Published in final edited form as:

Optom Vis Sci. 2009 June ; 86(6): E653. doi:10.1097/OPX.0b013e3181a6a237.

Development of Rod Function in Term Born and Former Preterm Subjects

Anne B. Fulton, MD, Ronald M. Hansen, PhD, and Anne Moskowitz, OD, PhD

Department of Ophthalmology, Children's Hospital and Harvard Medical School, Boston, Massachusetts

Abstract

Purpose—Provide an overview of some of our electroretinographic and psychophysical studies of normal development of rod function and their application to retinopathy of prematurity (ROP).

Methods—Electroretinographic (ERG) responses to full-field stimuli were recorded from dark adapted subjects. Rod photoreceptor sensitivity, S_{ROD} , was calculated by fit of a biochemical model of the activation of phototransduction to the ERG a-wave. Dark adapted psychophysical thresholds for detecting 2° spots in parafoveal (10° eccentric) and peripheral (30° eccentric) retina were measured and the difference between the thresholds, Δ_{10-30} , was examined as a function of age. S_{ROD} and Δ_{10-30} in term born and former preterm subjects were compared.

Results—In term born infants, (1) the normal developmental increase in S_{ROD} changes proportionately with the amount of rod visual pigment, rhodopsin, and (2) rod mediated function in central retina is immature compared to that in peripheral retina. In subjects born prematurely, deficits in rod photoreceptor sensitivity persist long after active ROP has resolved. Maturation of rod mediated thresholds in the central retina is prolonged by mild ROP.

Conclusions—Characterization of the development of normal rod and rod mediated function provides a foundation for understanding ROP.

Keywords

retina; infants; retinopathy of prematurity; electroretinography; psychophysics

The retina, an accessible part of the nervous system in which sensory and neural processes can be studied using non-invasive procedures, is immature at birth and continues to develop postnatally. We have tested hypotheses about the normal immature neurosensory retina in infants and children.¹⁻²³ In this paper, we present two main concepts about the development of normal scotopic function that have emerged from these studies and their application to one pediatric retinal disorder, retinopathy of prematurity (ROP).

One concept concerns immaturity of the rod photoreceptors. At term birth, all retinal layers are present and the number of retinal cells remains about constant through ensuing years.²⁴ Thus, our early studies that documented differences between infant and adult electroretinographic (ERG) responses to full-field stimuli suggested immaturities of the retinal cells.^{1, 25, 26} The ERG data, as well as psychophysical data,^{7, 18, 21} identified the rod photoreceptor as a site of critical immaturity in young infants. This led us to determine the growth curve for the rod visual pigment, rhodopsin,²⁷⁻²⁹ and to study phototransduction

processes in infants.^{6, 20} We found that the amount of rhodopsin increases during development^{28, 29} and that rhodopsin content scales the kinetics of activation and deactivation of phototransduction in dark adapted infants.^{6, 19} We have backed up these conclusions about development of human rods with studies of rat rods.³⁰⁻³⁵

The second concept is that development of central retinal function is delayed relative to that in more peripheral retina. Delayed development of the central retina pertains to both rod^{12, 17, 36} and cone²² mediated function; this paper considers rod function only. In keeping with the delayed developmental elongation of the parafoveal rod outer segments,³⁶⁻³⁸ psychophysically determined parafoveal thresholds of young infants are elevated relative to peripheral thresholds.^{12, 17, 36}

Herein we provide an overview of some electroretinographic and psychophysical studies of the development of normal rod and rod-driven function. We have applied our measurement and analytical procedures to investigation of pediatric retinal disorders³⁹⁻⁴³ and illustrate this by presenting some data obtained in ROP.⁴⁴⁻⁴⁹ ROP is the most common pediatric retinal disease to cause life-long, bilateral visual impairment.⁵⁰

The coincidence of age at onset of ROP⁵¹ and acceleration of the rhodopsin growth curve (Figure 1) alerted us to the pivotal role of the immature rods in the ROP disease process. Specifically, it is not until the age at which rapid increase in rhodopsin content and developmental elongation of the rod photoreceptor outer segments is in progress that ROP makes its clinical appearance, which is marked by the formation of abnormal retinal blood vessels.⁵¹ We theorized that rods have a pivotal role in ROP because, on one hand, the developing rods' escalating demand for aerobic energy contributes to the relative hypoxia of the neural retina that, in turn, drives development of the abnormal retinal vasculature.⁵² On the other hand, incompletely met energy demands can injure the developing rods.⁵³⁻⁵⁵ We hypothesized that (1) such injury would cause rod dysfunction in ROP subjects, and (2) the late maturing rods in the central retina would be particularly vulnerable to the effects of ROP, even if mild. We have tested these hypotheses using electroretinographic and psychophysical procedures.

