ARVO 2017 Annual Meeting Abstracts

152 Nystagmus and Gaze Holding
Sunday, May 07, 2017 3:15 PM–5:00 PM
Room 324 Paper Session
Program #/Board # Range: 860–866
Organizing Section: Eye Movements/Strabismus/Amblyopia/
Neuro-Ophthalmology

Program Number: 860
Presentation Time: 3:13 PM–3:30 PM
Visual Acuity Development with Infantile Nystagmus: Prediction of Visual Acuity Limits
John P. Kelly1, 2, James O. Phillips1, Avery H. Weiss1, 2.
1Ophthalmology OA.5.342, Seattle Children’s Hospital, Seattle, WA;
2Ophthalmology, University of Washington, Seattle, WA.

Purpose: Visual acuity (VA) is typically reduced in observers with infantile nystagmus (IN) without an afferent disorder. However, eye movements (e.g., eXpanded Nystagmus Acuity Function or NAFX) are poor at predicting VA in IN subjects (r2 < 0.20 across studies).

Also, IN subjects don’t show an improvement in VA when motion blur is eliminated by flashing visual targets. A concern is that image motion during early visual development reduces VA in IN (e.g., motion amblyopia). In contrast, the immaturity of the infant visual system should be more tolerant to retinal image motion due to IN.

This study provides predictions of eye velocity that should limit visual acuity across infant development and compares the prediction with eye movement recordings.

Methods: Nine children (1-4 years age) with idiopathic IN had visual acuity measurements (Teller Acuity Cards or letter optotypes) and eye movement recordings (confocal OCT/SLO imaging in one child). Prediction models of image motion that limits visual acuity development was derived from development of fovea anatomy and from adult data (adjusted for age). Eye movements were collected by VOG.

Results: All subjects showed brief periods (at least 17 - 200 ms) of eye velocity below the predicted value that would limit visual acuity for age. The percentage of time eye velocity was below the predicted limit varied from 14% to 51% across subjects. In subjects with pendular nystagmus, the turn-around points of the waveform were the only locations that did not limit visual acuity. Confocal SLO in a subject with pendular nystagmus showed the fovea was not matched to the target at these turn-around points. Age was not correlated with the percentage of time eye velocity was below the lower limit for age, nor the standard deviation or maximum duration of these low eye velocity periods. Longitudinal visual acuity development was not differentially affected by nystagmus waveform.

Conclusions: The model predicted all subjects had periods during which the visual system could sample high spatial frequency information. Therefore, retinal image motion due to nystagmus was not predicted to limit visual acuity development but indicates the visual system must compensate for improper foveation. Our model can help determine criteria of eye velocity to detect periods of assumed foveation across age.

Commercial Relationships: John P. Kelly, None;
James O. Phillips, None; Avery H. Weiss, None
Support: William O. Rogers Trust Fund, and by the Anderson and Peter G. La Haye charitable contributions

Program Number: 861
Presentation Time: 3:30 PM–3:45 PM
Comparison of retinal development in idiopathic infantile nystagmus and nystagmus associated with albinism, PAX6 mutations and achromatopsia
Mervyn G. Thomas1, Viral Sheth1, Gail Maconachie1, Sarim Ather1, Rebecca J. McLean1, Frank A. Proudlock2, Susanne Kohl1, Bart P. Leroy1, Anthony T. Moore1, Irene Gottlob3, Anthony T. Moore1, Irene Gottlob3,1 Ulverscroft Eye Unit, University of Leicester, Leicester, United Kingdom; 2Ophthalmology, UCSF, San Francisco, CA; 3Ophthalmology, Childrens Hospital of Philadelphia, Philadelphia, PA; 4Ophthalmology, University of Tübingen, Tübingen, Germany.

Purpose: Infantile nystagmus (IN) is a genetically heterogeneous disease which can arise due to mutations in genes expressed within the developing retina. Previous work has focussed on documenting the foveal defects associated with IN. We aimed to characterise the intra-retinal abnormalities (foveal and parafoveal) associated with IN.

Methods: OCTs (Copernicus HR, 3µm axial resolution; protocol: 7x7mm, 743x75: AxB) were obtained from 108 IN patients due to FRMD7 mutations (n=45), PAX6 mutations (n=15), albinism (n=34) and achromatopsia (n=14). OCTs were obtained from controls (n=52). Thickness measurements were obtained from a single fovea B-scan. Custom scripts in ImageJ were used for segmentation and deriving intra-foveal thickness measurements. Nasal and temporal parafoveal thickness measurements represent average measurements between 1mm to 3mm on either side of the fovea.

