Experientia 40 (1984), Birkhäuser Verlag, CH-4010 Basel/Switzerland

Mini Reviews

Developmental physiological optics and visual acuity: a brief review

by J. V. Odom and M. Green

Department of Ophthalmology, School of Medicine, West Virginia University Medical Center, Morgantown (West Virginia 26506, USA), and School of Optometry, Indiana University, Bloomington (Indiana 47401, USA)

Summary. The development of optical and neural factors affecting visual acuity is reviewed with the aim of determining the age at which the relationship between optical and neural factors become mature. Delayed development of extrastriate cortical and indirect visual pathways may account for differences in acuity assessed by preferential looking and pattern reversal VEPs.

Key words. Visual acuity; optics, developmental physiological; developmental physiological optics; optical factors; neural factors; visual pathways.

Beginning in the 1950's, a number of investigators have used behavioral and electrophysiological techniques to examine the development of human infants' visual acuity (for reviews see Dobson and Teller[13] and Harter et al.[20]). In general, acuity has been observed to develop rapidly during the first months of life and to approach normal adult levels (6/6) between six months[20, 21, 49, 50] and five to ten years of age[6, 12, 13, 27, 34, 35]. Interpretations of human visual development, especially acuity development, have concentrated on the role of central nervous system maturation[6, 10, 12, 13, 20, 21, 27, 32–35, 49, 50] as the mechanism underlying functional change. Differences between the estimates of various methods have been primarily attributed to differences in the stimulus characteristics or differences between the methods and the criteria used to determine thresholds[13, 49]. The above factors influence acuity estimates and possibly affect estimates of the rate at which normal vision develops. However, acuity as assessed in adults is influenced by processing before and after the striate cortex, including optical, neural and experimential variables and the development of these factors influences the development of visual function.

Classically, visual resolution has been explained in terms of 1) the optical properties of the eye and photoreceptors, 2) retinal neural processing, and 3) central neural processing (for reviews see Westheimer[56] and Riggs[43]). This article reviews the current literature and outlines current knowledge of the maturation of the optical and neural factors affecting acuity. The development of each of these three determinants of visual acuity is reviewed. An effort is made to identify the ages at which the relationships between external stimuli, anatomical and physiological variables become constant or invariant. The constancy of a relationship between some anatomical or physiological variable and external events is likely to be more important for function than the variable itself. For example, it is probably less important for the determination of acuity that visual cells, whether in the retina or cortex, have a certain number or number per unit area (density) as that they have a fixed, invariant relationship to visual angle, so that the same number of cells are excited by stimulation of an object of fixed size. Thus, one might expect that visual acuity would be adult-like at that period in development when the number of photoreceptors, ganglion cells, or cortical cells stimulated by a visual angle of some size is the same as in adults rather than at that point at which the absolute number of cells in a certain area of retina or cortex is the same as in the adult.

Optical development

The clarity of the image stimulating the retina depends on the optics of the eye. Several factors determine image quality including 1) clarity of the ocular media, 2) refractive error of the unaccommodated eye (determined primarily by the eye's total refractive power and axial length), 3) ability to accommodate, 4) depth of focus, and 5) retinal illuminance (a function of pupil area). The changes in infancy related to changing retinal image quality are poorly documented.

Newborns have clear ocular media (see Boettner and Walter[9]). Their pupils are smaller in diameter, so that even as late as three months of age the area of the pupil is only about 80% that of adults (based on Banks[5]). The effect of the resulting 0.1–0.2 log unit decrease in retinal illuminance on visual function is unknown. However, the smaller pupil size also means that young infants have much greater depth of focus[17].

This greater depth of focus especially in young infants, has important implications and correlations with the development of other visual functions. During the first year defocus impairs acuity relatively less than in adults[42], so that errors in refraction[4, 20, 38] have less impact on the determination of acuity. Similarly, the inability of the young infant to accommodate[4, 22, 38, 56] probably has little impact on visual acuity, and the improvement of accommodation in the early months is correlated with decreased depth of focus.

Two-thirds of newborn infants have astigmatism of 0.5 D or more[8]. The incidence of clinically significant astigmatism is greatest during the first nine months and decreases thereafter[2, 39]. Despite the fact that astigmatism influences visual preferences, few infant astigmats develop meridional amblyopia[3, 18]. The greater depth of focus of the infant eye during the early months may diminish what would otherwise be detrimental effects of astigmatism.

Infants' eyes are smaller than those of adults. They are shorter in axial length[28, 31] and greater in corneal curva-

ture[31] so that the total refractive power is greater (85 D vs 60 D)[30]. Although there is considerable individual variation, on average newborn infants' eyes are myopic by about 1–3 diopters[4, 21, 22, 30]. Older infants tend to be hyperopic.