Methods and Results

Full-Field Electroretinography. Rod Photoreceptor Function

We recorded ERG responses to full-field stimuli in dark adapted, awake infants using a corneal contact electrode (Figure 2A). The full-field ERG evaluates the function of the retina as a whole. ERG responses to a several log unit range of stimulus intensities were recorded and a-waves, which represent rod photoreceptor activity, were analyzed using mathematical models.⁵⁶⁻⁵⁹ In these models, S_{ROD} is a sensitivity parameter related to the gain of the activation of phototransduction. It is based on the time constants of the molecular processes that are initiated with photon absorption by rhodopsin.^{58, 59}

In normal term born infants, we found that the growth curve for S_{ROD} ⁶ is similar to that for rhodopsin.²⁸ In infants and children born prematurely and tested at post term ages, we found ERG evidence of persistent rod dysfunction long after active ROP disease had resolved (Figure 3).^{46, 48} In the majority of subjects with mild, untreated ROP (30 of 40), S_{ROD} was below average; by clinical criteria, their ROP had resolved without residua. Of the 11 subjects with more severe ROP treated by laser ablation of the peripheral avascular retina at preterm ages, seven had S_{ROD} values below the 95% prediction limit for normal; the area of ablated retina did not account for the deficits in S_{ROD} . None of the ROP subjects had retinal detachments. In the subjects who never had ROP (N=17), S_{ROD} values were distributed around the average normal value.

Psychophysical Delta 10-30 (Δ_{10-30}) Test. Rod Mediated Function in Central Retina

In contrast to ERG responses to full-field stimuli in which spatial information is lacking, behavioral responses to stimulation of small patches of retina can be studied using psychophysical procedures (Figure 2B). The area of central retina with delayed rod outer segment development is too small (<5% of the total retinal area) to have a detectable impact on ERG responses. We devised a psychophysical procedure in which the dark adapted threshold in parafoveal retina was compared to the threshold in peripheral retina.³⁶ Stimulus conditions were selected such that in adults, thresholds are equal at the two sites; that is, delta 10-30 (Δ_{10-30}) in adults is zero.

We used a two-alternative, spatial forced-choice preferential looking procedure to estimate dark adapted thresholds in 2° diameter patches of parafoveal (10° eccentric) and peripheral (30° eccentric) retina (Figure 4). We presented test stimuli on the right or left of a rear projection screen. A fix and flash paradigm was used to control the retinal site stimulated.⁶¹ An adult observer, unaware of the position of the test spot, reported the direction of the infant's looking behavior, right or left. For speed, and thus feasibility for evaluating infants, we used a rapid, up-down staircase.⁶² In basic work, we have shown that thresholds obtained using the staircase are in good agreement with those obtained using the method of constant stimuli.⁷

In healthy term born 10 week olds, we found that the parafoveal threshold was more elevated than the peripheral threshold. The course of maturation was such that threshold at both sites reached adult values by age 6 months.^{12, 17}

We used the Δ_{10-30} procedure to test the hypothesis that ROP alters the course of development of the rods in the late maturing central retina. We found that in infants with a history of mild, untreated ROP which had resolved completely and spontaneously, the course of maturation of the thresholds was prolonged (Figure 5A) compared to that in normal term born infants.⁴⁴ In former preterms who never had ROP (Figure 5B), the course of maturation of the thresholds was indistinguishable from that in term born infants.

Discussion

The results shown in Figures 3 and 5 illustrate application of some of the methods that we have used in studies of normal retinal development to ROP. Long after active ROP has resolved, deficits in rod photoreceptor sensitivity persist (Figure 3). In the central retina, maturation of rod mediated thresholds is prolonged by mild ROP (Figure 5A). In rat models of ROP, the fine structure of the rods is altered⁵⁴ and S_{ROD} is attenuated^{53, 55, 63} in a fashion similar to that in human ROP subjects (Figure 3). Furthermore, in rat models, rod dysfunction antedates⁵⁵ and predicts⁵³ subsequent ROP vascular status, and early pharmaceutical intervention that targets fundamental rod function improves vascular outcome.⁶⁴ These preclinical data offer a new and promising perspective on treatment of human ROP.

