for cholinergic ligands—are likely to induce the degeneration of AChR (*11*) or affect transmembrane ion exchange (*12*), resulting in muscle weakness. Failure to precipitate *Narke* AChR suggests that our monoclonal antibody is directed to a particular determinant present on mammalian AChR.

The fact that antibodies to human AChR share some idiotype specificities suggests that the number of idiotypic determinants is limited (*13*). Thus, it might be possible to prepare specific immunosuppressants by raising antibodies against different types of idiotypic determinants on molecules of human antibody to AChR.

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Eye Movements of Preschool Children

Abstract. *Accurate recordings of eye movements of children 4 and 5 years old show that their eye movements differed from those of adults. During maintained fixation, saccades were large (1° to 2°) and smooth eye movement speeds were high (45 minutes of arc per second). Saccade latencies were highly variable during target step tracking. Smooth pursuit latencies were longer than those of adults. These hitherto unknown characteristics limit a child's ability to use eye movements to acquire visual information.*

Eye movements are essential for effective visual processing. For example, saccades bring selected retinal images to the central fovea where visual acuity is best. Once the image is foveal, saccades and smooth eye movements must maintain fixation so that visual details can be discerned. Despite the importance of eye movements, little is known about their development (*1*).

We undertook to study oculomotor development by making accurate recordings of the two-dimensional eye movements of two preschool children, Philip (4 years 7 months) and Jennifer (5 years 3 months) (*2*). These children were asked to perform simple oculomotor tasks, which were chosen because they require little instruction and have been studied carefully in adults (*3*). We found that the children did not fixate as well as adults. This result has implications for understanding the development of visual processing.

The children were asked to fixate a small bright stationary point. This target, displayed on a cathode-ray tube located at optical infinity, was visible in an otherwise darkened room. The children were asked to "look at the star" and reminded to do so throughout the recording sessions (*4*).

Fixation by preschool children is not like adult fixation. The children's line of sight was unstable. This finding is best summarized by the two-dimensional scatter of the line of sight, specifically, the mean bivariate contour ellipse area—

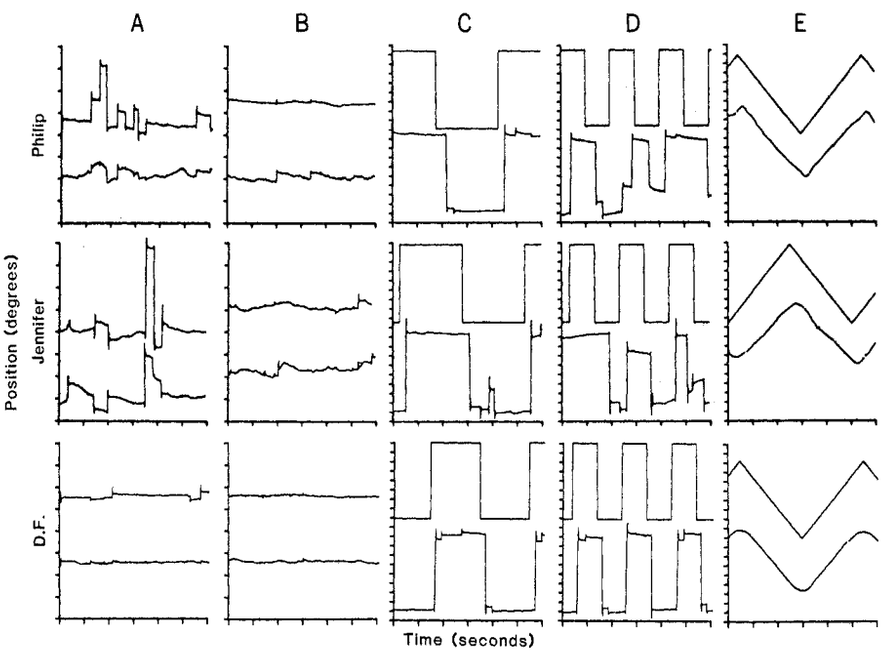

Fig. 1. Representative eye movement records. The time scale shows 1-second intervals and the position scale, 1° rotations. (A) Fixation of a stationary target. Top traces show horizontal and bottom traces vertical eye movements. Saccades (high-velocity rotations of the eye) 1° or larger are frequent in the children's records. The large overshoots at the end of saccades are caused in part by slippage of the crystalline lens in its capsule. (B) Examples of saccade-free intervals during fixation. (C) Saccadic tracking of low-frequency periodic horizontal target steps (0.4 step per second). Top traces show the stimulus and bottom traces horizontal eye movements. (D) Saccadic tracking of higher frequency target steps (1 step per second). (E) Smooth pursuit of periodic horizontal constant velocity (2.4° per second) target motion. Top traces show the stimulus and bottom traces, horizontal eye movements. Saccades have been removed from these records. Eye traces were corrected for the changes in position introduced by saccades by assuming that smooth eye movements continued during the saccade at the velocity present just before saccade onset.