Results: Foveal hypoplasia was seen in all patients with albinism (grades 1-4) and PAX6 mutations (grades 1-3). Only a proportion of patients (12/45) with FRMD7 mutations had foveal hypoplasia (all grade 1). Parafoveal nerve fibre layer (NFL) was significantly thinner in all groups compared to controls (p<0.0001). PAX6 mutations were associated with the thinnest NFL, however this reduction was confined to the nasal parafovea. FRMD7 and achromatopsia groups had significant reduction to both nasal and temporal NFL. The parafoveal ganglion cell layer and inner plexiform (GCL+IPL) complex and outer plexiform layer (OPL) was significantly reduced in PAX6, albinism and achromatopsia (p<0.01). Patients with achromatopsia had significantly thinner foveal and parafoveal outer nuclear layer (ONL) in comparison to the other groups and controls. No significant differences were noted in parafoveal ONL between PAX6, albinism, FRMD7 and controls.

Conclusions: This study highlights the specific retinal defects in patients with IN. Patients with albinism had more severe grades of foveal hypoplasia compared to the other groups. We report for the first time the significant changes to the intra-foveal layers in PAX6, albinism and achromatopsia. The NFL loss was most severe in patients with PAX6 mutations. Consistent with cone photoreceptor loss, achromatopsia patients had a reduction in the ONL thickness at the fovea and parafovea.

Commercial Relationships: Mervyn G. Thomas, None;
Viral Sheth, None; Gail Maconachie, None; Sarim Ather, None; Rebecca J. McLean, None; Frank A. Proudlock, None; Susanne Kohl, None; Bart P. Leroy, None; Anthony T. Moore, None; Irene Gottlob, None
Support: This study was supported by the Ulverscroft foundation, the Medical Research Council (MRC), London, UK (grant number: MR/J004189/1 and MRC/N004566/1) and Fight for Sight (ref: 5009/5010). Author MGT is supported by the NIHR (#2980).

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Prenatal Exposure to Cocaine, Amphetamines and Methadone Disrupts the Development of Gaze Holding Circuits

Avery H. Weiss1,2, James O. Phillips1,2, John P. Kelly1,2. 1Ophthalmology, University of Washington, Seattle, WA; 2Ophthalmology, University of Leicester, Leicester, United Kingdom.

**Purpose:** Directional sensitivities to nasal vs temporal and superior vs inferior motion are set prenatally by Starburst retinal ganglion cells which express specific cocaine and amphetamine regulated transcripts (CART). The directional specificity of this circuit is set by the neuronal connectivity between the dendritic branches of amacrine and ganglion cells whose axons project to downstream pre-motor neurons. We postulated that prenatal exposure to cocaine and methamphetamine would perturb the neuronal circuitry underlying gaze holding and conjugate eye movements.

**Methods:** Eight children (mean age 3.4y) with documented prenatal and/or perinatal exposure to cocaine/methadone and/or amphetamine were studied. All had normal or nearly normal visual acuities and examinations of the anterior and posterior segments were normal. Each child had assessments of gaze holding, vertical saccades and vertical optokinetic nystagmus (OKN) quantified by binocular video-oculography (VOG).

**Results:** Six of 8 subjects had gaze holding instabilities; 4 had asymmetric, horizontal, pendular nystagmus and 2 had conjugate horizontal jerk nystagmus. Average gains for saccades to point targets stepped upward 5deg, 10deg and 20deg were 1.0±0.55, 0.82±0.48 and 0.8±0.36, respectively. Average gains for saccades stepped downward 5deg, 10deg and 20deg were 0.57±0.22, 0.73±0.22, and 0.87±0.36, respectively. Average OKN gains for horizontally-oriented gratings drifted at velocities of 15, 30 and 45deg/s were respectively 1.03±0.44, 0.69±0.35 and 0.84±0.22 in the upward direction and 0.38±0.18, 0.69±0.35 and 0.54±0.22 in the downward direction.

**Conclusions:** Our data show that infants with prenatal exposure to cocaine, amphetamines or methadone were likely to exhibit gaze-holding instabilities. All subjects generated vertical saccades and vertical OKN across velocities with similar gains in the upward and downward direction except for target steps of 5deg and velocities of 15deg/s. We hypothesize that prenatal exposure to these drugs may lead to dysregulation of the CART resulting in the failure of DSGC to connect with the appropriate downstream neurons. The resulting failure to organize target neurons into precise neural circuits may account for the gaze-holding instabilities.