The dark adapted rod photoreceptors do not tell the whole story about retinal function in normal development or in ROP. Scotopic ERG and psychophysical data provide evidence that the postreceptor retina re-organizes both in normal development and during the evolution and resolution of ROP.^{14-16, 18, 21, 23, 47, 48, 65} Cone photoreceptor and cone-driven postreceptor ERG responses to full-field stimuli are also immature, but in keeping with their earlier anatomic development,²⁴ cones are relatively more mature than rods²⁰ and are less affected by ROP;⁴⁵ possibly earlier maturation is protective. Cone-driven postreceptor function in the central retina is remarkably immature in young term born infants²² and is altered by mild ROP in a fashion that forecasts⁶⁶ structural changes in the neurovascular retina, which we have demonstrated using high resolution imaging techniques.⁶⁷

More remains to be learned about both scotopic and photopic processes in the normal, immature mammalian retina. For instance, retinal adaptation in steady state conditions^{18, 21, 47} and during recovery from light exposure^{8, 26} warrant further study. ERG and psychophysical investigations in the living eye in animal models and in patients will surely continue to identify disease processes and guide the design of novel treatments.

Acknowledgments

Supported by National Institutes of Health grant R01-EY10597.

References

1. Fulton A, Hansen R. Background adaptation in human infants: Analysis of b-wave responses. *Doc Ophthalmol Proc Ser* 1982;31:191–7.
2. Fulton, A.; Hansen, RM. Stimulus response functions for the scotopic b-wave. In: Heckenlively, JR.; Arden, GB., editors. *Principles and Practice of Clinical Electrophysiology of Vision*. 2nd. Cambridge, MA: The MIT Press; 2006. p. 473–8.
3. Fulton AB, Hansen RM, Westall CA. Development of ERG responses: the ISCEV rod, maximal and cone responses in normal subjects. *Doc Ophthalmol* 2003;107:235–41. [PubMed: 14711155]
4. Fulton AB, Hansen RM. Scotopic stimulus/response relations of the B-wave of the electroretinogram. *Doc Ophthalmol* 1988;68:293–304. [PubMed: 3402318]
5. Fulton AB, Hansen RM. The rod sensitivity of dark adapted human infants. *Curr Eye Res* 1992;11:1193–8. [PubMed: 1490337]
6. Fulton AB, Hansen RM. The development of scotopic sensitivity. *Invest Ophthalmol Vis Sci* 2000;41:1588–96. [PubMed: 10798680]
7. Fulton AB, Hansen RM, Yeh YL, Tyler CW. Temporal summation in dark-adapted 10-week old infants. *Vision Res* 1991;31:1259–69. [PubMed: 1891817]
8. Hansen RM, Fulton AB. Pupillary changes during dark adaptation in human infants. *Invest Ophthalmol Vis Sci* 1986;27:1726–9. [PubMed: 3793401]
9. Hansen RM, Fulton AB. Pupillary changes during dark adaptation in human infants. *Invest Ophthalmol Vis Sci* 1986;27:1726–9. [PubMed: 3793401]
10. Hansen RM, Fulton AB. Scotopic optokinetic nystagmus thresholds in 10-week-old infants. *Invest Ophthalmol Vis Sci* 1994;35:1246–9. [PubMed: 8125736]
11. Hansen RM, Fulton AB. Rod-mediated increment threshold functions in infants. *Invest Ophthalmol Vis Sci* 2000;41:4347–52. [PubMed: 11095637]
12. Hansen RM, Fulton AB. The course of maturation of rod-mediated visual thresholds in infants. *Invest Ophthalmol Vis Sci* 1999;40:1883–6. [PubMed: 10393066]
13. Hansen RM, Fulton AB. Psychophysical estimates of ocular media density of human infants. *Vision Res* 1989;29:687–90. [PubMed: 2626826]
14. Hansen RM, Fulton AB. Electroretinographic assessment of background adaptation in 10-week-old human infants. *Vision Res* 1991;31:1501–7. [PubMed: 1949619]
15. Hansen RM, Fulton AB. Scotopic center surround organization in 10-week-old infants. *Vision Res* 1994;34:621–4. [PubMed: 8160381]
16. Hansen RM, Hamer RD, Fulton AB. The effect of light adaptation on scotopic spatial summation in 10-week-old infants. *Vision Res* 1992;32:387–92. [PubMed: 1574853]
17. Hansen RM, Fulton AB. Dark-adapted thresholds at 10- and 30-deg eccentricities in 10-week-old infants. *Vis Neurosci* 1995;12:509–12. [PubMed: 7654607]
18. Hansen RM, Fulton AB. Rod-mediated increment threshold functions in infants. *Invest Ophthalmol Vis Sci* 2000;41:4347–52. [PubMed: 11095637]
19. Hansen RM, Fulton AB. Recovery of the rod photoresponse in infants. *Invest Ophthalmol Vis Sci* 2005;46:764–8. [PubMed: 15671311]
20. Hansen RM, Fulton AB. Development of the cone ERG in infants. *Invest Ophthalmol Vis Sci* 2005;46:3458–62. [PubMed: 16123452]

