THE CLASSIFICATION OF AMBLYOPIA ON THE BASIS OF VISUAL AND OCULOMOTOR PERFORMANCE*

BY *Suzanne P. McKee,* PhD (BY INVITATION), *Clifton M. Schor,* OD, PhD (BY INVITATION), *Scott B. Steinman,* OD, PhD (BY INVITATION), *Nance Wilson,* BA (BY INVITATION), *Gary G. Koch,* PhD (BY INVITATION), *Sonia M. Davis,* MS (BY INVITATION), *Charlene Hsu-Winges,* MD (BY INVITATION), *Susan H. Day,* MD (BY INVITATION), *Christine L. Chan,* OD (BY INVITATION), *J. Anthony Movshon,* PhD (BY INVITATION), *Merton C. Flom,* OD, PhD (BY INVITATION), *Dennis M. Levi,* OD, PhD (BY INVITATION), AND *John T. Flynn,* MD

INTRODUCTION

AMBLYOPIA IS MOST SIMPLY DEFINED AS A LOSS OF VISUAL ACUITY WITHout an identified organic cause.[1] Traditionally, the amblyope is classified as strabismic, anisometropic, refractive, or deprivational according to the accompanying conditions thought to be responsible for the acuity loss.[2,3] Although it is widely recognized that these classes are neither particularly uniform nor discriminative, there is no established means of classifying amblyopia on the basis of visual function alone. Our primary objective was to create a classification system for amblyopia based on a broad spectrum of clinical, psychophysical, and oculomotor abnormalities—a system that could supplement or perhaps supplant the traditional approach leading to better diagnosis and treatment. We report here the results from a *pilot* study showing that this objective is feasible.

*From the Smith-Kettlewell Eye Research Institute, Berkeley; University of California, Berkeley; University of Missouri, St Louis; University of North Carolina, Chapel Hill; Kaiser Permanente, Northern California; New York University; University of Houston; Bascom Palmer Eye Institute, University of Miami School of Medicine. Supported in part by National Eye Institute grant U10-EYO7657.

The limited goals of this preliminary feasibility study were to determine whether (1) an experimental system could be designed and constructed that would be suitable for testing a large number of naive amblyopic and normal subjects, (2) a single study center would be able to recruit enough cooperative amblyopic subjects to produce a substantial number of statistically defined categories to be generated by cluster analysis[4,5] of psychophysical and oculomotor data, and (3) these categories would not be redundant with traditional clinical measures (eg, Snellen visual acuity, strabismic diagnosis).

We report the results from a pilot study showing that these objectives are attainable.

MATERIALS AND METHODS

POPULATION

Two hundred fifteen naive subjects between the ages of 8 and 35 years, including 82 amblyopes, 73 recovered amblyopes, 40 nonamblyopic strabismic or anisometropic ("at risk") subjects, and 20 normal subjects, participated in this study (Table I).

TABLE I: STUDY POPULATION

CONDITION	DIAGNOSIS				TOTAL
	AMBLYOPIC	"AT RISK"	RECOVERED	NORMAL	
Normal	0	0	0	20	20
Strabismic	38	25	49	0	112
Anisometropic (pure)	33	11	13	0	57
Refractive	2	4	8	0	14
Deprivational	6	0	2	0	8
Other	3	0	1	0	4
Total	82	40	73	20	215

DEFINITIONS

For purposes of this study, an *amblyope* was considered to be anyone with best corrected Snellen visual acuity worse than or equal to 20/40 in one or both eyes. *Recovered* amblyopes were subjects with a history of, or prior treatment for, amblyopia (eg, patching therapy) who currently had a visual acuity of better than 20/40 in each of their eyes. *Anisometropia* was defined as a difference of 1 diopter (D) or greater between the refraction of the two eyes. *High refractive errors* were defined as greater than 4 D of hyperopia, myopia, or astigmatism. Subjects were designated *at risk* if

the visual acuity in each of their eyes was better than 20/40 and they had never been treated for amblyopia, but were suffering from one of the conditions commonly associated with amblyopia (eg, strabismus, anisometropia). *Control* subjects had acuities of better than 20/40 in both eyes, no prior treatment for amblyopia, and none of the conditions associated with amblyopia. Subjects were assigned to only one associated condition according to the following hierarchy: deprivational, strabismic, anisometropic, refractive, or normal.

CLINICAL EXAMINATION

Each subject was given a thorough clinical examination[6,7,8] before the laboratory measurements were done. In addition to standard measures of acuity (Snellen chart) and refraction, tests of ocular alignment, fixation behavior, and binocular functioning were included in the clinical protocol (Appendix). The clinicians used the results of their examination plus the prior history to specify a diagnosis (amblyopic, recovered, "at risk," or normal) and an associated condition (strabismus, anisometropia, large refractive error, or deprivation).

LABORATORY MEASUREMENTS

We selected the laboratory tests according to three criteria:

- The presence of a significant body of data demonstrating abnormal performance in amblyopia,
- The existence of models of the physiological factors limiting test performance, and
- The feasibility of using the proposed test on a large number of naive subjects.

Thus, measures of color vision and flicker were excluded because there is little evidence of abnormality in amblyopia. Similarly, measures of cognitive functioning were excluded, since there is no widely accepted model of their physiologic basis. Measures of the entire contrast sensitivity function and peripheral acuity function were excluded because the time available for testing each subject did not permit such extensive measurements.

The selected test battery included the following tests:

1. Two measurements of *visual acuity*: letter acuity measured with the Log-MAR chart[9] and grating acuity measured with a sinusoidally varying luminance pattern.[10,11]

2. Two measures of *contrast sensitivity*: the lowest contrast letters correctly identified on a Pelli-Robson chart[12] and the minimum contrast required to detect a luminous edge.[13]

3. Two measures of *hyperacuity*: vernier acuity for a repetitive pattern of offset bars[14] and horizontal and vertical bisection acuity for three small, bright squares.[15]

4. Three measures of *oculomotor performance*: OKN velocity for a 0.8 cycles-per-degree grating moving at 11 degrees per second,[16] pursuit velocity for a large cross moving at 3 degrees per second,[17] and latencies and amplitudes for 3-degree horizontal and vertical saccades.[18]

5. A binocular summation test, originally included in the battery, proved too difficult for naive subjects. A recently developed test of motion, binocularly sensed,[19] has been substituted and the subjects tested since the pilot study, but was not tested on the pilot subjects themselves.