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a measure analogous to the standard deviation of the line of sight on a single meridian (*5*). The children's scatter was more than 100 times as large as typical adult values [Philip's mean = 9,438 (minutes of arc)^2 and Jennifer's mean = 24,278 (minutes of arc)^2] (*3*). An adult subject (D.F., 21 years old) whose eye movements were recorded with the same instrument and who, like the children, had no prior experience as a subject, had a mean bivariate area of 144 (minutes of arc)^2—a value typical of other adult subjects (*3*).

Saccades were primarily responsible for the children's relatively large scatter (Figs. 1A and 2A) (*6*). The children's saccades were, on the average, 4 to 15 times as large as the average size of saccades made by adults when they fixate (*3, 7, 8*). The fixation of D.F. is illustrated in Figs. 1A and 2A (*6*). Although the children's saccades were much larger than adult saccades, they occurred almost as frequently. On the average, Philip made 1.3 and Jennifer 1.1 saccades per second. These values fall near the low end of typical adult saccade rates (*3, 7, 8*). Only rarely did Philip and Jennifer choose not to make a saccade for more than 2 seconds (Fig. 1B).

The children's smooth eye movements were similar to the smooth eye movements of adults in that both have effective slow control (*9*); both children's eyes remained almost as stable as the inexperienced adult's when saccades were not made (Fig. 1B). The distribution of 100-msec smooth eye movement velocities (Fig. 2B) have means near 0 minute of arc per second. This means that the children's smooth eye movements, like the adult's, do not cause the line of sight to drift far away from the target. However, the larger variances of the children's velocity distributions mean that the retinal image speeds of the children were often higher than the speeds of the adult (*10*).

We also examined the children's ability to fixate a moving target. Both children were able to use saccades to track periodic horizontal target steps when step frequency was low (0.4 step per second) (Fig. 1C). When step frequency was higher (1 step per second), the children had difficulty controlling the timing of their saccades. Latencies were often very long (1/2 to 1 second), and tracking saccades were occasionally made well before the target step (Fig. 1D). Adults track such steps with ease, making saccades of relatively uniform latencies (Fig. 1, C and D) (*11*).

The children, like adults, could use smooth eye movements to pursue repetitive horizontal target motions of constant velocity (Fig. 1E) but unlike adults, they did not anticipate the change in direction of the target (*11, 12*). The children waited about 200 msec before changing direction.

Thus, preschool children do not perform simple oculomotor tasks as adults do. This fact has a number of implications. The children's high retinal image velocities may impair vision. Their large saccades introduce fixation errors which may also impair vision. The difficulty children have controlling saccades when they fixate or track may limit their ability to use saccades to acquire information from visual displays. These results suggest that differences in the effectiveness of visual processing between preschool children and adults may be caused, at least in part, by incomplete oculomotor development (*13*).

This suggestion also applies to differences in visual performance between infants and adults. For example, the infant's spatial contrast sensitivity function for sinusoidal gratings peaks at a much lower spatial frequency than the adult's (*14*). Similar shifts in peak frequency can be produced in adults by artificially imposing high-speed retinal image motion on the grating (*15*). Thus, high retinal image speeds in infants could account for the shape of their contrast sensitivity function. Drawing conclusions about visual development on the basis of an infant's visual performance without knowledge of the infant's eye movements or retinal image speeds (*14, 16*) may, therefore, be premature.

We do not know why preschool children's eye movements are not like adult eye movements. Perhaps children have not yet learned efficient oculomotor skills. This suggestion is plausible for saccades. The saccades adults use to fixate a stationary target or to scan a visual display show features characteristic of overlearned motor habits (*9, 17*). Preschool children are not noted for their repertoires of such habits. They do not typically touch-type, play tennis, or even write their names rapidly and neatly. Regardless of the reasons preschool children's eye movements are different from adult eye movements, however, the fact

