High heterogeneity in the receptive-field subunit maps of multiple nearby neurons in infant V2

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Purpose: We previously reported that chronic monocular defocus (-3D or -10D) between 3 and 12 weeks of age leads to amblyopia in monkeys, and that the receptive-field (RF) subunit maps of multiple nearby V2 neurons in these amblyopic monkeys are substantially different from each other. The magnitude of this map heterogeneity is highly correlated with the degree of binocular suppression in V2 and also with the depth of amblyopia of individual monkeys (reduced grating and vernier acuity). To gain insights into how these neural and perceptual anomalies may be developmentally linked, we compared the RF subunit maps of multiple nearby V2 neurons in ‘normal’ infant monkeys.

Methods: We recorded from multiple V2 neurons in anesthetized monkeys at 4 and 8 weeks of age. We employed dense white noise stimuli and standard unit recording methods. Spiking data were analyzed using Local Spectral Reverse Correlation (LSRC) to reveal the RF subunit maps of individual neurons. The heterogeneity of the subunit maps was quantified by calculating the differences in the preferred orientations and spatial frequencies between all pairs of subunits.

Results: At 4 weeks of age, the subunit maps of nearby neurons were very different from each other although the subunit map of each neuron was normal (i.e., homogeneous). This heterogeneity in RF subunit maps between nearby neurons was similar to that found in adult amblyopic monkeys. However, this large heterogeneity of the subunit maps disappeared by 8 weeks of age.

Conclusions: We conclude that early binocular imbalance rapidly initiates robust binocular suppression in V1 and V2, which in turn disrupts the normal maturation of the intrinsic connections in V2 and/or the feedback connections from higher-order visual areas, resulting in the observed abnormally high heterogeneity of subunit maps between nearby multiple neurons. These results support the clinical opinion that the corrective procedures for binocular imbalance (hence reductions of binocular suppression) at the earliest possible age may be beneficial in preventing the emergence of amblyopia.

Commercial Relationships: Bin Zhang, None; Xiaofeng Tao, Guofu Shen, None; Janice M. Wensveen, None; Earl L. Smith, None; Yuzo M. Chino, None

Support: R01 EY-008128 (YC), R01 EY-003611 (ELS), & Core Grant P30 EY-007551

Program Number: 3813
Presentation Time: 3:45 PM–4:00 PM
High heterogeneity in the receptive-field subunit maps of multiple nearby neurons in infant V2

Disconnection of ipsilateral FEF from the attention network in strabismic amblyopia during coherent motion task

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Purpose: Anecdotally it has been suggested that the amblopic eye of strabismic amblyopes is less able and slower to drive eye movements than the fellow eye. Thus we compared speed threshold performance and brain activation during motion salience and voluntary saccade tasks in adult strabismic amblyopes and controls.

Methods: Psychophysical speed thresholds for target detection were measured in 8 strabismic amblyopes and 8 normal participants prior to fMRI scanning of a motion salience task and a task requiring voluntary saccades to horizontal stimulus position changes. Activation and functional networks between ROIs including parieto-frontal attention network, Frontal Eye Fields and V1 were examined.

Results: Significantly impaired speed thresholds for target detection were seen through the strabismic amblyopic eye compared to thresholds through the fellow eye or control eyes when determining the direction of motion of the coherently moving dots task. BOLD activation in V1, IPS and FEF was also weaker for both tasks, following viewing through the amblyopic eye compared to activation through the fellow or control eyes. Correlational connections between key nodes of the visual attention network activated by the amblyopic eye were abnormal in the motion salience task, with the FEF ipsilateral to the amblyopic eye isolated from all other nodes. By contrast, the functional connections of this network were normal for the voluntary saccade task.

Conclusions: Lower motion thresholds and less BOLD activation of the parieto-frontal network through the amblyopic eye indicate a requirement for longer exposure time for discrimination of the moving target during amblyopic eye driven movements compared to those through the fellow eye or control eyes. A specific deficit in functional connectivity was also seen between V1 and the frontal eye field ipsilateral to the strabismic eye during the motion salience task but not during the voluntary saccade task.

Commercial Relationships: Sheila G. Crewther, None; Hao Wang, None; Mingiong Liang, None; Tao Yu, None; Jian Wang, None; David P. Crewther, None; Robin Laycock, None; Zheng Yin, None

Program Number: 3814
Presentation Time: 4:00 PM–4:15 PM
Disconnection of ipsilateral FEF from the attention network in strabismic amblyopia during coherent motion task

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Purpose: Rapid alternating occlusion (RAO) is used to treat amblyopia. The neural mechanism, however, is not well studied. To test the neural interactions during RAO, we measured Visual Evoked Potentials (VEPs) under different dichoptic conditions.

