Effects of Extraocular Muscle Surgery on 15 Patients With Oculo-Cutaneous Albinism (OCA) and Infantile Nystagmus Syndrome (INS)

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• PURPOSE: **The purpose of this report is to characterize the clinical and electrophysiological effects of extraocular muscle surgery in 15 patients with oculo-cutaneous albinism (OCA) and infantile nystagmus syndrome (INS). Our hypothesis is that surgery on the extraocular muscles of patients with OCA and INS changes their nystagmus and their visual function.**

• DESIGN: **Interventional, prospective, cohort, noncomparative case series.**

• METHODS: **All 15 patients had surgery on all four virgin horizontal recti; three for strabismus alone, three for nystagmus alone, five for an eccentric gaze null zone alone, and four for an eccentric gaze null zone plus strabismus. All patients have been followed for at least six months. All 15 patients had the subjective outcome measure of pre- and postoperative binocular best optically corrected acuity (BBOCA). Objective outcome measures included anomalous head posture (AHP) in nine patients, eye movement recording measures of expanded nystagmus acuity function (NAFX) in 10 patients, null zone position (NUZP) and null zone width (NUZW) in 10 patients, and foveation time (FOV) in nine patients.**

• RESULTS: **The results are summarized as follows; BBOCA increased 0.1 LogMar or greater in 14 of 15 patients. In those operated on for an AHP with or without associated strabismus the AHP improved significantly (*P* < .01 for all). The NAFX, NUZP, NUZW, and FOV measured from eye movement recordings showed persistent, significant increases in all patients (*P* < .01 for all).**

• CONCLUSIONS: **This report adds to the evidence that surgery on the extraocular muscles in patients with INS has independent neurologic and visual results. (Am J Ophthalmol 2004;138:978–987. © 2004 by Elsevier Inc. All rights reserved.)**

Accepted for publication July 13, 2004.

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ALBINISM IS NOT A SINGLE ENTITY BUT REPRESENTS a heterogeneous group of inherited disorders of pigmentation. Despite a wide variety of manifestations, all forms of albinism are characterized by varying degrees of several ocular features, including: nystagmus, photophobia, reduced visual acuity, and a lack of stereopsis.[1–3] Involuntary ocular oscillations that begin in infancy and are associated with OCA have been classified in many ways, resulting in some confusion and disagreement among clinicians, physiologists, psychologists, and bioengineers.[1,4,5] The recently sponsored National Eye Institute Workshop on Classification of Eye Movement Abnormalities and Strabismus (CEMAS) has attempted to resolve some of these issues.[5] The CEMAS working group publication outlining a definition of INS is used in this study. Nystagmus in infancy may also be attributable to structural disease of the brainstem and cerebellum, much the same as nystagmus in adulthood.[4–7,8] Other clinical characteristics with variable association include: increased intensity with fixation, decreased intensity with sleep; variable intensity in different positions of gaze (null positions); changing direction in different positions of gaze (neutral positions); decreased intensity with convergence (damping); anomalous head posturing; strabismus; and the increased incidence of significant refractive errors. Infantile nystagmus syndrome is the predominant type of nystagmus associated with albinism.[1,9]

Patients with INS and OCA usually have significantly diminished visual acuity, regardless of whether they have associated visual sensory defects. The visual acuity may be inversely related to the intensity of the nystagmus in

  0002-9394/04/$30.00
doi:10.1016/j.ajo.2004.07.029

TABLE 1. Patient Characteristics

PT No.	Age	F/U	Diagnosis	AHP	Surgery
1	43.1	25	OCA/amblyo/OND	Yes	N + S
2	16.6	19	INS/OND/OCA	No	T
3	31.5	36	INS/albinism/on hypoplasia	Yes	N
4	42.6	28	INS/OCA/amblyo OS/ONH	Yes	N + S
5	38.6	16	INS/OND/OCA	Yes	N
6	4.1	22	INS/OCA/OND	Yes	N
7	13.0	12	INS/OCA/Astig/ONH/amblyo OS	Yes	N + S
8	15.0	13	INS/OCA/Astig/ONH/amblyo OS	No	S
9	6.0	6	INS/OCA/Astig/ONH/amblyo OD	Yes	N + S
10	5.0	6	INS/OCA/Astig/ONH	No	S
11	2.5	12	INS/OA	Yes	N
12	8.5	12	INSOA/CP	No	T
13	4.0	14	INS/OCA	Yes	N
14	3.5	12	INS/OCA/SOD/ONH/amblyo OD	No	S
15	4.0	15	INS/OCA	No	T

PT No. = patient number; Age = age in years at time of surgery; F/U = follow up in months; INS = infantile nystagmus syndrome; AHP = anomalous head posture; amblyo = amblyopia; OND = optic nerve dysplasia; SOD = septo-optic dysplasia; OA = ocular albinism; ONH = optic nerve hypoplasia; Astig = astigmatism. N = eccentric Null zone surgery; S = strabismus surgery; T = tenotomy surgery alone; N + S = eccentric null zone plus strabismus surgery.

patients whose ocular motor system can utilize a reduction in nystagmus intensity and in whom no other sensory defect is present (for example, foveal, or optic nerve hypoplasia). In such cases, a decrease in the nystagmus may produce an increase in visual function.[1,9–12]

One of the most common features of the INS waveforms is the presence in segments of the slow phase wherein the eyes remain at or close to the point of desired fixation with little or no movement.[13–15] These "foveation periods" have been shown to enhance visual acuity. The accuracy and duration of foveation has been directly linked to visual acuity.[13–15] If these periods can be lengthened or increased by the patient (adaptation) or by therapeutic interventions (that is, medicines, surgery, contact lenses, biofeedback) the patient's visual acuity may be increased.