21. Hansen RM, Fulton AB, Harris SJ. Background adaptation in human infants. *Vision Res* 1986;26:771–9. [PubMed: 3750858]
22. Hansen RM, Moskowitz A, Fulton AB. Multifocal ERG responses in infants. *Invest Ophthalmol Vis Sci* 2009;50:470–5. [PubMed: 18719077]
23. Moskowitz A, Hansen RM, Fulton AB. ERG oscillatory potentials in infants. *Doc Ophthalmol* 2005;110:265–70. [PubMed: 16328935]
24. Hendrickson, AE. The morphologic development of human and monkey retina. In: Albert, DM.; Jakobiec, FA., editors. *Principles and Practice of Ophthalmology: Basic Sciences*. Philadelphia: Saunders; 1994. p. 561-77.
25. Fulton AB, Hansen RM. Electoretinography: application to clinical studies of infants. *J Pediatr Ophthalmol Strabismus* 1985;22:251–5. [PubMed: 4078668]
26. Fulton AB, Baker BN. The relation of retinal sensitivity and rhodopsin in developing rat retina. *Invest Ophthalmol Vis Sci* 1984;25:647–51. [PubMed: 6724834]
27. Fulton AB, Dodge J, Hansen RM, Schremser JL, Williams TP. The quantity of rhodopsin in young human eyes. *Curr Eye Res* 1991;10:977–82. [PubMed: 1959384]
28. Fulton AB, Dodge J, Hansen RM, Williams TP. The rhodopsin content of human eyes. *Invest Ophthalmol Vis Sci* 1999;40:1878–83. [PubMed: 10393065]
29. Fulton AB, Dodge J, Schremser JL, Armstrong A, Lanier F, Dawson WW, Williams TP. The quantity of rhodopsin in human eyes. *Curr Eye Res* 1990;9:1211–6. [PubMed: 2091900]
30. Alpern M, Fulton AB, Baker BN. “Self-screening” of rhodopsin in rod outer segments. *Vision Res* 1987;27:1459–70. [PubMed: 3445480]
31. Dodge J, Fulton AB, Parker C, Hansen RM, Williams TP. Rhodopsin in immature rod outer segments. *Invest Ophthalmol Vis Sci* 1996;37:1951–6. [PubMed: 8814134]
32. Fulton AB, Baker BN. The relation of retinal sensitivity and rhodopsin in developing rat retina. *Invest Ophthalmol Vis Sci* 1984;25:647–51. [PubMed: 6724834]
33. Fulton AB, Graves AL. Background adaptation in developing rat retina: an electoretinographic study. *Vision Res* 1980;20:819–26. [PubMed: 7467136]
34. Fulton AB, Hansen RM, Findl O. The development of the rod photoresponse from dark-adapted rats. *Invest Ophthalmol Vis Sci* 1995;36:1038–45. [PubMed: 7730013]
35. Fulton, AB.; Hansen, RM.; Dodge, J.; Williams, T. Photoreceptor development and photostasis. In: Williams, TP.; Thistle, AB., editors. *Photostasis and Related Phenomena*. New York: Plenum Press; 1998. p. 189-98.
36. Fulton, A.; Hansen, RM.; Dorn, E.; Hendrickson, A. Development of primate rod structure and function. Vital-Durand, F.; Atkinson, J.; Braddick, OJ., editors. Oxford: Oxford University Press; 1995. p. 33-49.
37. Dorn EM, Hendrickson L, Hendrickson AE. The appearance of rod opsin during monkey retinal development. *Invest Ophthalmol Vis Sci* 1995;36:2634–51. [PubMed: 7499086]
38. Hendrickson AE, Drucker D. The development of parafoveal and midperipheral retina. *Behav Brain Res* 1992;19:21–32. [PubMed: 1388798]
39. Cooper LL, Hansen RM, Darras BT, Korson M, Dougherty FE, Shoffner JM, Fulton AB. Rod photoreceptor function in children with mitochondrial disorders. *Arch Ophthalmol* 2002;120:1055–62. [PubMed: 12149059]
40. Cox GF, Hansen RM, Quinn N, Fulton AB. Retinal function in carriers of Bardet-Biedl syndrome. *Arch Ophthalmol* 2003;121:804–10. [PubMed: 12796250]
41. Elias ER, Hansen RM, Irons M, Quinn NB, Fulton AB. Rod photoreceptor responses in children with Smith-Lemli-Opitz syndrome. *Arch Ophthalmol* 2003;121:1738–43. [PubMed: 14662594]
42. Moskowitz A, Hansen RM, Akula JD, Eklund SE, Fulton AB. Rod and rod-driven function in achromatopsia and blue cone monochromatism. *Invest Ophthalmol Vis Sci* 2009;50:950–8. [PubMed: 18824728]
43. Lu M, Hansen RM, Cunningham MJ, Eklund SE, Fulton AB. Effects of desferoxamine on retinal and visual function. *Arch Ophthalmol* 2007;125:1581–2. [PubMed: 17998528]
44. Barnaby AM, Hansen RM, Moskowitz A, Fulton AB. Development of scotopic visual thresholds in retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 2007;48:4854–60. [PubMed: 17898313]