STATISTICAL ANALYSIS

Cluster analysis[4,5] is a statistical method for grouping together subjects who perform similarly on a variety of measurements; it identifies those individuals in a pool who share sufficiently many common characteristics, as measured by the laboratory variables, that they form a cluster is significantly different from other such clusters.

Approximately 50 laboratory variables were available for analysis, including measures of central tendency and variability. Only results from the weaker eye, as defined by Snellen acuity, were used.

Each subject was ranked on every variable, and their ranks served as the basis of the analysis. The 50 rankings were reduced to 12 summary variables; each summary variable is an average of a set of highly correlated variables, determined by factor analysis.[20] The summary variables have the advantages of reducing within-subject variability and allowing a less computationally intensive analysis: an appropriate strategy for our pilot data. The 12 summary variables are: Pelli-Robson contrast sensitivity, hyperacuity thresholds, and means and standard deviations of OKN, pursuit, saccadic amplitude and latency, edge contrast threshold, and grating acuity (cycles per degree).

Cluster analysis was then performed on the summary variables using the average density method.[21] Seventeen clusters were identified as groups of subjects that were significantly different from their nearest neighbor group, based on a pseudo t^2 test.[23] A tree diagram of the clusters is depicted in Fig 1.

Eight clusters, containing eight or fewer subjects each, were merged with larger clusters to which they were most likely to belong, via prediction from linear and logistic regression.[24] This resulted in a final nine

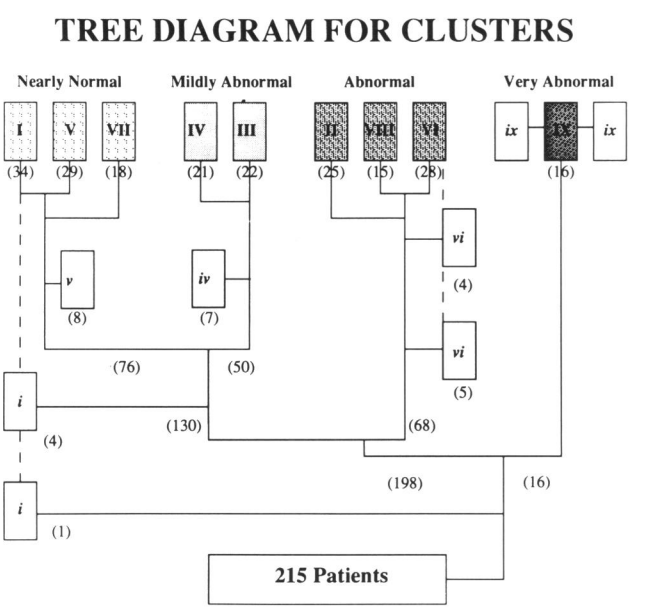


FIGURE 1
Tree diagram of clusters defined by statistical analysis.

clusters. Linear and logistic regression determined that cluster membership expressed more variation between subjects than could be explained by clinical diagnosis, associated condition, and visual acuity.

RESULTS

After the nine clusters had been defined by statistical analysis of the laboratory measurements, the membership of each cluster was examined post hoc to determine how many normal, "at risk," recovered, and amblyopic subjects were in each cluster (Fig 2), and what their associated conditions were (Fig 3). Most of the clusters contained some subjects from every diagnostic category and associated condition. There were no purely anisometropic, purely strabismic, or purely deprivational clusters. Similarly, there were no clusters that contained only amblyopes, because some recovered amblyopes and "at risk" subjects have some of the same visual or oculomotor deficiencies as amblyopes. There were also no clusters that contained only normal subjects, because, again, some recovered amblyopes and "at risk" subjects shared some visual and oculomotor characteristics with normal.

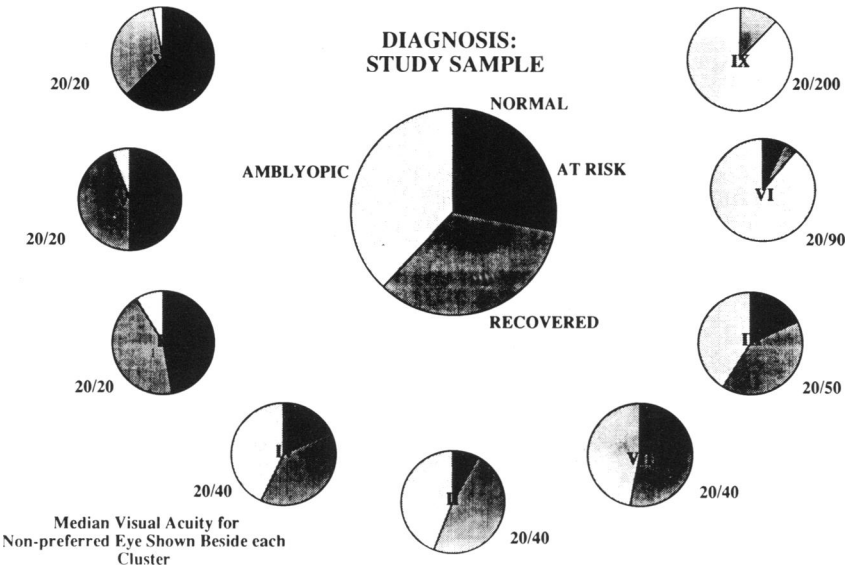


FIGURE 2
Division of clusters according to diagnosis: normal, "at risk," recovered, and amblyopic subjects.