The surface area of the retina (posterior half of the newborn's eye) is only half that of adults (based on Lotmar[30]). The shorter nodal distance[30] and (presumably) a constant linear distance between the fovea and optic disc account for the greater reported angle between the optical and visual axes observed in newborns (8° vs 1° for adults)[48].

The first year of life is one of rapid growth and change in the eyes. At birth the retinal image subtending 1° has only 70% of the adult linear extent and 50% of the areal extent (based on Lotmar[30]).

Individual children show marked fluctuations in refractive error on successive examination. The picture is more stable for averaged population data. Axial length of the eye, and especially vitreal length, increases into adulthood[28, 51], but there is little change in the refractive power[51], refractive error[51], or visual acuity[16] after the age of three. Increasing axial length is compensated for by decreased corneal curvature[30]. According to Larsen[28], this stabilizaiton occurs in humans within the first year of life and probably within the first few postnatal months. Results of animal experiments suggest a similar picture[19, 45, 46]. After an initial postnatal period of rapid growth in axial length, adult refractive power is obtained, and all subsequent changes in ocular dimensions are compensatory, tending to maintain a constant refractive power.

Therefore, our best knowledge suggests that within the first few postnatal months, the linear extent of a visual angle reaches its adult value. Whether the neural system subtended by that visual angle is mature remains to be answered. In the next section, evidence regarding the time at which 1) a visual angle projects onto the same number of foveal cones as in the adult and 2) whether the connections between those cones and their ganglion cells are sufficiently mature to support adult-like function will be examined.

Retinal development

At birth, the inner retinal layers still lie above the foveal cones which are shorter and thicker than in the adult[1, 31]. By four months of age, development of the foveal pit is virtually complete[31]. Available data on other mammals is consistent with the human data. During the period from birth to adulthood, the region of rod free cones in the rhesus monkey decreases in diameter from 800 to 200 μm[23] (260 μm in adult human[41]) and the cones became more densely packed by a factor of four, suggesting a parallel relationship between foveal diameter and cone density[23]. Figure 6 of Hendrickson and Kupfer[38] indicates that foveal diameter of infant macaques is only slightly larger than the adults' (300 μm) at four months and fully adult by seven months. Because the interconnections of cones, bipolars, and ganglion cells are made prior to the displacement of the ganglion cells from the fovea, one may infer that the linear extent of the receptive fields of macular ganglion cells is fixed at some point between one and seven months in the monkey[23]. Using a conversion factor of one month of a monkey's development equals four months of human development, one might infer that between four and 28 months of age humans would reach a similar developmental stage (suggested by Teller[13]).

Similar observations have been made in the cat. The linear extent of kitten receptive field centers in the area centralis is fixed shortly after eye opening (3 weeks). Subsequent decrease in angular subtense is attributable primarily to the increased posterior nodal distance[19, 45, 46]. The relationship of the linear extent of ganglion cell receptive fields to visual angle is not known in humans. However, relationship of pattern-reversal elicited electroretinograms to pattern size in 3.5-month-old infants is more similar to that of adults than VEPs, suggesting ganglion cell receptive fields in infants and adults subtend more similar visual angles than do cortical receptive fields[40].

Much of the improvement in visual acuity observed during the first few months of life may be attributed to retinal development.

Total retinal area increases postnatally, but mitosis ceases in any retinal area as the rods and cones appear, so after birth there are no new retinal cells [31]. Therefore, if the density of central receptors is increasing and the total number of cells is constant, as retinal area is increasing, one would predict a decrease in peripheral receptor density and an increase in the linear extent of peripheral receptive fields. The time course of the development of adult-like peripheral receptive fields may be much longer than for the central retinal receptive fields responsible for acuity. After the first few months the greatest changes in visual function may be in the periphery possibly accounting for the increased extent of visual fields in older infants[55].

Central neural development

Mature retinal function is a necessary but insufficient condition for the development of adult-like visual acuity. Mature cortical function is also required.

Of the little quantitative information available on the development of the human cortex, the most comprehensive source is the work of Conel[11, 14, 54]. At birth, the visual cortex and other visual areas vary greatly in relative maturity with A17 being the most mature, and relative maturity declining with more anterior location. During the first year, the order of relative maturity remains A17, A18, A19, A21, and A8[11]. Ablation studies indicate that A17 is the locus of fine pattern vision[7, 36]. Development of human A17 is particularly rapid in the first six months, both in changes in the thickness of cellular layers[11] and increased numbers of dendritic processes[54]. The changes during the first half year of life coincide with a period of rapid improvement in optical quality, retinal development and improvements in acuity.