45. Fulton AB, Hansen RM, Moskowitz A. The cone electroretinogram in retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 2008;49:814–9. [PubMed: 18235032]
46. Fulton AB, Hansen RM, Petersen RA, Vanderveen DK. The rod photoreceptors in retinopathy of prematurity: an electroretinographic study. *Arch Ophthalmol* 2001;119:499–505. [PubMed: 11296015]
47. Hansen RM, Fulton AB. Background adaptation in children with a history of mild retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 2000;41:320–4. [PubMed: 10634637]
48. Moskowitz A, Hansen R, Fulton A. Early ametropia and rod photoreceptor function in retinopathy of prematurity. *Optom Vis Sci* 2005;82:307–17. [PubMed: 15829858]
49. Reisner DS, Hansen RM, Findl O, Petersen RA, Fulton AB. Dark-adapted thresholds in children with histories of mild retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 1997;38:1175–83. [PubMed: 9152237]
50. Steinkuller PG, Du L, Gilbert C, Foster A, Collins ML, Coats DK. Childhood blindness. *J AAPOS* 1999;3:26–32. [PubMed: 10071898]
51. Palmer EA, Flynn JT, Hardy RJ, Phelps DL, Phillips CL, Schaffer DB, Tung B. Incidence and early course of retinopathy of prematurity. The Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Ophthalmology* 1991;98:1628–40. [PubMed: 1800923]
52. Fulton AB, Akula JD, Mocko JA, Hansen RM, Benador IY, Beck SC, Fahl E, Seeliger MW, Moskowitz A, Harris ME. Retinal degenerative and hypoxic ischemic disease. *Doc Ophthalmol* 2009;118:55–61. [PubMed: 18483822]
53. Akula JD, Hansen RM, Martinez-Perez ME, Fulton AB. Rod photoreceptor function predicts blood vessel abnormality in retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 2007;48:4351–9. [PubMed: 17724227]
54. Fulton AB, Reynaud X, Hansen RM, Lemere CA, Parker C, Williams TP. Rod photoreceptors in infant rats with a history of oxygen exposure. *Invest Ophthalmol Vis Sci* 1999;40:168–74. [PubMed: 9888440]
55. Reynaud X, Hansen RM, Fulton AB. Effect of prior oxygen exposure on the electroretinographic responses of infant rats. *Invest Ophthalmol Vis Sci* 1995;36:2071–9. [PubMed: 7657546]
56. Cideciyan AV, Jacobson SG. An alternative phototransduction model for human rod and cone ERG a-waves: normal parameters and variation with age. *Vision Res* 1996;36:2609–21. [PubMed: 8917821]
57. Hood DC, Birch DG. Rod phototransduction in retinitis pigmentosa: estimation and interpretation of parameters derived from the rod a-wave. *Invest Ophthalmol Vis Sci* 1994;35:2948–61. [PubMed: 8206712]
58. Lamb TD, Pugh EN Jr. A quantitative account of the activation steps involved in phototransduction in amphibian photoreceptors. *J Physiol* 1992;449:719–58. [PubMed: 1326052]
59. Pugh EN Jr, Lamb TD. Amplification and kinetics of the activation steps in phototransduction. *Biochim Biophys Acta* 1993;1141:111–49. [PubMed: 8382952]
60. The International Classification of Retinopathy of Prematurity revisited. *Arch Ophthalmol* 2005;123:991–9. [PubMed: 16009843]
61. Schneck ME, Hamer RD, Packer OS, Teller DY. Area-threshold relations at controlled retinal locations in 1-month-old infants. *Vision Res* 1984;24:1753–63. [PubMed: 6533998]
62. Wetherill GB, Levitt H. Sequential estimation of points on a psychometric function. *Br J Math Stat Psychol* 1965;18:1–10. [PubMed: 14324842]
63. Liu K, Akula JD, Falk C, Hansen RM, Fulton AB. The retinal vasculature and function of the neural retina in a rat model of retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 2006;47:2639–47. [PubMed: 16723481]
64. Akula JD, Kubota R, Hansen RM, Tzekov R, McGee D, Fulton AB. Effects of a vitamin-a derivative (ag-787-14-2) on retinal function in oxygen-induced retinopathy. *Invest Ophthalmol Vis Sci* 2008;49 E-Abstract 2629.
65. Akula JD, Mocko JA, Moskowitz A, Hansen RM, Fulton AB. The oscillatory potentials of the dark-adapted electroretinogram in retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 2007;48:5788–97. [PubMed: 18055833]