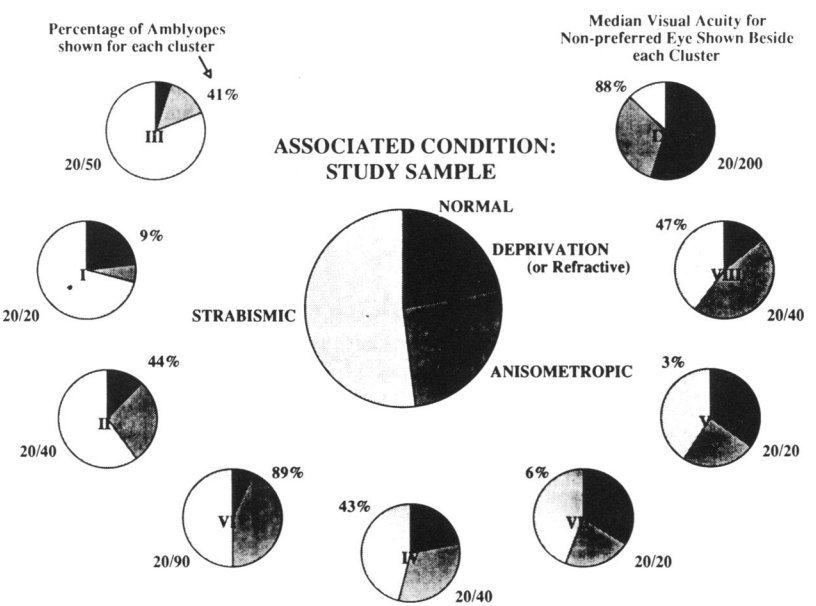


FIGURE 3
Breakdown of clusters according to associated condition: normal, deprivation, anisometropia, strabismic.

Nevertheless, on the basis of their median Snellen acuity (20/20 or better in both eyes), three of the nine clusters (1, 5, and 7) could be termed normal. Each of these three clusters contained a very tiny proportion of amblyopes as well as a higher proportion of normal control subjects than our sample as a whole. The characteristics of one of these "normal" clusters are quite instructive (Fig 4). The defining variables for this cluster were elevated hyperacuity thresholds (compared with normal) and a marked nasal-to-temporal asymmetry in OKN velocities. In short, this cluster was not truly normal; it contained a sizable number of recovered amblyopes and "at risk" subjects whose visual function showed residual anomalies. The associated conditions for this cluster are shown in Fig 4; the *black bar* reflects the proportion of subject in the sample as a whole, and the *hatched bar* shows the composition of this cluster. This cluster is slightly more strabismic (about 70%) than the sample as a whole, but the other two "normal" clusters also contained a sizable proportion of strabismics (about 40%), and their defining variables, on average, were distinctly normal on every measured dimension. Thus, associated condition is not generally a good predictor of cluster membership.

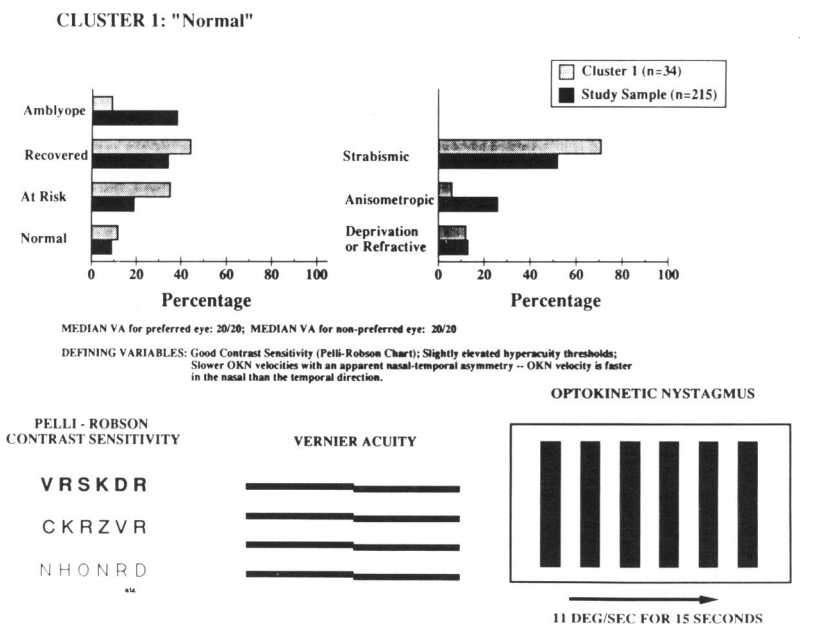


FIGURE 4
Characteristics of "normal" cluster (cluster 1).

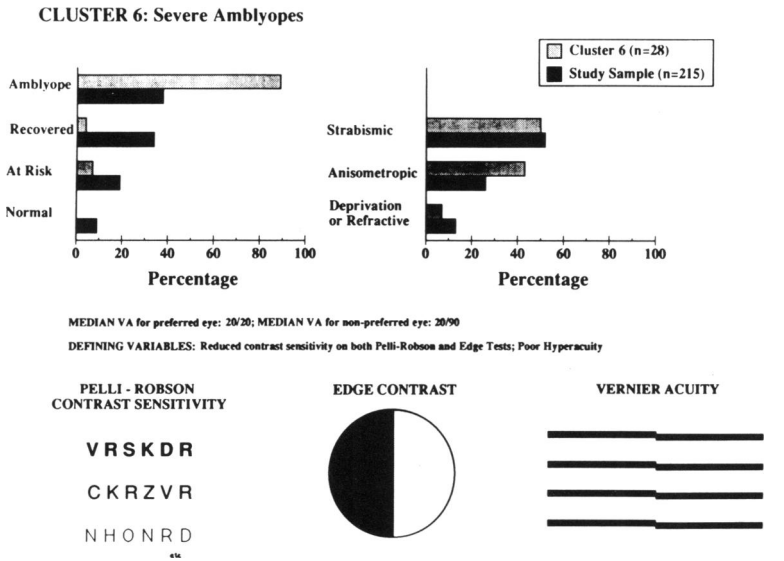


FIGURE 5
Characteristics of "strongly abnormal" cluster (cluster 6). This cluster was defined by visual abnormalities.