**Commercial Relationships:** Avery H. Weiss, James O. Phillips, None; John P. Kelly, None

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**Program Number:** 862
**Presentation Time:** 3:45 PM–4:00 PM
**Prenatal Exposure to Cocaine, Amphetamines and Methadone Disrupts the Development of Gaze Holding Circuits**

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**Program Number:** 863
**Presentation Time:** 4:00 PM–4:15 PM
**Hypothermia and the Effect of Infantile Nystagmus on Postural Control in Neonates**

Frank A. Proudlock1, Tharsica Sivagnanasithayar1, Rebecca J. McLean1, Philip Duke1, Rakesh Patel1, Irene Gottlob1, Zhanhan Tu1. 1Ulverscroft Eye Unit, University of Leicester, Leicester, United Kingdom; 2Neuroscience, Psychology and Behaviour, University of Leicester, Leicester, United Kingdom; 3Division of Audiology, De Montfort University, Leicester, United Kingdom.

**Purpose:** The impact of infantile nystagmus (IN) on postural control is poorly understood. IN is often associated with other visual diseases, such as albinism leading to poor stereovision and foveal hypoplasia reducing the quality of central vision. We investigated the role of central binocular and peripheral monocular visual fields for postural responses in IN compared to controls. To explore the contribution of vision relative to other sensory inputs we used: (1) a sway-referenced (SR) platform to reduce somatosensory inputs, and (2) the phenomenon ofvection to motion.

**Methods:** Postural responses in the anterior-posterior (A-P) plane were recorded using an Equitest system (Neurocom) in 20 participants with IN (unassociated: n=9; albinism: n=11) and 15 age-matched controls under the following conditions: (1) eyes closed compared to static visual stimuli in the central or peripheral fields (AP) using a Cervical Range Of Motion device and best binocular acuity (BVA) using standardized acuity testing, nystagmus function (NF) using eye movement recordings and contrast sensitivity (CS) using the CSV1000 device in primary position.

**Results:** Ages ranged from 5-85 yrs (ave 27 yrs), 59% male, follow up ranged from 1-10 years (ave 2 yrs). 14 (82%) had diagnosed CNS disease, 15 (88%) had a clinical AHP, 6 (35%) had other eye diseases, 9 (53%) had associated strabismus and all had oscillopsia and/or decreased BVA and CS compared to normal for age. After eye muscle surgery there were significant, persistent group improvements in NF, BVA, AHP, SD, CS, and SO after surgery (P<.0012 to <0.05). Those will alcohol related CNS disease responded the least to surgery while children (<18 years) improved the most. Two patients required reoperation for a consecutive strabismus. There were no serious complications.

**Conclusions:** DBN patients commonly have associated central nervous system abnormalities and may be offered standard eye muscle surgery in addition to known medical treatments to improve associated abnormal visual system signs and symptoms.

**Commercial Relationships:** Richard W. Hertle, None; Ashraf Ahmad, None

**Clinical Trial:** Database Registry Akron Children's Hospital Institutional Review Board, 110201

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**Program Number:** 864
**Presentation Time:** 4:15 PM–4:30 PM
**Contribution of Central and Peripheral Visual Cues to Postural Control in Infantile Nystagmus**

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**Program Number:** 865
**Presentation Time:** 4:45 PM–5:00 PM
**The Impact of Infantile Nystagmus on Postural Control in Neonates**

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**Program Number:** 866
**Presentation Time:** 5:00 PM–5:15 PM
**The Impact of Infantile Nystagmus on Postural Control in Neonates**

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under both fixed and SR platform conditions; (2) simulated 3D sinusoidal visual motion (0.05–4Hz) in the A-P plane in the central and peripheral visual fields to generate frequency response functions (static platform only). Responses were quantified using spectral analysis of sway in the A-P plane.

Results: For the fixed platform condition, no significant differences in postural responses were observed between eyes closed compared to static visual stimuli in the central or peripheral fields for all participant groups. However, for the SR platform condition, the presence of either central or peripheral field static visual stimuli dramatically reduced postural sway compared to the eyes closed condition in the control group (p<0.001). In contrast, in the IN group, central static visual stimuli moderately reduced postural sway compared to eyes closed, with peripheral stimuli making less difference. Frequency response functions were similar for simulated central and peripheral motion in controls. In contrast, in participants with IN (albinism and unassociated), motion in the peripheral visual field led to a distinct peak of instability at 0.5Hz but not for motion in the central visual field.

Conclusions: Individuals with IN rely less on vision in general for postural control compared to controls, particularly on peripheral visual information. They also have a propensity to experiencing vection for sinusoidal motion at 0.5Hz in the peripheral visual field leading to postural instability which might have functional implications.

Commercial Relationships: Frank A. Proudlock: None; Rebecca J. McLean, None; Philip Duke, None; Rakesh Patel, None; Irene Gottlob, None; Zhanhan Tu, None
Support: Fight for Sight, UK (Nystagmus Network Small Grant Award, grant number: 24NN14)

Program Number: 865
Presentation Time: 4:30 PM–4:45 PM

Optimising visual attention in children with autism spectrum disorder: a comparison of fixation distributions viewing singing and speech
Larry A. Abel1, Grace A. Thompson2,3. 1Optometry & Vision Sciences, University of Melbourne, Parkville, VIC, Australia; 2Melbourne Conservatorium of Music, The University of Melbourne, Melbourne, VIC, Australia.