In cats, the high spatial frequency cut-off (acuity) of 1) central retinal ganglion x-cells[26]; 2), central, LGN x-cells[26]; 3) visually evoked potential (VEP) estimated acuity[15]; and 4) behaviorally assessed acuity[37] are roughly parallel in their development, approaching

adult levels at roughly 12 weeks. In humans, there appears to be a dissociation between the ages at which adult, normal acuity is reached depending on the measure. Most VEP estimates of visual acuity indicate normal adult acuity is reached at about six months[12, 32, 49, 50] while it is not reached until several years of age using behavioral tasks[13, 34]. The differences in visual acuity development assessed electrophysiologically or behaviorally may reflect: 1) the different criteria employed to determine acuity[13, 49], 2) the use of a pattern preference criterion which underestimates the discriminative capacities of infants[27] or 3) that different neural mechanisms are being assessed using behavioral and electrophysiological tests.

Several lines of evidence provide indirect support of the third possibility. The retina[31] and the LGN parvocellular layers[20, 24, 32, 49, 50] mature at about six months of age, about the same time that VEP acuity is adult-like; the LGN magnocellular layers mature at 2–3 years[13, 24, 34], about the same time as preferential looking indicates adult-like acuity. The functional significance of these two LGN divisions is unclear. They may represent x- and y-cell segregation[24, 29, 44, 53] or they may represent segregation of cells responsive to color contrast from those responsive to luminance contrast[47].

Several authors attribute differential development of infant visual behaviors during early life to differential development of neural subsystems[10, 33]. In addition to direct x- and y-cell pathways which pass through the LGN to A17, an indirect y-cell pathway passes through the superior colliculus and pulvinar on its way to the cortex[29, 44, 53]. Also, there are strong interconnections between A18, A19 and A21 and these subcortical structures[29, 44, 53]. The relative immaturity of A18, A19, and A21 compared to A17 suggests that those visual functions controlled by those cortical areas would be delayed in their development relative to striate cortical acuity[10, 33].

Indirect evidence of a differential maturation of different neural subsystems is provided by VEPs. An early component of the VEP is unrelated to infants visual attention for different spatial frequencies at less then 45 days of age but is related at two months and older. Conversely a later component which is highly correlated with preferences at two months and less is unrelated to infants preferences at older ages[21, 25, 27]. A related observation is that an evoked potential component (CII) elicited by pattern appearance which, presumably, originate in A18 or A19[25, 52] is absent in young infants. When these later developing pattern-appearance elicited VEP components are used to estimate visual acuity development, the relationship between the VEP and behavioral acuity is much closer[12].

Acknowledgment. This research was supported by NIH grant EY03781. Reprint requests to Dr J. Vernon Odom, Morgantown.