Two of the clusters (6 and 9) were "strongly abnormal": median acuity of the weaker eye was 20/90 in cluster 6 and 20/200 in cluster 9) (Figs 5 and 6). Three fourths of the subjects in both of these clusters were amblyopes, and the remainder were either in the recovered or "at risk" categories. Interestingly, one of these very abnormal clusters was defined by visual abnormalities (poor contrast sensitivity and poor hyperacuity) (Fig 5), and the other by oculomotor abnormalities (slow and highly variable OKN, highly variable pursuit) (Fig 6). The associated conditions for the clusters are shown in the figures. Clearly, one of these clusters, defined by sensory abnormalities, contains many strabismic and anisometropic amblyopes, and the other, defined by oculomotor abnormalities, is dominated by deprivation amblyopes.

The median visual acuity of the weaker eye in the remaining four clusters was 20/40 to 20/50, the range associated with mild to moderate amblyopia. Each of these clusters was defined by a different mixture of laboratory variables. For example, in one cluster, good contrast sensitivity, as measured by the edge and Pelli-Robson tests, was coupled with slightly impaired grating acuity and very slow pursuit velocities. Not all "bad things" go together!

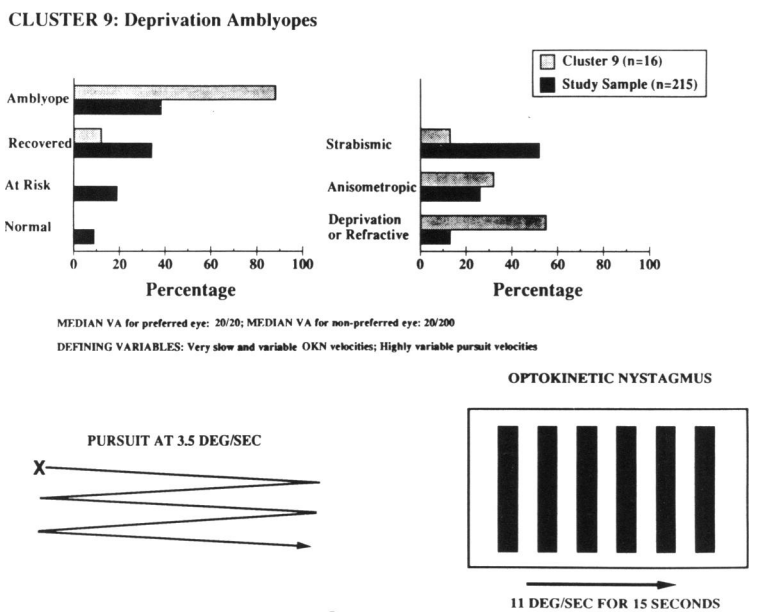


FIGURE 6
Characteristics of "strongly abnormal" cluster (cluster 9). This cluster was defined by oculomotor abnormalities.

Finally, stepwise linear regression models were also run, allowing Snellen visual acuity and clinical diagnostic categories and associated conditions to be predictors in addition to the 12 grouped laboratory variables. Generally, they were found *not* to be significant predictors after the laboratory variables were controlled for. As a test of cluster validity, discriminant analysis was conducted on the nine clusters; it grouped subjects into their correct clusters 63% of the time.

DISCUSSION

These results are examined from two standpoints: (1) what the clusters tell us thus far and (2) what promising leads are to be followed up in the full-scale study.

The results of this pilot study indicate that there may be a rationale for diagnosing amblyopia on the basis of functional visual loss instead of the traditional classification scheme based on associated condition (eg, strabismus, anisometropia, deprivation).

Though not apparent at this time, these clusters, or some derivative of

them that emerges as the study progresses, may provide new and useful insights into the pathogenesis of amblyopia that our current clinical classification system does not.

In addition to the patient history and diagnosis, the clinical protocol contains a number of clinical tests that are commonly used to detect suppression, eccentric fixation, angle of deviation, and other items useful in a complete ophthalmologic examination of amblyopia. These tests were used by the clinicians to assess clinical diagnosis and associated condition, but they can also be used as separate variables in defining the clusters. They have not yet been incorporated into the statistical analysis. One of the difficulties is that many of the measurements are not continuous, so the subjects cannot be ranked. The few measurements that are continuous, such as the difference in refractive power of the eye in anisometropia, will be used as cluster predictors (like clinical diagnosis or Snellen acuity) to determine if the laboratory variables account for all sources of variances associated with these clinical measurements. Categorical measurements (eg, suppression [yes or no], type of therapy) can be used retrospectively to identify the medical characteristics of the nine clusters. For example, are the amblyopes with suppression, found in different clusters from those without suppression?

It should be emphasized in considering these results that they preliminary. On completion of the larger study of some 500 amblyopic, recovered, "at risk," and normal subjects (now under way), with use of the best measuring techniques developed during this pilot, we should have a clearer picture of the pattern of functional abnormalities associated with each cluster.

What are some of the questions that can be addressed by the full scale study?

Many studies[24-29] have suggested that strabismic amblyopes and purely anisometropic (without accompanying strabismus) amblyopes have different visual losses. In particular, some studies have found that strabismic amblyopes have much worse hyperacuity thresholds than anisometropic amblyopes. Other studies have noted significant spatial biases in the hyperacuity responses of strabismic amblyopes compared with anisometropic amblyopes. The full-scale study will permit comparison of the hyperacuity measurements for these two classes of amblyope. What differences persist between the two classes if they are initially matched for grating acuity and for contrast sensitivity?

