Ryan Gise
Resident Physician, Department of Pediatrics
Morgan Stanley Children's Hospital of New York Presbyterian Hospital
Columbia University Medical Center

Detection of Amblyopia via Retinal Rivalry

1.) Study purpose and Rationale

Amblyopia or lazy eye is the most common cause of vision loss in children in USA with an estimated of 100,000 cases each year. In this condition the eye and visual system are intact but due to anisometropia, strabismus, or unfavorable eye structure one eye is preferentially used. The ability to resolve images with the not favored eye progressively declines and, if untreated, the result is legal blindness in that eye. This disease is usually curable if detected and treated by 6-8 years of age. Despite current screening techniques, many cases go undetected until the vision loss is irreversible.

The standard testing method today is testing each eye using a Snellen distance reading chart. Problems with this method include (1) the child can memorize the chart or peak around a covered eye and disguise an amblyopic eye and (2) the child must be able to recognize letters or numbers. A binocular test eliminates the problem of a monocular test where peaking around the covering eye can give erroneous results. One study in Taiwan found that distance visual acuity testing when administered by registered nurses to have a sensitivity of 74.7 and a specificity of 90.8.[1]

Rivalry measurement using complementary colors was first described by Johnson in patients with optic nerve disease. He showed that the side opposite the nerve defect dominated rival preference.[2] Using a similar technique for color rivalry, Hofeldt and Hofeldt showed that patients with amblyopia have a large sensory defect in the eye with amblyopia and that the sensory defect is positively correlated with the severity of amblyopia.[3]

2.) Study Design and Statistical Analysis

The proposed technique is a binocular test that uses an interactive video program on an iPhone in conjunction with a 3 dimensional viewer made by the toy company Hasbro to separate binocular stimuli. The stimuli, which may be other than letters and numbers, are presented in a game format that is fun and non-threatening for children. The development of such an interactive testing technique with common portable devices has the potential of screening for amblyopia any child. The degree of retinal rivalry is determined by the patient's choice of the brighter image as a sequence of test stimuli are presented. The control objects have similar brightness and are normally chosen with equal likelihood between eyes.

The following parameters will be analyzed:

A. Age vs. ability to perform the test.

B. Sensitivity and specificity of detecting amblyopia

C. Rival scores of normal subjects vs. patients with amblyopia

D. Rival scores of patients with amblyopia vs. severity of amblyopia

E. Rival scores of normal subjects vs. abnormal subjects with conditions other than amblyopia

F. Rival score change and the change in the severity of amblyopia following treatment.

We will need 70 patients in each group so that the study will reach statistical significance with a p value <0.05 and Power of 0.80. This will be able to see a sensitivity of 90% and a Specificity of 99%.

Statistical analysis will be performed using ANOVA, one-way analysis of variance to compare the variance of two independent samples.

3.) Study Procedure

The subjects will be patients who come to my office for pediatric ophthalmic consultation. A complete pediatric ophthalmic examination including visual acuity measurement, stereopsis and fusion measurements, refraction, retinoscopy, eye muscle balance, pupillary examination, and retinal examination would otherwise still be performed as part of their medical care. Their ages, underlying ophthalmic condition and its severity, and their treatment will be recorded in the office chart.

The test and video game are described in developmentally appropriate terms to English speaking children and their guardian. After assent from the child and informed consent from the guardian are obtained the rivalry test is presented. The rivalry test is completely interactive and relies solely on the subject's response. After verbal instructions are given, the subject looks through the MY3D viewer made by the toy manufacturer Hasbro at a Keynote presentation on an iPhone screen where additional instruction is presented by a narrator. A series of parallel Keynote images on the iPhone is presented in a video game format. The test stimuli consistent of simultaneous presentation of identical night skies to each eye. The test objects are presented simultaneously to each eye against this background but vary in their location and brightness. The patient choses the brighter object by pressing on the corresponding side of the iPhone screen through the MY3D viewer. Their responses are recorded by the iPhone as right eye or left eye. The disparity in stimulus brightness between eyes is varied from screen to screen to define a threshold for detection by each eye and thereby the status of retinal rivalry.

The rivalry score is difference between the right/left preference for pairs of test stimuli. No preference yields a rival score of 0, complete dominance yields a score of 100%. The stimulus pair could be shapes, numbers, or letters.

4.) Study Drugs: Not Applicable

5.) Medical Devices

iPhone 5 made by Apple

MY3D stereoviewer for iPhone made by Hasbro

6.) Study Questionnaires: Not Applicable

7.) Study Subjects

Inclusion and exclusion criteria: English speaking children presenting for consultation to my medical practice who receive a complete pediatric ophthalmic examination will be offered the opportunity to participate in the study. Children who have an urgent problem, have had recent surgery, and who are severely disabled will be excluded.

Number of enrollment: The critical age of diagnosis of amblyopia is prior to 7 years of age so there is time for adequate treatment. A goal is to study at least 70 children with amblyopia, suspicion of amblyopia, or who have been treated for amblyopia between 3 and 7 years and 24 age matched normal controls for a total of 70 subjects.

8.) Recruitment of Subjects

Recruitment will be via the private practice of Steven Kane, MD, PhD, at the time of consultation.

9.) Confidentiality of Study Data

Data sheets will be compiled and given a case number. Only the patient's office chart in possession of Dr. Steven Kane will contain both the patient's name and case number.

10.) Potential Conflict of Interest

11.) Location of Study

12.) Potential Risks

There are no potential risks from playing this video game beyond what is encountered in daily life. No harmful events, outcomes, or occurrences related to this research are foreseen.

13.) Potential Benefits

Such a screening device for amblyopia would be useful for the general ophthalmologists,

optometrists, pediatricians, and schools or other pediatric screening facilities.

The individual patients in this study will not benefit directly from the research. Pediatric ophthalmologists have the diagnostic ability to identify children with amblyopia and do not need a computerized sensory testing program; however, such a device would be a time-saving method for diagnosis and for following the progress of therapy.

14.) Alternative Therapies

Patients can choose not to participate without consequence for their medical care. There is no therapeutic arm of this study.

15.) Compensation to Subjects: Not Applicable

16.) Costs to Subjects: None

17.) Minors as Research Subjects

Consent will be obtained following the scheduled examination by Dr. Steven Kane and after the study is verbally described by either Dr. Steven Kane or Dr. Ryan Gise to the child and a guardian. The child's assent will be required and documented in the chart. A consent form requiring the guardian's signature will be used.

18.) Radiation or Radioactive Subjects: Not Applicable

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[1] Chang CH et al, Screening Amblyopia of Preschool Children with Uncorrected Vision and Stereopsis Tests in Eastern Taiwan. *Eye* (2007); 21, 1482-1488.

[2] Johnson L. The relative afferent defect and a novel method of fusion recovery with the Worth 4-dot test. Arch Ophthalmol 1996;114:171-5.

[3] Hofeldt TS, Hofeldt AJ. Measuring colour rivalry suppression in amblyopia. Br J Ophthalmol 1999;83:1283-6.