after birth. Thus, at least in the cat, the onset of the critical period appears to coincide with the period of most rapid geniculate cell growth and the period of most synapse formation in both the geniculate and visual cortex. Although not as well defined, in the Garey *et al.* study (*7*), the end of all geniculate cell growth coincided well with the end of the critical period. If this relationship holds for other animals, including man, the most crucial period in the development of the human geniculo-cortical system (and possibly the visual system as a whole) would be the first 24 months of life. My data, however, suggest the possibility of two phases to the critical period for the human visual system. The period of susceptibility for the parvocellular layer cells would extend throughout the first year whereas, for the magnocellular layer cells, this period would continue until the end of the second year.

The results may also explain some of the findings reported for studies of visual deprivation. Physiological studies (*9*) have shown that Y cells in the cat LGN are affected relatively more by early visual deprivation than are X cells. In addition, anatomical studies in the visually deprived cat, dog, and monkey (*5, 6, 9*) have shown that the larger geniculate cells are reduced in size more than the smaller geniculate cells. These physiological and anatomical findings can be related by evidence suggesting that the larger geniculate cells correspond to the Y cells while the smaller geniculate cells correspond to X cells (*10*). In the monkey, cells in the magnocellular layer can be functionally classified as Y cells, and those of the parvocellular layer fall into the X cell classification (*11*). My results show that the time required to reach adult size is about twice as long for the large geniculate cells than for the small ones. Accordingly, cells of the magnocellular layer should experience a period of susceptibility that is approximately twice as long as that encountered by those in the parvocellular layer and might thus be subject to greater structural and functional changes. During development, the X and Y cells might compete with each other for synaptic space on cortical cells (*12*). By maturing faster, the smaller geniculate cells may gain an advantage in this competition that would show up dramatically when the system is visually deprived. Given the relative effects of deprivation in the monocular and binocular segments of the visual system (*13*), both mechanisms may play roles in producing the changes seen.

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9 August 1977