1 Abramov, I., Gordon, J., and Hendrickson, A., Postnatal development of the infant retina. Invest. Ophthal. vis. Sci. suppl. *20* (1981) 46.
2 Atkinson, J., Braddick, O., and French, J., Infant astigmatism: its disappearance with age. Vision Res. *20* (1980) 891–893.
3 Atkinson, J., and French, J., Astigmatism and orientation preference in human infants. Vision Res. *19* (1979) 1315–1317.
4 Banks, M.S., Infant refraction and accommodation. Int. Ophthal. Clin. *20* (1980) 205–232.
5 Banks, M.S., The development of visual accommodation during early infancy. Child Dev. *51* (1980) 646–666.
6 Beazley, L.D., O'Connor, W.M., and Illingworth, D.J., Adult levels of anisotropy and contrast threshold in 5-year-olds. Vision Res. *22* (1982) 135–138.
7 Berkley, M.A., and Sprague, J.M., Striate cortex and visual acuity functions in the cat. J. comp. Neurol. *187* (1979) 679–702.
8 Blomdahl, S.S., Ultrasonic measurements of the eye in the newborn infant. Acta ophthal. *49* (1979) 1048–1059.
9 Boettner, E.A., and Walter, J.R., Transmission of the ocular media. Technical Documentary Report No. MRL-TDR-62-34. Wright-Patterson Air Force Base, 1962.
10 Bronson, G., The postnatal growth of visual capacity. Child Dev. *45* (1974) 873–890.
11 Conel, J.L., The Postnatal Development of the Human Cerebral Cortex, vols. 1–8. Harvard University Press, Cambridge 1939–1963.
12 De Vries-Khoe, L.H., and Spekreijse, H., Maturation of luminance and pattern EPs in man. Doc. ophthal. Proc. Ser. *31* (1982) 461–475.
13 Dobson, V., and Teller, D.Y., Visual acuity in human infants: a review and comparison of behavioral and electrophysiological studies. Vision Res. *18* (1978) 1469–1483.
14 Eichorn, D.H., Biological correlates of behavior, in: Child Psychology, part 1. Ed. H.W. Stevenson. 63rd Yearbook of the National Society for the Study of Education. University of Chicago Press, Chicago 1963.
15 Freeman, D.N., and Marg, E., Visual acuity development coincides with the sensitive period in the kitten. Nature *254* (1975) 614–615.
16 Friendly, D.S., Preschool visual acuity screening tests. Trans. Am. ophthal. Soc. *76* (1978) 383–480.
17 Green, D.G., Powers, M.K., and Banks, M.S., Depth of focus, eye size and visual acuity. Vision Res. *20* (1980) 827–835.
18 Gwiazda, J., Brill, S., Mohindra, I., and Held, R., Infant visual acuity and its meridional variation. Vision Res. *18* (1978) 1557–1564.
19 Hamasaki, D.I., and Sutija, V.G., Development of x- and y-cells in kittens. Exp. Brain Res. *35* (1979) 9–23.
20 Harter, M.R., Deaton, F.K., and Odom, J.V., Pattern visual evoked potentials in infants, in: Visual Evoked Potentials in Man: New Developments, p. 332–352. Ed. J.E. Desmedt. Clarendon Press, Oxford 1977.
21 Harter, M.R., Deaton, F.K., and Odom, J.V., Maturation of evoked potentials and visual preference in 6–45-day-old infants: Effects of check-size, visual acuity, and refractive error. EEG clin. Neurophysiol. *42* (1977) 595–607.
22 Haynes, H.M., White, B.L., and Held, R., Visual accommodation in human infants. Science *148* (1965) 528–530.
23 Hendrickson, A., and Kupfer, C., The histogenesis of the fovea in the macaque monkey. Invest. Ophthal. vis. Sci. *15* (1976) 746–756.
24 Hickey, T.L., Postnatal development of the human lateral geniculate nucleus: Relationship to a critical period for the visual system. Science *198* (1977) 836–838.
25 Hoffmann, R.F., Developmental changes in human infant visual-evoked potentials to patterned stimuli recorded at different scalp locations. Child Dev. *49* (1978) 110–118.
26 Ikeda, H., Visual acuity, its development and amblyopia. R. Soc. Med. *73* (1980) 546–555.
27 Karmel, B.Z., and Maisel, E.B., A neuronal activity model for infant visual attention, in: Infant Perception: From Sensation to Cognition, vol. I: Basic Visual Processes, pp. 78–131. Eds L.B. Cohen and P. Salapatek. Academic Press, New York 1975.
28 Larsen, J.S., The sagittal growth of the eye. IV: Ultrasonic Measurement of the axial length of the eye from birth to puberty. Acta ophthal. *49* (1971) 873–886.
29 Lennie, P., Parallel visual pathways: A review. Vision Res. *20* (1980) 562–594.
30 Lotmar, W., A theoretical model for the eye of new-born infants. Albrecht v. Graefes Arch. klin. exp. Ophthal. *198* (1976) 179–185.