Purpose: Many children with autism spectrum disorder (ASD) are at risk of social isolation and limited social development due to difficulties with gaze and visual attention to people. Studies have shown that children with ASD may prefer music to other stimuli. We hypothesised that a short video of a singer would elicit more attention to the performer, particularly to her face, than a video of her reading a story and that the child’s familiarity with the song and story would enhance attention.

Methods: 16 children aged 7-10 (14 M, 2 F) with ASD took part. Stimuli were 4 videos 1 minute long. Content was a favourite song or story of the child, along with a song and story which were the same for all children. The performer, her clothing, lighting and sound level were the same across tasks. Props were a pair of drums for the songs and a storybook of similar size for the stories. Eye movements were recorded with an Eyelink 1000; areas of interest (AOIs) were defined for the face, prop and body. 3-way repeated measures ANOVAs were used to examine the proportion of total dwell time, the proportion of total fixations and pupil area for each AOI in each trial.

Results: For dwell time proportion, a significant interaction was found for familiarity*AOI (F=7.45, p=.004), with gaze time to the face being increased for familiar trials (Table 1). Similarly, medium*AOI was significant (F=6.01, p=.013), with increased gaze time to the face and body and decreased time to the prop for the songs (Table 2). The same patterns were seen for proportion of fixation counts to the AOIs (familiarity*AOI F=4.97, p=.016; medium*AOI F=10.33, p=.001). For the pupil, only familiarity and AOI were significant; pupils were larger for familiar stimuli (F=16.70, p=.001) and for the face and prop (F=6.8, p=.015), with the body eliciting less dilation.

Conclusions: As hypothesised, the videos of singing attracted children’s gaze to the performer more than did those of her reading a story. Familiarity with the material being performed also attracted more attention to her face. Familiarity and gaze to the face also increased arousal, as indexed by pupil dilation. Observation by children with ASD of a singer, particularly one performing their favourite songs, may be a useful intervention for improving their social engagement skills.

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Dwell time proportion, familiarity*AOI

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Dwell time proportion, medium*AOI

Commercial Relationships: Larry A. Abel, None; Grace A. Thompson, None
Support: Melbourne Neuroscience Institute Interdisciplinary Seed Funding Scheme

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Program Number: 866
Presentation Time: 4:45 PM–5:00 PM
Out of the blue: Effects of blue-filtering lenses on EEG and eye movements during reading

Purpose: Increased blue-light exposure from computer screens has been linked to fatigue in screen-based working conditions, leading to the development of blue-filtering lenses. Despite this recent trend, behavioral and physiological evidence for the efficacy of such lenses is scarce. Here, we investigate potential differences in comprehension, brain wave activity, and eye movements, when people read texts with or without blue-filtering lenses.

Methods: 34 participants (24 males, students, mean age=23.5y) with normal visual acuity (0.1±0.1logMar) and right eye dominance. The task consisted of reading 6 texts with different topics taken from the Korea academic aptitude test, with each text displayed for 120s and followed by comprehension questions. During the experiment, brain waves were recorded with a 24-channel electroencephalogram setup (Neurofax JE120A, 1kHz), and chin-rest-stabilized eye movements were recorded with a calibrated, monitor-based eye tracker (Tobii XL120, 120Hz). Each text contained 250 Korean words, and each syllable subtended 0.5deg visual angle. Three slides were read with blue-filtering lenses (transmittance 0% below 390nm, HOYA), and three lights with normal vision (with counter-balanced order).

Results: Analyses used non-parametric tests in Matlab for the normal and filtered conditions on questionnaire performance, eye movement measures, and EEG band power extracted at standard frequency bands. There was no significant difference in performance (p=.578). For eye movements, the filtered condition had significantly fewer saccades per slide (244 vs 301) with longer duration (244ms vs 213ms) and length (4.1deg vs 3.6deg) (all p<.001, Fig.1). EEG analysis showed significant decreases in alpha power and increases in delta power (Fig.2) for several sites in the filtered condition.

Conclusions: Although we found no performance differences, several frontal EEG sites involved in attentional processes were affected by filtering, suggesting increased levels of attention. Similarly, participants made fewer and longer saccades in the filtered condition, confirming a more efficient processing of the text information. These results demonstrate for the first time clear physiological effects of blue-filtering lenses even for short usage durations.

Fig.1 Eye movement measures for normal and filtered conditions including p-value

Fig.2 Significant sites for alpha-decreases (red) and delta-increases (green)

Commercial Relationships: Hyongsok Ryu, None; Christian Wallraven, None