The role of eye oscillations in determining visual acuity in infantile nystagmus

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Purpose: Controversy exists regarding the role of eye oscillations in degrading visual acuity in infantile nystagmus (IN). These have important implications for treatments aimed at improving vision in IN by reducing nystagmus. We take advantage of changes in nystagmus occurring in IN when maintaining different gaze angles to explore within- and between-subject differences in nystagmus in relation to visual acuity (VA). The effect of retinal deficits were also compared using optical coherence tomography (OCT).

Methods: Nystagmus (EyeLink, SR Research) and distance VA were recorded at 7 different horizontal gaze angles (at 10° intervals) in 46 participants with IN. Nystagmus intensity and expanded nystagmus acuity function (NAFX) were calculated for each gaze angle. Only participants with nystagmus intensity ranges >33.3% of mean intensity / NAFX were included (16 Idiopathic, 21 albinism, 6 retinal disease). Foveal hypoplasia was assessed using OCT B-scan images through the foveal center. Regression analysis was used to estimate within-subject measures of r, slope and intercept for each participant. Linear mixed models were used to explore within- and between-subject factors by including mean intensity or NAFX in the model.

Results: Between-subject measures (i.e. mean) of intensity and NAFX were not significant predictors of VA in statistical models for any of the three disease groups (p>0.1). In contrast, within subject repeated measures of intensity and NAFX measures were mostly significant (p=0.001 and 0.15 for idiopathies, 0.001 and 0.001 for albinism, 0.06 and 0.03 for retinal diseases for intensity and NAFX, respectively). However, individual slopes were shallow and showed a wide degree of variation (e.g. mean±SD=0.036±0.029 and 0.037±0.076 change in logMAR lines for every 1°/s change in nystagmus intensity, for idiopaths and albinism, respectively).

Conclusions: We find that within-subject changes in nystagmus intensity and foveation are strongly associated with VA concluding that nystagmus oscillations can play a role in degrading VA. However, slopes of within subject nystagmus measures show high variability with average values indicating that a large change in nystagmus is necessary to effect a relatively small change in VA (e.g. in idiopathies and albinism >25°/s mean difference in intensity is required to cause a change of 1 logMAR line, where the mean intensity = 18°/s)

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Electrical Stimulation of the rostral Superior Colliculus in Strabismic Monkeys alters Strabismus Angle

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Purpose: Disruption of binocular vision during the early critical period leads to eye misalignment in humans and in macaque monkey models. A recent study in normal monkeys has demonstrated vergence related activity in the rostral part of the Superior Colliculus (SC) and electrical stimulation in this area leads to divergence and convergence eye movements when looking at a near target. The purpose of our study was to determine the role of the rostral Superior Colliculus in maintaining eye misalignment in strabismic monkeys.

Methods: Three juvenile optical prism-reared strabismic monkeys previously trained in oculomotor tasks were used as a model of developmental strabismus in this study. Electrical stimulation was delivered to the intermediate and deep layers of the rostral Superior Colliculus via the recording microelectrode (400Hz, 0.5s duration, 20-50uA). Scleral search coils were used to record movements of both eyes. The goal of the analysis was to examine changes in alignment and conjugacy of saccades during electrical stimulation.

Results: Electrical stimulation in the rSC resulted in small amplitude (<5deg) staircase saccades with both horizontal and
vertical components as predicted from the topographic map within the Superior Colliculus. Electrical stimulation of rostral sites also resulted in changes in horizontal strabismus angle, i.e., a shift towards exotropia/esotropia (4/6 sites divergent change; 2/6 sites convergent change). Although electrical stimulation frequently leads to saccades with both horizontal and vertical components, i.e., oblique saccades, there was minimal change in vertical misalignment. The change in misalignment was due to a combination of disconjugate saccades and post-saccadic drift. The saccade disconjugacy was relatively small compared to the change in misalignment in 4/6 sites (ratio of amplitude of saccade disconjugacy to change in alignment < 0.3). Further saccade disconjugacy and the final change in misalignment were sometimes in opposite directions and not consistently related to the amplitude of the saccade.

**Conclusions:** Electrical stimulation of rostral Superior Colliculus of strabismus monkeys produces a change in horizontal eye alignment and disconjugate saccadic eye movements. The mechanisms for saccade disconjugacy and change in alignment due to rSC stimulation may be different.

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**Congenital and Acquired Exotropia: Underlying Mechanisms**

**Purpose:** To determine the rate of deterioration of intermittent exotropia (IXT) in children without treatment over 3 years.

**Methods:** 183 children 3 to 10 years of age with previously untreated IXT and near stereoacuity of 400 arc sec or better were randomly assigned to an observation group as part of a randomized trial. Observation was defined as no IXT treatment other than refractive correction for 3 years unless deterioration criteria were met at 3 months, 6 months, or 6 month intervals thereafter until 3 years post-randomization. Protocol-allowed exceptions for starting treatment were overwhelming social concern, debilitating diplopia, and/or failure to maintain stereoacuity age norms. The primary outcome was deterioration by 3 years, defined as achieving a motor criterion (constant XT of 10pd or greater at distance and near) or a near stereoacuity criterion (decrease of 2 octaves or more from best previous measure), assessed by a masked examiner. For analysis, participants were also counted as having deteriorated if they were prescribed any treatment other than refractive correction without first meeting motor or stereoacuity deterioration criteria. The cumulative probabilities of meeting deterioration criteria by 1, 2, and 3 years and 95% confidence intervals (CI) were calculated using Kaplan-Meier survival analysis.