66. Fulton AB, Hansen RM, Moskowitz A, Barnaby AM. Multifocal ERG in subjects with a history of retinopathy of prematurity. *Doc Ophthalmol* 2005;111:7–13. [PubMed: 16502302]
67. Hammer DX, Iftimia NV, Ferguson RD, Bigelow CE, Ustun TE, Barnaby AM, Fulton AB. Foveal fine structure in retinopathy of prematurity: an adaptive optics Fourier domain optical coherence tomography study. *Invest Ophthalmol Vis Sci* 2008;49:2061–70. [PubMed: 18223243]

Figure 1.

Rhodopsin growth curve and the preterm onset of ROP. Rhodopsin content is plotted as percent of the adult mean.²⁸ The large arrow indicates the age at which prethreshold ROP is diagnosed.

⁵¹ The small arrow indicates a preterm age.

Figure 2.

Procedures for assessment of retinal function in dark adapted infants. **(A)** Electroretinography. A 10 week old infant is positioned under an integrating sphere that is used for presenting full-field stimuli. A bipolar contact electrode on the infant's right eye registers changes in the transretinal potential, the ERG, that are evoked by brief flashes of light. **(B)** Psychophysical Δ_{10-30} test. An older infant reaches toward a test spot presented on a rear projection screen. For younger infants, an adult observer reports on every trial the infant's looking response to the right or left of the screen. Details of the procedure are given in Barnaby *et al.*⁴⁴ A color version of this figure is available online at www.optvissci.com.

Figure 3.

Rod photoreceptor sensitivity, S_{ROD} , in former preterms. The solid curve represents the average normal growth curve for S_{ROD} ; dashed lines show the upper and lower 95% prediction limits of normal.⁶ Each symbol represents one subject with ROP category as indicated in the key. The 50% point on the S_{ROD} growth curve is at approximately 10 weeks post term and thus within the 95% confidence interval for the growth curve for rhodopsin.²⁸ Re-plotted from Fulton *et al.*⁴⁶ and Moskowitz *et al.*⁴⁸ with additional data added.

Figure 4.

Psychophysical Δ_{10-30} test. **(A)** ROP zones and location of stimuli on the retina. The position of the parafoveal and peripheral stimuli (filled circles) are superimposed on the circular diagram of the ROP zones.⁶⁰ **(B)** Schematic diagram of the screen and stimuli. The 2° diameter stimuli at the parafoveal (10° eccentric) and peripheral (30° eccentric) sites are indicated. The + indicates the central fixation display. Re-plotted from Figure 1 in Barnaby *et al.*⁴⁴

Figure 5.

Dark adapted thresholds in former preterms. The difference between parafoveal and peripheral thresholds (Δ_{10-30}) is plotted as a function of corrected age. Panel A shows data from subjects with a history of mild, untreated ROP (N=12); panel B shows data from former preterms who never had ROP (N=12). Data points from an individual are connected by line segments. Values above zero indicate that the parafoveal threshold was elevated relative to the peripheral threshold. In term born infants aged 6 months, as in adults, Δ_{10-30} is zero. The dashed lines in each panel indicate the upper and lower limits of the 99% prediction interval of normal. Re-plotted from figures 2 and 3 in Barnaby *et al.*⁴⁴