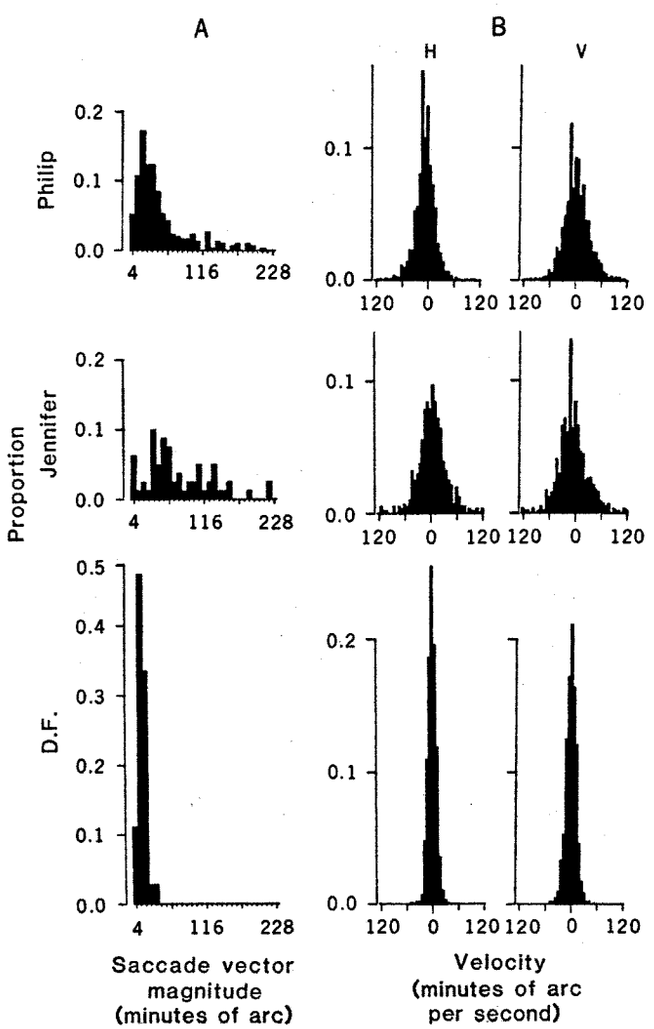

Fig. 2. (A) Histograms of saccade vector magnitudes during fixation of a stationary target. Bins are 8 minutes of arc wide. Philip's histogram is based on 301 saccades, Jennifer's on 79 saccades, and D.F.'s on 35 saccades. A portion of these saccades (10 for Philip and 17 for Jennifer) were larger than 228 minutes of arc. (B) Histograms of 100-msec horizontal (*H*) and vertical (*V*) smooth eye movement velocities during fixation of a stationary target. Bins are 6 minutes of arc per second wide. Rightward and upward eye velocities are plotted to the right of zero. Philip's histograms are based on 1505 velocity samples, Jennifer's on 542, and D.F.'s on 954.

remains that their oculomotor performance can limit their visual abilities. These limitations must be taken into account when interpreting their visual performance.

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2. Eye movements were recorded with a double Purkinje image eye tracker (SRI Generation III) [T. N. Cornsweet and H. D. Crane, *J. Opt. Soc. Am.* **63**, 921 (1973)]. The noise level of the tracker, expressed as the standard deviation of position of an artificial eye, was 0.5 minute of arc on the horizontal and 0.67 minute of arc on the vertical meridian. The tracker is insensitive to head translation. Voltage outputs of the tracker were filtered at 50 Hz (−3 dB) and fed to an analog-to-digital converter that sampled eye position at 100 Hz. Movements of the right eye were recorded with the left eye occluded and the head stabilized by a bite board.
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4. Alignment and calibration were carried out in the first session. Calibration factors were determined from the children's tracking of a large-amplitude (8.2°), low-frequency (0.4 step per second) square wave (Fig. 1C). Median eye position was estimated for intervals between the large tracking saccades. The children's calibration factors were within the 10 percent range of variation we have measured with a large sample of adults whose calibration factors have been measured with the same instrument in lengthy and elaborate calibration sessions. Both children remained attentive and cooperative throughout. They were willing and able to sit still, bite on the bite board, and look at the target for many consecutive minutes during each recording session. No special procedures were used to reward or to train the children in order to facilitate comparison with prior studies of adults. The correlation between the children's eye movements and the general pattern of target motions (Fig. 1) suggests that they understood and were trying to follow our simple instructions to look at the target.
5. The bivariate contour ellipse area [(minutes of arc)^2], as calculated, describes the region in which the line of sight was located 68 percent of the time.
6. Saccade vector magnitudes were measured by taking the differences between the steady-state saccade-offset and -onset eye positions. The large overshoots at the end of saccades (Fig. 1A) were not included in the measures of saccade vector magnitude. These large overshoots are generated by movements of the fourth Purkinje image when the crystalline lens moves within the lens capsule because of inertia.
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10. Mean retinal image vector speed (that is, mean eye speed averaged over all 100-msec saccade-free intervals) was 42.3 minutes of arc per second for Philip [standard deviation (S.D.) = 21.7, N = 1505] and 47.5 minutes of arc per second for Jennifer (S.D. = 26.3, N = 542). The average retinal image vector speed of D.F. was 13.7 minutes of arc per second (S.D. = 9.0, N = 954). D.F.'s retinal image speeds fell within the range of retinal image speeds of other adults [(*9, 11*); A. Skavenski, R. Hansen, R. M. Steinman, B. J. Winterson, *Vision Res.* **19**, 675 (1979)].
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13. Preschool children may perform as well as adults when visual tasks do not require precise fixation. For example, recent reports suggest that visual acuity reaches adult levels by about 2 years of age [D. L. Mayer and V. Dobson, *Invest. Ophthalmol. Visual Sci.* **19**, 566 (1980)]. Stimuli in this study were large (9°) high-contrast square wave gratings. Thus, saccades on the order of several degrees would still permit the bars of the grating to remain imaged on the fovea. The contribution of retinal image speed to performance of this task is more difficult to evaluate because performance of some visual tasks is not impaired by imposed retinal image motion slower than 2° per second [B. J. Murphy, *Vision Res.* **18**, 521 (1978); G. Westheimer and S. P. McKee, *J. Opt. Soc. Am.* **65**, 847 (1975)].
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16. It is not likely that poor visual resolution would produce high retinal image speeds in infants or children, because characteristics of smooth eye movements during slow control or smooth pursuit are largely independent of target contrast and luminance [B. J. Winterson and R. M. Steinman, in (*12*); R. B. Post, C. S. Rodemer, J. Dichgans, H. W. Leibowitz, *Invest. Ophthalmol. Visual Sci.* **18** (Suppl.), 140 (1979)].
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Increased Axonal Proteolysis in Myelin-Deficient Mutant Mice