Is the better eye of the amblyopic observer really "normal"? A comparison of the best eye of the normal subjects with the best eye of the amblyopic subjects on the psychophysical variables, as well as the ocu-

lomotor variables, is well within the power of this study. Our pilot study indicated that there were no significant differences, but a more definitive answer will emerge from the main study. These are but a few of the many issues that can be explored in depth with a large-scale study of amblyopia.

The long-term goals of this study, identified at its conception, remain to provide probes into amblyopia as it develops among the infant, toddler, or child. The tests that are used in this study are amenable, with modification, to be employed as diagnostic tools in the evaluation of preverbal and early verbal children. By providing insights into which visual behaviors—sensory or motor or both—provide the basis of membership in a given cluster, we may, in fact, be identifying functions lost or impaired together during visual development.[30]

REFERENCES

1. Parks MM: *Ocular Motility and Strabismus*. New York, Harper & Row, 1975, pp 85-91.
2. Burian HM, von Noorden GK: *Binocular Vision and Ocular Motility*. St Louis, CV Mosby, 1974, p 219.
3. American Academy of Ophthalmology Basic & Clinical Science Course. Section VI: *Binocular Vision and Ocular Motility*. San Francisco, American Academy of Ophthalmology, 1984, p 49.
4. SAS Institute Inc: *SAS/STAT User's Guide, Version 6*, 4th ed, Vol 1 and 2. Cary, NC, SAS Institute Inc, 1989.
5. Everitt BS: *Cluster Analysis*. 2nd ed, London, Heineman Education Books Ltd, 1980.
6. American Academy of Ophthalmology Basic & Clinical Science Course. Section VI: *Binocular Vision and Ocular Motility*. San Francisco, American Academy of Ophthalmology, 1984, pp 51-53.
7. Duke-Elder S, Wybar K: Ocular motility and strabismus, in *System of Ophthalmology, Vol 6*. St Louis, CV Mosby, 1973, pp 295-301.
8. Parks MM: *Ocular Motility and Strabismus*. New York, Harper & Row, 1975, pp 85-91.
9. Early treatment. Diabetic Retinopathy Study (ETDRS) Manual of Procedure.
10. Gestalder RJ, Green DG: Laser interfero metric acuity in amblyopia. *J Pediatr Ophthalmol Strabismus* 1971; 8:251-256.
11. Levi DM, Harwerth RS: Spatio-temporal interactions in anisometropic and strabismic amblyopia. *Invest Ophthalmol Vis Sci* 1977; 16:90-95.
12. Pelli DG, Robson JG, Wilkins AJ: The design of a new letter chart for measuring contrast sensitivity. *Clin Vis Sci* 1988; 2:187-199.
13. Levi DM, Harwerth RS, Pass AF, et al: Edge-sensitivity mechanisms in humans with abnormal visual experience. *Exp Brain Res* 1981; 43:270-280.
14. Levi DM, Klein S: Differences in vernier discrimination for gratings between strabismic and anisometropic amblyopes. *Invest Ophthalmol Vis Sci* 1982; 23:398-407.
15. Bedell HE, Flom MC, Barbeito R: Spatial aberrations and acuity in strabismus and amblyopia. *Invest Ophthalmol Vis Sci* 1985; 26:909-916.
16. Schor CM: A directional impairment of eye movement control in strabismus amblyopia. *Invest Ophthalmol* 1971; 14:692-697.
17. Schor CM, Hallmark KW: Slow control of eye position in strabismic amblyopia. *Invest Ophthalmol Vis Sci* 1980; 19:668-683.
18. Schor CM, Levi DM: Disturbances of small field horizontal and vertical OKN in amblyopia. *Invest Ophthalmol Vis Sci* 1980; 19:668-683.
19. Shadlen M, Carney T: Mechanisms of human motion perception revealed by a new cyclopean illusion. *Science* 1986; 232:95-97.

20. Sokal RR, Michener CD: A statistical method for evaluating systematic relationships. *Univ Kansas Sci Bull* 19??; 38:1409-1438.
21. Milligan GW, Cooper MC: An examination of procedure for determining the number of clusters in a data set. *Psychometrika* 1985; 50:159-179.
22. Kleinbaum DG, Kupper LI, Muller KE: *Applied Regression Analysis and Other Multivariable Methods*. 2nd ed, Boston, PWS-Kent, 1988.
23. Hosmer DW, Lemeshow S: *Applied Logistic Regression*. New York, John Wiley & Sons, 1989.
24. Levi DM, Klein SA: Vernier acuity, crowding and amblyopia. *Vision Res* 1983; 23:1005-1017.
25. Hess RF, Baker CL: Assessment of retinal function in severely amblyopic individuals. *Vision Res* 1989; 24:1367-1376.
26. Hess RF, Campbell FW, Greenhalgh T: On the nature of the neural abnormal in human amblyopia: Neural aberrations and neural sensitivity loss. *Pflugers Arch* 1978; 377:201-207.
27. Levi DM, Carkeet A: Amblyopia: A consequence of abnormal visual development, in K Simons (ed): *Infant Vision: Basic and Clinical Research*. Committee on Vision, Commission on Behavior and Social Sciences and Education, National Research Council. New York, Oxford University Press. In Press.
28. Flynn JT: Amblyopia revisited. *J Pediatr Ophthalmol Strabismus* 1991; 28:183-201.
29. Steinman SB, Levi DM, McKee SP: Discrimination of time and velocity in the amblyopic visual system. *Clin Vis Sci* 1988; 2:226-276.
30. Levi DM: The "spatial grain" of the amblyopic visual system. *Am J Optom Physiol Optics* 1988; 65:767-786.

APPENDIX

PATIENT BACKGROUND DATA

Patient Number _____ Location of psychophysical test _____

Patient Name _____

Age _____ If under 18, see *Parent or Guardian*
Kaiser medical record # _____
Address _____
_____

Day Phone _____ Day phone is: ☐ Mother's
Evening Phone _____ ☐ Father's
Time to call _____ ☐ Patient's
☐ Other _____

Referring Doctor

Name _____
Address _____
Telephone _____
Date of first exam on record with this Doctor _____

Examining Doctor

Name _____
Date of this exam _____

Parent or Guardian

Name _____
Relationship _____

PATIENT HISTORY

Patient Number _____

Patient Name _____

Presenting Diagnosis

Current diagnosis the patient has been told he or she has.