31 Mann, I., The Development of the Human Eye, 3rd ed. Grune and Stratton, New York 1964.
32 Marg, E., Freeman, D.N., and Peltzman, P., Visual acuity development in human infants: Evoked potential measurements. Invest. Ophthal. *15* (1976) 150–153.
33 Maurer, D.T., and Lewis, T.L., A physiological explanation of infants' early visual development. Can. J. Psychol. *33* (1979) 232–252.
34 Mayer, D.L. and Dobson, V., Visual acuity development in infants and young children as assessed by operant preferential looking. Vision Res., in press.
35 Mayer, M.J., Development of anisotropy in late childhood. Vision Res. *11* (1977) 703–710.
36 Miller, M., Pasik, P., and Pasik, T., Extrageniculostriate vision in the monkey, VII Contrast sensitivity functions. J. Neurophysiol. *43* (1980) 1510–1526.
37 Mitchell, E.D., Griffin, F., Wilkinson, F., Anderson, P., and Smith, M.L., Visual resolution in young kittens. Vision Res. *16* (1976) 363–366.
38 Mohindra, I., and Held, R., Refraction in humans from birth to five years. Doc. ophthal. Proc. Ser. *28* (1981) 19–27.
39 Mohindra, I., Held, R., Gwiazda, J., and Brill, S., Astigmatism in infants. Science *202* (1978) 329–331.
40 Odom, J.V., Maida, T., Dawson, W.W., and Romano, P., Human pattern-evoked retinal and cortical potentials: spatial tuning and development, in: Evoked Potentials II. Eds. R.H. Nodar and C. Barber. Butterworth Publ., Stoneham, Massachusetts, in press.
41 Oesterberg, G., Topography of the layer of rods and cones in the human retina. Acta ophthal. suppl. *6* (1935) 1–102.
42 Powers, M.K., and Dobson, V., Effects of focus on visual acuity in human infants. Vision Res. *22* (1982) 521–528.
43 Riggs, L.A., Visual acuity, in: Vision and Visual Perception, pp. 321–349. Ed. C.H. Graham. Wiley and Sons, New York 1965.
44 Rodieck, R.W., Visual pathways. A. Rev. Neurosci. *2* (1979) 193–225.
45 Rusoff, A.C., Development of ganglion cells in the retina of the cat, in: Developmental Neurobiology of Vision, pp. 19–30. Ed. R.D. Freeman. Plenum Press, New York 1979.
46 Rusoff, A.C., and Dubin, M.W., Development of receptive-field properties of retinal ganglion cells in kittens. J. Neurophysiol. *40* (1977) 1188–1198.
47 Shapley, R.M., Kapan, E., and Soodak, R.E., Spatial summation and contrast sensitivity of x and y cells in the lateral geniculate nucleus of the macaque. Nature *292* (1981) 543–545.
48 Slater, A.M., and Findlay, J.M., Binocular fixation in the newborn baby. J. exp. Child Psychol. *20* (1975) 248–273.
49 Sokol, S., Measurement of infant visual acuity from pattern reversal evoked potentials. Vision Res. *18* (1978) 33–39.
50 Sokol, S., and Dobson, V., Pattern reversal visually evoked potentials in infants. Invest. Ophthal. vis. Sci. *15* (1976) 58–62.
51 Sorsky, A., Benjamin, B., and Sheridan, M., Refraction and its components during the growth of the eye from the age of three. Medical Research Council Special Report Series 301. Her Majesty's Stationery Office, London 1961.
52 Spekreijse, H., Maturation of contrast EPs and development of visual resolution. Archs. ital. Biol. *116* (1978) 358–369.
53 Stone, J., Parallel processing in the visual system: The classification of retinal ganglion cells and its impact on the neurobiology of vision. Plenum Press, New York, 1983.
54 Takashima, S., Chan, F., Becker, L.E., et al., Morphology of the developing visual cortex of the human infant. J. Neuropath. exp. Neurol. *39* (1980) 487–501.
55 Tronick, E., Stimulus control and the growth of the infant's effective visual field. Percept. Psychophys. *11* (1972) 373–376.
56 Westheimer, G., Visual acuity. A. Rev. Psychol. *16* (1965) 359–380.

0014-4754/84/111178-04$1.50 + 0.20/0

Have we underestimated the importance of the thymus in man?

by M.D. Kendall

Department of Anatomy, St. Thomas's Hospital Medical School, Lambeth Palace Road, London SE1 7EH (England)

Summary. Recent immunological research has concentrated on the complex and subtle interactions between T cells, B cells and accessory cells. In these studies, little attention has been given to the adult thymus gland. Modern textbooks of disease and anatomy all stress that the gland undergoes fatty involution with age in man but omit reference to the statements here and there in the literature that the gland is active and produces lymphocytes throughout life. To suggest that the bone marrow, which also builds up fat throughout life, is atrophic and not important to adult man would deny all modern hematological concepts. Yet few people today take a parallel view of the thymus except perhaps those investigating aging and thymic hormones. In both of these areas of research it is obvious that the thymus must be active throughout life for continued good health.
This brief review urges that a thorough understanding of the vital importance of the thymus in adult life is now needed. From it could emerge a new philosophy on the treatment of immune diseases in both the young (SCID and AIDS patients) and in the aged (autoimmune conditions and cancers) and it would aid our treatment of patients recovering from illnesses and from many drug treatments.
Key words. Thymus; thymic hormones; thymic atrophy.

The current awareness of the central role of the immune system to healthy life has been endorsed by the increased prevalence in the young of SCID (Severe Combined Immunodeficiency Disease), AIDS (Acquired Immune Deficiency Syndrome) and the great incidence of infectious diseases, autoimmune conditions and cancers in the aged[81] now that life expectancy has risen.

In all of the above conditions, the functional capacity of the T cells, and hence of the B cells, appears crucial to the course of the diseases. It is surprising, therefore, that so little attention is paid in adult man to the organ that produces the T cells of the body. Earlier research into thymic size and activity has resulted in most current textbooks dismissing the thymus as an atrophic or-