Abstract. *Protein degradation within retinal ganglion cell axons in vitro is 50 to 110 percent faster than normal in mutant mice exhibiting deficiencies of myelin in the central nervous system. Proteolysis is increased proximally and distally within retinal ganglion cell axons of mice carrying the jimpy mutation or its allele, myelin synthesis deficiency, and is increased distally within those axons of quaking mice. The proteolytic defect is axon (neuron)-specific since the rate of protein degradation within glial cells is normal. Increased axonal proteolysis does not bear a simple relation to hypomyelination since shiverer, another mouse mutant deficient in central myelin, displayed normal rates of axonal protein degradation under the same conditions. These observations suggest an abnormal axon-glial interaction in mice with primary glial defects and raise the possibility that the functioning of histologically normal axons (neurons) may be altered in dysmyelinating diseases.*

Biochemical interactions between neurons and glia seem to be important in normal brain development (*1*). The interplay between axons and glia during myelinogenesis has been well documented (*2, 3*), although our understanding of these interactions at the molecular level is limited. In large part, this limitation stems from the problem of distinguishing biochemical events in neurons from those in glia, while preserving the anatomical relationships between these cells.

A strategy was developed that permits proteolysis to be studied specifically within the axons of mouse retinal ganglion cells (RGC) and separately within neighboring glial cells throughout postnatal development (*4, 5*). After labeling RGC proteins in vivo by intravitreal injection of radioactively labeled amino acid, I exploited the ability of the neuron to segregate by axoplasmic transport a population of labeled proteins that is specifically neuronal in origin. Glia in the optic pathway were selectively labeled in vitro by taking advantage of the negligible protein synthetic capacity of axons (*6*). Proteolysis in RGC axons or glial elements of the primary optic pathway was studied in vitro in the excised, but intact, optic nerves to preserve anatomic relationships. The rates of protein degradation measured under these conditions approximate those estimated in vivo (*4*).

This approach was applied to mice with genetic disorders that profoundly impair myelin formation but apparently spare neurons and their processes (*7–11*). In two mutant strains, jimpy (*jp* and *jp^{msd}*) (*7–9*) and quaking (*qk*) (*8*), protein degradation at physiological *p*H was abnormally elevated within RGC axons but not in adjacent glial cells. Since the primary genetic defect in *jp* and *qk* mice is believed to reside in glial cells (*12*), the observation that neuronal proteolysis is increased suggests that axon-glial interactions, and possibly neuronal function, are abnormal in these mice.

Mice, originally from Jackson Laboratories (Bar Harbor), were bred in controlled-environment rooms on a 12-hour day-night cycle. The *jp* mutation, a sex-linked recessive trait (*7, 8*), was bred on a C57BL/6J-CBA hybrid background.

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