Check one of the following diagnoses:
- ☐ 1 = Amblyopic
- ☐ 2 = Normal (no amblyopia)
- ☐ 3 = Unable to specify
- ☐ 4 = No information

Check all conditions that apply:
- ☐ Strabismic
- ☐ Anisometric
- ☐ Refractive
- ☐ Deprivational
- ☐ Other _____

Date of Birth: _____

Pregnancy and Delivery Complications:
- ☐ 0 = no information
- ☐ 1 = none
- ☐ 2 = positive (specify) _____

Birth Weight _____ pounds, _____ ounces. (Best guess is OK)

Apgar: _____ (1 min)
_____ (5 min)

Cerebral Palsy:
- ☐ 0 = no information
- ☐ 1 = none
- ☐ 2 = positive (specify) _____

Seizures:
- ☐ 0 = no information
- ☐ 1 = none
- ☐ 2 = positive

If positive, check all that apply:
- ☐ Febrile
- ☐ Ongoing
- ☐ On medication

Other Growth and Developmental Abnormalities:
- ☐ 0 = no information
- ☐ 1 = none
- ☐ 2 = positive (specify) _____

Race:
- ☐ 0 = no information
- ☐ 1 = white
- ☐ 2 = black
- ☐ 3 = hispanic
- ☐ 4 = asian
- ☐ 5 = other

Sex:
- ☐ 0 = no information
- ☐ 1 = female
- ☐ 2 = male

Family History

For parents, check applicable boxes.
For siblings, specify number that apply (excluding patient).

Relative	Don't know	Surgery	Strabismus	Amblyopia	Glasses	Other (specify below)
Mother						
Father						
# of siblings						

Total Number of Siblings (excluding patient): _____

Any other comments on family history:

Age of onset of signs/symptoms _____ months. (Best guess is OK)
☐ Check if not applicable.

Prior Treatment for Amblyopia:
☐ 0 = no information
☐ 1 = none
☐ 2 = positive

Ocular Therapy History: (check all that apply)

Rx for Amblyopia	Rx for other reasons	
☐	☐	No information
☐	☐	None
☐	☐	Patch
☐	☐	Glasses
☐	☐	Atropine Penalization
☐	☐	Pleoptics
☐	☐	Opaque Contact Lenses
☐	☐	Cambridge Therapy
☐	☐	Surgery
☐	☐	Miotics
☐	☐	Prisms
☐	☐	Orthoptic Exercises
☐	☐	Other _____

Any other comments on treatment history (times, etc):

Age at surgery 1 _____ years.
surgery 2 _____ years.
surgery 3 _____ years.

Best Visual Acuity Achieved with corrections and therapy:

OD ____/____

OS ____/____

Other Amblyogenic conditions: (check all that apply)

- ☐ No information
- ☐ None
- ☐ Ptosis
- ☐ Ulcer
- ☐ Cataract
- ☐ Other _____

Sources of patient history information: (check all that apply)

- ☐ No information
- ☐ Examining doctor
- ☐ Other doctor
- ☐ Vision screener
- ☐ Kaiser records
- ☐ Parent
- ☐ Patient
- ☐ Other _____

PATIENT CLINICAL EXAM

Visual Acuity

Current Spectacle Rx:	VA at 6 meters	VA at 1/3 meter
OD ____D. sph ____D. cyl × ____	____/____	____/____
OS ____D. sph ____D. cyl × ____	____/____	____/____

Check if patient did not bring glasses ☐

Check if patient has no Rx ☐

Manifest Refraction (dry): VA at 6 meters VA at 1/3 meter

OD _____D. sph _____D. cyl × ____ ____/____ ____/____
OS _____D. sph _____D. cyl × ____ ____/____ ____/____

Visual Acuity with:		VA at 6 meters	VA at 1/3 meter
Log 2 NDF	OD	____/____	____/____
	OS	____/____	____/____
Single Symbols	OD	____/____	____/____
	OS	____/____	____/____

Chart type: (check one) Chart Luminance _____ ft. candles.

- ☐ 1 = Snellen optotype
- ☐ 2 = Projectochart
- ☐ 3 = Other _____

Pupil Exam: (check all that apply)

- ☐ No information
- ☐ Normal to light and near
- ☐ Marcus Gunn + _____ (log units)
- ☐ Rapid escape
- ☐ Anisocoria
- ☐ Other _____

Nystagmus: (check all that apply)

- ☐ No information
- ☐ None
- ☐ Pendular
- ☐ Jerk
- ☐ Latent
- ☐ Other _____

Strabismus Evaluation

Horizontal Angle: (check all that apply in each column)

At 6 meters	At 1/3 meter
☐ No information	☐ No information
☐ No strabismus	☐ Strabismus
☐ Esotropia	☐ Esotropia
☐ Exotropia	☐ Exotropia
☐ 'A' pattern	☐ 'A' pattern
☐ 'V' pattern	☐ 'V' pattern
☐ Other _____	☐ Other _____

Size of deviation in primary position:

_____ p.d. at 6 meters _____ p.d. at 1/3 meter

Method of measurement: (check one)

☐ 1 = corneal light reflex
☐ 2 = Krimsky
☐ 3 = prism cover
☐ 4 = other _____

Vertical Deviation: (check all that apply in each column)

At 6 meters	At 1/3 meter
☐ No information	☐ No information
☐ No strabismus	☐ No strabismus
☐ RHT (primary position)	☐ RHT (primary position)
☐ LHT (primary position)	☐ LHT (primary position)
☐ DVD	☐ DVD
☐ Other _____	☐ Other _____

Size of deviation in primary position:

_____ p.d. at 6 meters _____ p.d. at 1/3 meter

Method of measurement: (check one)

☐ 1 = corneal light reflex
☐ 2 = Krimsky
☐ 3 = prism cover
☐ 4 = other _____

Binocular Functions

Large and Small Worth 4-dot: (check one in each column)

At 6 meters	At 1/3 meter
☐ 0 = no information	☐ 0 = no information
☐ 1 = normal	☐ 1 = normal
☐ 2 = diplopia - homonymous	☐ 2 = diplopia - homonymous
☐ 3 = diplopia - heteronymous	☐ 3 = diplopia - heteronymous
☐ 4 = suppression RE	☐ 4 = suppression RE
☐ 5 = suppression LE	☐ 5 = suppression LE

Red Glass: (check one in each column)

At 6 meters	At 1/3 meter
☐ 0 = no information	☐ 0 = no information
☐ 1 = normal	☐ 1 = normal
☐ 2 = diplopia - homonymous	☐ 2 = diplopia - homonymous
☐ 3 = diplopia - heteronymous	☐ 3 = diplopia - heteronymous
☐ 4 = suppression RE	☐ 4 = suppression RE
☐ 5 = suppression LE	☐ 5 = suppression LE

Base up/down to elicit response?

(Y/N) _____ (Y/N) _____

Bagolini Lenses Patient percept:

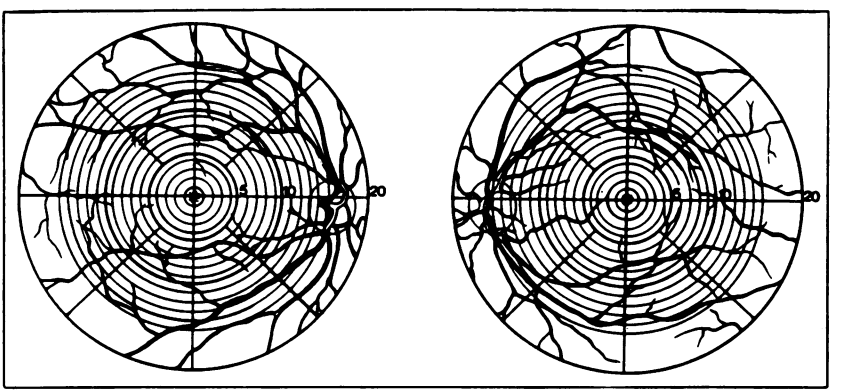
At 6 meters	At 1/3 meter
☐	☐

Check one per column:

☐ 0 = no information	☐ 0 = no information
☐ 1 = normal	☐ 1 = normal
☐ 2 = diplopia - homonymous	☐ 2 = diplopia - homonymous
☐ 3 = diplopia - heteronymous	☐ 3 = diplopia - heteronymous
☐ 4 = suppression RE	☐ 4 = suppression RE
☐ 5 = suppression LE	☐ 5 = suppression LE

Cycloplegic (wet) Refraction:			VA at 6 meters	VA at 1/3 meter
OD ____D. sph	____D. cyl × ____		____/____	____/____
OS ____D. sph	____D. cyl × ____		____/____	____/____

Fixation



Check one per column:

Right Eye	Left Eye
☐ 0 = no information	☐ 0 = no information
☐ 1 = foveal, steady	☐ 1 = foveal, steady
☐ 2 = foveal, unsteady	☐ 2 = foveal, unsteady
☐ 3 = central, unsteady	☐ 3 = central, unsteady
☐ 4 = eccentric, parafoveal	☐ 4 = eccentric, parafoveal
☐ 5 = eccentric, macular	☐ 5 = eccentric, macular
☐ 6 = eccentric, paramacular	☐ 6 = eccentric, paramacular
☐ 7 = eccentric, disk region	☐ 7 = eccentric, disk region
☐ 8 = eccentric, other _____	☐ 8 = eccentric, other _____
☐ 9 = nystagmiform	☐ 9 = nystagmiform
Eccentricity fixation (degrees) _____	Eccentricity fixation (degrees) _____
Drift direction (degrees) _____	Drift direction (degrees) _____

Optic disk:
- ☐ 0 = no information
- ☐ 1 = normal
- ☐ 2 = abnormal (specify) _____

Macula:
- ☐ 0 = no information
- ☐ 1 = normal
- ☐ 2 = abnormal (specify) _____

Photos taken:
- ☐ 0 = no information
- ☐ 1 = yes
- ☐ 2 = no

Clinical Diagnosis

Your evaluation based on this exam.

Check one of the following diagnoses:
- ☐ 1 = Amblyopic
- ☐ 2 = Normal (no amblyopia)
- ☐ 3 = Unable to specify
- ☐ 4 = No information

Check all conditions that apply:
- ☐ Strabismic
- ☐ Anisometric
- ☐ Refractive
- ☐ Deprivational
- ☐ Other _____

DISCUSSION

DR MARSHALL M. PARKS. The authors' goal was to establish a new amblyopia classification and to develop tests that can improve the method of determining the resolving power of the eye and that can define amblyopic features other than simply a resolving power abnormality. They question the validity of the traditional classification of amblyopia that is based on the associated conditions of strabismus, anisometropia, and deprivation or refractive disorders.

This paper is a preliminary report about a pilot study; the main study is ongoing. It is an opportunity for this society to view the cutting edge of a clinical research project on amblyopia. This study reports on 215 subjects between 8 and 35 years of age (Table I).

TABLE I: STUDY POPULATION

CONDITION	NO.	%
Strabismus	109	51
Anisometropia	58	27
Refractive (deprivation)	28	13
Normal controls	20	9

Eighty-two (38%) of the 215 subjects had amblyopia, defined as less than 20/40 Snellen acuity. Seventy-three (34%) had recovered amblyopia, with better than 20/30 Snellen acuity in each eye. Forty (19%) were considered "at risk" for amblyopia, defined as having better than 20/30 Snellen acuity in each eye without prior therapy but having either strabismus, anisometropia (a difference of 1 D between the two eyes), or a high refractive error in both eyes of greater than 4 D of myopia, hypermetropia, or astigmatism. Twenty subjects (9%) were controls, having better than 20/40 Snellen acuity in both eyes without strabismus, anisometropia, or high refractive errors (Table II).