Methods: Subjects (n=5) underwent an eye screening and had no history of ocular pathologies, refractive error less than 5.00D sphere and/or 2.50D cylinder and no anisometropia greater than

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The amplitude of the 2nd H is higher for interocular delays less than frequencies lower than 8Hz (p=0.69). During binocular dichoptic the results of the monocular experiment showed that the disks were alternatively presented to each eye at 7Hz while we introduced an onset delay in one of the two disks ranging from 10 to 71ms. Recordings were Fast Fourier Transformed. ANOVA and two-tailed Student’s t-tests (α=0.05) were used to compare frequencies and amplitudes of first and second harmonics (H).

**Results:** The results of the monocular experiment showed that the amplitude of the 2nd H for alternating frequencies up to 8Hz with a peak at 7Hz (p=0.019). The results of the third experiment showed that the amplitude of the 2nd H is higher for interocular delays less than ~20ms (p=0.037) and longer than ~40ms (p<0.001) with a trough between 30 and 40ms.

**Conclusions:** The difference in amplitude of the 2nd H between the first and the second experiment indicates that the 2nd H of the second experiment reflects enhanced binocular activity for alternating frequencies between 6 and 8Hz. The increased 2nd H amplitude for interocular delays below 20ms can only be explained by binocular summation. This series of experiments offers the first evidence that RAO promotes binocular interactions based on VEP results.

**Commercial Relationships:** Hilary A. Hamer, None; Andrew McLeod, None; Athanasios Panorgias, None

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**Program Number:** 3816  
**Presentation Time:** 4:30 PM–4:45 PM  
**Home use binocular dichoptic video content treatment for amblyopia-pilot study**  
Chaim Stolovitch. Ophthalmology, Tel Aviv Medical center, Tel Aviv, Israel.

**Purpose:** To assess home use device for treatment of Amblyopia using dynamically altered dichoptic presentation of video contents without patching.

**Methods:** 25 subjects, age 4-8 years, with refractive/strabismic or combined amblyopia, with visual acuity ≤ 20/50 in the amblyopic eye were enrolled prospectively. The device used software that dynamically alters any video content dichoptically, using video goggles, in which reduced contrast of the content is presented to the good eye. All the children had best corrected refraction glasses for at least 3 months prior to treatment and were reluctant for further patching or using atropine. All were instructed to use the device for 30-60 min daily, viewing passively child/animated TV shows at home without patching. Visual Acuity was assessed at baseline and after 4, 8 and 12 weeks of treatment. VA was assessed in 15 and 12 patients at week 24 and week 36 respectively after termination of treatment. Visual acuity was measured with M&S VA computerized system and the results were transformed and expressed in logMar unit. Statistical analysis was done using Wilcoxon T-test related samples.

**Results:** 17 patients completed 8 weeks of treatment and 16 patients 12 weeks. Base line Mean VA in the amblyopic eye was 0.648 (+0.1898). At 4 week visit, mean VA improved significantly to 0.46 (0.1828 ± 0.1443 lines) in the amblyopic eye(P<0.0004), at 8 weeks visit mean VA improved to 0.3940(0.254 ± 0.1687 lines, P=0.00437) and at 12 weeks to 0.3860(0.2582 ± 0.1853 lines, P=0.00098) from base line VA. 15 patients were examined after cessation of treatment at week 24 with a very small change in mean VA -0.12 line(P=0.575) from Last mean VA measurements at week 12. 12 patients return for last visit at week 36 with very small detrioration of mean VA: -0.086 line(P=0.0593) from mean VA at week 12 which was not statistically significant.8 patients completed 4 weeks of Sham protocol with no improvement (mean change in VA of amblyopic eye 0.0063 ±0.1653,P=0.4226) from base line VA. Compliance was excellent:100% of the recommended time and even up to 110% in some kids who would not stop viewing their favorite movies.

**Conclusions:** Passive viewing of dynamically altered dichoptic presentation of any video content achieved very good results at 4 weeks of treatment with further improvement after 8 week without patching. The improvement sustained for at least 6 months. It has the potential to be used as treatment for Amblyopia.

**Commercial Relationships:** Chaim Stolovitch, None 
**Support:** Visior Technologies Ltd.

**Clinical Trial:** NCT02003235

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**Program Number:** 3817  
**Presentation Time:** 4:45 PM–5:00 PM  
**Greater eye movement disconjugacy with near fixation in amblyopia during binocular viewing is associated with increased microsaccade rate**  
Howard S. Ying1, Soollenah Rhiu1, Connie Yang2, Vivian Xu2, Robert Geary2, Boris I. Gramatikov2, David L. Guyton2, Kristina Irisch2. Ophthalmal & Visual Sciences, Boston University School of Medicine, Boston, MA; Ophthalmology, The Johns Hopkins University, Baltimore, MD; Ophthalmology, Hallym University College of Medicine, Hwasong, Korea (the Republic of).