**Results:** Of the 183 participants, 151 (83%) completed the study. The cumulative probability of deterioration was 9% (95% CI = 5% to 14%) by 1 year, 14% (95% CI = 10% to 21%) by 2 years, and 15% (95% CI = 10% to 22%) by 3 years. Of the 25 cases of deterioration by 3 years, 2 had constant XT 10pd or greater at distance and near, 11 had a near stereoacuity decrease of 2 octaves or more from the best previous measure, and 12 started treatment without meeting motor or stereoacuity deterioration criteria (8 were protocol-allowed exceptions). The cumulative probability of meeting the motor or stereoacuity deterioration criteria by 3 years was 8% (95% CI = 5% to 13%).

**Conclusions:** Over a 3-year period, deterioration of IXT is uncommon among children 3 to 10 years of age with IXT who are observed without treatment. These data on the natural history of childhood IXT provide an important new context for discussions of management between parents and eye care providers.

**Commercial Relationships:** Susan A. Cotter, None; Brian G. Mohney, Daniella L. Chandler, None; Jonathan M. Holmes, David B. Petersen, Raymond T. Kraker, David K. Wallace, Marshall B Ketchum University, Fullerton, CA; Mayo Clinic, Rochester, MN; Jaeb Center for Health Research, Tampa, FL; Mayo Clinic, Rochester, MN; Rocky Mountain Eye Care Associates, Salt Lake City, UT; Duke Eye Center, Durham, NC.

**Purpose:** To determine the rate of deterioration of intermittent exotropia (IXT) in children without treatment over 3 years.

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Magnetic Resonance Imaging (MRI) Demonstrates Vergence Compensation of Strabismus By Differential Compartmental Mechanisms

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**Purpose:** Differential compartmental function of extraocular muscles (EOMs) has been demonstrated by MRI during normal adduction, convergence, & vertical fusional vergence (VFV). We asked how vergence controls intermittent strabismus.

**Methods:** We studied 1 patient with 25° intermittent exotropia (IXT), and another with 3° intermittent hypertropia (IHT). Surface coil MRI was repeated in fusing & deviated conditions with 1 eye aligned, as confirmed by optic nerve position on MRI. Contractility, indicated by change in posterior partial volume (PPV), was analyzed in medial (equatorial insertion, torsion) & lateral (posterior insertion, vertical) SO compartments, superior & inferior horizontal rectus compartments, and medial & lateral inferior rectus (IR) compartments.

**Results:** Distant target fusion in IXT was accomplished by 40% increase in PPV in the inferior compartment of the converging medial rectus (MRI), more than the 28% increase in the superior compartment, with uniform relaxation of both lateral rectus (LR) compartments. In the converging eye, PPV decreased 29% in the medial (torsional) SO compartment, without change in the lateral compartment. In the aligned eye, PPV decreased 20% in the lateral (vertical) SO, without change in the medial SO. There were no other significant PPV changes in other EOM compartments in either eye. In normal subjects, MRi has less contractility in adduction than superior compartment MRs in adduction, but similar in convergence. Near target fusion in IHT was accomplished in the infraducting eye by 11% PPV increase in the inferior rectus (IR) lateral compartment & 16% increase in the SO lateral compartment. In the aligned eye there was a 24% PPV decrease in the superior medial rectus (MR) compartment, and a 12% increase in the superior rectus. There were no other PPV changes in EOM compartments in either eye. This contractility is larger and different from normal VFV, where the LR superior compartment and IR medial compartment contract selectively in the infraducting eye.

**Conclusions:** Fusional vergence compensating for intermittent horizontal & vertical strabismus involves supranormal differential compartmental EOM patterns distinct from normal adduction, convergence, infraduction, & VFV (Demer and Clark, *J. Neurophysiol.* 113:2150-63, 2015). Surprisingly, SO participates differentially in compensation of both IHT & IXT, while MR does so in IHT.

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Altered Functional Connectivity of Primary Visual Cortex in Adult Comitant Strabismus: A Resting-State Functional MRI Study

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**Purpose:** The aim of this study was to examine the functional connectivity between primary visual cortex and other cortical areas during rest in normal subjects and patients with comitant strabismus using functional magnetic resonance imaging.

**Methods:** Prospective, observational study. Ten patients with comitant exotropia and eleven matched healthy subjects underwent resting functional magnetic resonance imaging (fMRI). Resting-fMRI was performed using a 3.0T MR scanner. fMRI data were analyzed using Statistic Parametric Mapping software (SPM2, London, UK) and Analysis of Functional Neuroimages software (AFNI).

**Results:** The resting-state functional connectivities of primary visual cortex were calculated in each group and compared between strabismic and normal control group. Compared to normal controls, functional dysconnectivity between primary visual cortex and other cortical areas exists in patients with comitant strabismus, especially the connectivity with visual cortex (BA19) and other oculomotor regions, such as frontal eye field (BA6) and cerebellum.

**Conclusions:** The fMRI results suggest that on-going and permanent cortical changes occur in patients with comitant strabismus. Disrupted brain functional connectivities are associated with abnormal eye movement and loss of stereopsis.

**Commercial Relationships:** Xiaohe Yan, None; Xiaoming Lin