TABLE II: STUDY POPULATION

CONDITION	NO.	%
Amblyopia	82	38
Recovered amblyopia	73	34
At risk	40	19
Control	20	9

The subjects were presented a battery of psychophysical and oculomotor tests that produced approximately 50 different variables. Only the OKN deviations, saccadic amplitude and latency, Pelli-Robson contrast sensitivity, edge contrast

threshold, grating acuity, and hyperacuity tests emerged as significant for analysis to create nine different clusters of subjects having similar test variables. These nine clusters of subjects were assessed against two factors; (1) the distribution of subjects who were amblyopic, recovered amblyopic, or at risk for amblyopia, and the normal controls and (2) the distribution of subjects with strabismus, anisometropia, and deprivation or refractive disorders.

The authors submit only three of the clusters of subjects for review in this paper; one illustrates what they consider "near normal," the second illustrations a cluster they describe as severe amblyopes, and the third illustrates a cluster of deprivation amblyope (Tables III, IV, and V).

TABLE III: "NEAR NORMAL" CLUSTER (n = 34)

CONDITION	NO.	%
Amblyopia	3/82	4
Recovered amblyopia	15/73	20
At risk for amblyopia	12/40	30
Normal controls	4/20	20
Strabismus	24/109	22
Anisometropia	2/58	3
Deprivation (refractive)	4/28	14

TABLE IV: "SEVERE AMBLYOPES" CLUSTER (n = 28)

CONDITION	NO.	%
Amblyopia	25/82	33
Recovered amblyopia	1/73	1
At risk for amblyopia	2/40	5
Normal controls	0/20	0
Strabismus	14/109	13
Anisometropia	12/58	21
Deprivation (refractive)	2/28	7

TABLE V: "DEPRIVATION AMBLYOPES" CLUSTER (n = 16)

CONDITION	NO.	%
Amblyopia	8/52	10
Recovered amblyopia	1/73	1
At risk for amblyopia	0/40	0
Normal controls	0/20	0
Strabismus	1/109	1
Anisometropia	3/58	5
Deprivation (refractive)	5/28	18

My concern is that the defining variables for the "near normal" cluster detected only 20% of the normal controls. Used as a screening test, this would lead to an overreferral rate of 80%. Also, these same variables failed to detect 4% of the amblyopic subjects. Therefore, I hope Doctor Flynn will address why the defining variables that sort out this cluster of patients seem to do such a poor job.

Similar problems also appear in the other two illustrated clusters. The cluster designated severe amblyopes includes 2 of the 40 at risk for amblyopia and 1 of the 73 recovered amblyopia subjects. Also, note the two deprivation amblyopia subjects, because the last cluster illustrates the deprivation amblyope. Are two of the five deprivation subjects listed here the same as those listed as severe amblyopes? Also, this cluster includes one recovered amblyopia subjects.

Perhaps Doctor Flynn will explain these apparent deficiencies and bolster my confidence that these methods of detecting amblyopia have potential for improving diagnosis and understanding of amblyopia. I do congratulate the authors on their assiduous search for other features of amblyopia that are not evaluated by simply assessing the resolution capability of the eye with Snellen acuity.

DR EDWARD L. RAAB. I agree with Doctor Parks' congratulatory comments to Doctor Flynn and his group. I have one question for Doctor Flynn. Would the information derived from this study be useful to us in the treatment of clinical situations where we have combined organic and amblyopia features? For instance, optic nerve hypoplasias with secondary strabismus, where we wonder about whether an individual would be treatable as partially amblyopic. It would be very important to have a clinical handle on something like that. It might, in answer to that question, force you to redefine amblyopia in terms of octaves of difference since even the better eye vision might not be as good as 20/40.

DR JOHN T. FLYNN. First of all, let me thank both Doctor Parks and Doctor Raab for their kind comments. When new ideas break new ground, they are not always easy to deal with. I have been introduced to new ideas such as cluster analysis, and let me explain if I can what cluster analysis is and does. Cluster analysis says here are all of the people who belong together because of their behavior on "this or that test." It does not care a hoot for those behaviors which they do not share. Now when we look at the median visual acuity of that cluster (remember that that means half the values are lower and half the values are higher), we find that the median visual acuity of some clusters containing amblyopes is 20/20. That median was assigned post hoc, not a priori. The behaviors themselves are what defines this individual cluster. The normals, only four of which were counted in cluster 1 are distributed to other clusters. It may very well be that these "normals" have tiny abnormalities in their visual behaviors which we pass off as normal and which, as we get more experience with the clusters, we may recognize that this does not really represent a difference. With regard to the deprivation amblyopes, the same thing can be said. Each subject appeared in one and only one cluster. The great proportion of the deprivation subjects were in cluster 9, but there were also deprivation subjects in other clusters whose behavior on the oculomotor and

psychophysical tests varied from that of cluster 9 and therefore they were included in other clusters. This is the principle underlying this type of research: we are beginning to look at amblyopia in terms of a group of behaviors for which a model is currently emerging from the study of infant visual development. For example, infant vision resolution acuity reaches normal by about 1 year. Infant vision stereoacuity is already in place by 3 months. Infant oculomotor behavior comes on line somewhere else in the time sequence. It is this model, if you will, which is driving this research. None of these tests are as yet ready for the clinic, yet 215 naive amblyopic and normal subjects were able to come into a laboratory and perform reliable and reproducible results on these psychophysical tests. The idea in the end would be to put in all our offices some form of a cartoon-type television display which would systematically test the sensory and motor behaviors in infants and toddlers. This is where we are hoping one day we will go with this study in addition to giving us a new look at amblyopia.