**Purpose:** To determine whether increased eye movement disconjugacy with near fixation in amblyopic subjects during binocular viewing is associated with changes in microsaccade parameters.

**Methods:** Binocular eye movements were recorded at 500 Hz using the EyeLink 1000 eye tracker (SR Research Ltd., Ontario, Canada). Eleven amblyopic subjects, age 8-45 years, were asked to fixate on a blue cross subtending 0.5° at a near distance of 57 cm or at a far distance of 4 m for 20-second epochs of binocular or monocular viewing. Microsaccade number, duration, peak velocity, direction, binocularity, and reversals of direction (square-wave jerk configuration) were recorded. Means and standard deviations were calculated, and significance testing was performed with the Student’s t-test.

**Results:** Amblyopic subjects during binocular viewing showed more microsaccades with near fixation (1.4±0.1 microsaccades/s) than with far fixation and (1.9±0.2 microsaccades/s; P=0.02) and fewer reversals in direction with near fixation than with far fixation (49±22 % near vs. 58±16 % far; P=0.01). Both viewing conditions showed similar microsaccade duration (95±200 ms vs. 66±83 ms) and peak velocity (42±28 deg/s vs. 37±18.5 deg/s).

**Conclusions:** Increased disconjugacy with near fixational eye movements for amblyopic subjects during binocular viewing is associated with an increase in the number of microsaccades in the same direction. This increase in microsaccade rate with near fixation may indicate subclinical manifest latent nystagmus possibly from increased suppression of the amblyopic eye during accommodation to the near target.

**Commercial Relationships:** Howard S. Ying, Lutronics, Inc. (C); SPOUSE - Takeda, Inc., REBIScan, Inc. (C); Johns Hopkins University (P); Soollenah Rhiu; Connie Yang, None; Vivian Xu, None; Robert Geary, Johns Hopkins University (P),
**Program Number:** 3819  
**Presentation Time:** 5:15 PM–5:30 PM  
**Detection of Amblyopia in Young Children via Retinal Rivalry Using a Video Game Styled Interface on a Tablet Device**  
**Ryan Gise**, **Steven Kane**, Ophthalmology, Albert Einstein College of Medicine/ Montefiore Medical Center, New York, NY; Ophthalmology, Columbia University Medical Center, New York, NY.  
**Purpose:** A great deal of time and effort had gone into developing new technologies to screen for amblyopia. Current photoscreeners are able to detect amblyopic risk factors but not quantify the degree or presence of amblyopia. The Snellen Eye Chart is both accurate and effective when used by a skilled ophthalmologist but there remains a great deal of inter-screener variability in the primary care setting between physicians and medical staff. We sought identify a screening method that would also be able to quantify the degree of amblyopia for children even before they can read letters on the Snellen Eye Chart. We performed a prospective, observational study of children with known amblyopia and without to determine if a test with a video game like interface could use retinal rivalry to detect and quantify amblyopia.  
**Methods:** For this study, we tested 16 Normal and 16 amblyopic children aged 3 to 7. Each was presented with a staircase algorithm of image sets of differing log units of brightness (0 to 1.8). It was designed by AMA Optics, Inc. for use on the iPad. The images were stacked on top of each other and the child was asked to determine the brighter object while wearing polarized sunglasses in order to separate the two eyes. The test was performed on each child twice and the results were recorded along with the visual acuity obtained at the child's ophthalmologic appointment that day and whether or not the child had amblyopia or was receiving treatment. The degree of brightness deficit between the two eyes was then compared to the visual acuity difference between the eyes for children with amblyopia.  
**Results:** All 16 Amblyopes with greater than 1 line disparity on the Snellen Eye Chart were detected and there were no false positives for children without Amblyopia. Thus, the sensitivity of the test was 100%. The test scores were consistently repeatable as indicated by highly correlated test and retest scores. (r=0.99, p <0.0001) The depth of defect reported and lines of acuity disparity were also highly correlated. (r=0.85, p<0.0001)  
**Conclusions:** The iPad can be used as a vehicle for a game-like program to accurately detect the presence of amblyopia in children, It may provide a useful tool for both screening in the primary care setting and for ophthalmologic professionals to follow the improvement of patients with amblyopia during treatment.  
**Commercial Relationships:** Ryan Gise, None; Steven Kane, None