There is no cure for many of the visual sensory system deficits that are associated with albinism and INS, that is, chiasmal, foveal, and optic nerve dysplasia. One goal of any treatment directed specifically at the INS should be to reduce the intensity of the nystagmus, thereby increasing the potential for more gaze angles during which foveation could take place, increasing foveation periods in the null position, or lowering slow-phase velocities during foveation periods. All these changes would act to increase the patient's visual acuity or other visual functions. This applies both to patients with and without associated sensory-system defects. These benefits were consistently observed in patients who underwent the Anderson-Kestenbaum surgical procedure (resection-recession surgery) although the procedure's primary purpose is to decrease torticollis in patients whose nystagmus intensity is least in gaze angles away from primary position.[16–19] It was originally designed to straighten these patients' face or head turn, which they were performing to maximize their visual acuity.[19–22]

The purpose of this report is to characterize clinical and electrophysiological effects of extraocular muscle surgery for numerous indications, that is, strabismus and/or head posturing in a prospective, cohort, noncomparative case series, of 15 patients with INS associated with oculo-cutaneous albinism.

MATERIALS AND METHODS

ALL TESTING WAS APPROVED BY THE INSTITUTIONAL REview Boards of The National Eye Institute, The National Institutes of Health, and Columbus Children's Hospital, Columbus Ohio. All procedures observed the declaration of Helsinki and informed consent/assent was obtained on all patients/families.

• **INCLUSION CRITERIA:** The patients who are the subject of this report had: Family and/or patient signed informed consent and assent; clinically diagnosed and electrophysiologically confirmed infantile nystagmus syndrome (old congenital nystagmus); clinically diagnosed oculo-cutaneous albinism (diffuse skin and hair hypopigmentation, diffuse iris transillumination, foveal and or optic nerve dysplasia, fundus hypopigmentation, strabismus, and anomalous VER showing predominantly crossed afferent visual system); best corrected binocular acuity $\geq$ to 20/200 (Log Mar 1.0); no current medicines that could influence the ocular motor system and no prior surgery on the extraocular muscles before the surgery performed by the author (R.W.H.); prospectively collected data for at least six months; optotype visual acuity testing (Early Treatment of Diabetic Retinopathy Study [ETDRS] or Amblyopia Treatment Study Protocol, that is, single surrounded HOTV);[23] and no age or gender requirements but were able to cooperate for visual acuity and electrophysiologic testing.

• **OUTCOME MEASURES:** The outcome measures for this study included: Pre- and postoperative (3 months) binocular best optically corrected (BBOC) acuity (15 patients); pre- and postoperative (6 to 28 months, Table 1) anomalous head posture (AHP) (9 patients); pre- and postoperative expanded nystagmus acuity function (6 to 28 months, Table 1) (NAFX) (10 patients); pre- and postoperative null zone position (6 to 28 months, Table 1) (NUZP) (10 patients); pre- and postoperative null zone width (6 to 28 months, Table 1) (NUZW) (10 patients); and pre- and postoperative foveation time (6 to 28 months, Table 1) (FOV) (9 patients).

• **CLINICAL EXAMINATION PROCEDURES:** All 15 patients underwent the following routine clinical evaluations. Visual acuity testing was performed with refraction in place, both binocularly and monocularly, using the EDTRS chart or the amblyopia treatment study single, surrounded, HOTV optotype protocol.[23] Binocular function was assessed using the Worth 4-dot test at distance and near with the Randot® preschool stereoacuity test. Ocular motor examination also included a determination of heterophoria/tropia at distance (6 m) and near (33 cm) in all diagnostic positions of gaze using the simultaneous prism cover test and alternate prism cover test. Versions and ductions were examined and color vision was tested using Ishihara color plates. The ocular examination also included cycloplegic refraction, tonometry, slit-lamp and ophthalmoscopic examination of the anterior and posterior segments, and fundus photographs when pathology was observed. Clinical evaluation of the ocular motor oscillations included examination and measurement of any anomalous head posture and changes in the oscillation in primary position, at near, and in diagnostic positions of gaze under monocular and binocular conditions. Strabismus was defined as any hetereotropia in primary position. An eccentric null position was defined both clinically and by eye movement recordings (see below). There was a "significant" head position if one was observed during fixation at distance and/or measured by eye movement recordings, at $\geq$10 degrees horizontally, $\geq$6 degrees vertically, or $\geq$6 degrees torsionally.

• **OCULAR MOTILITY RECORDINGS:** All 15 patients had eye movement recordings. The presentation of stimuli and the acquisition, display, and storage of data were controlled by a series of PCs using standard Microsoft and Matlab software and specially designed and created software such as Visual and EXperimentation (VEX) and a Real-time EXperimentation (REX) packages.

The horizontal and vertical eye movement recordings were made using an IR reflection method; the system bandwidth was 0 to 500 Hz. The signals were calibrated (using the end of the fast phase during the nystagmus cycle) at the beginning of the recording session by having the patient fixate small target lights located on a screen at a distance of 1 m. Data were sampled at 500 Hz to 1 kHz.

Calibration was accomplished monocularly by placing an opaque trial frame occluder in the eye movement recording system over one eye and using 3 degree pictures or stationary 1 degree targets presented on a screen at a distance of 1 m from the patient. The patients were seated with their head stabilized by means of a chin cup and headrest and instructed to look at targets at $\pm$15 degrees or $\pm$20 degrees horizontally and $\pm$10 degrees vertically. After calibration all recording sessions followed the same protocol. The patient was required to fixate between 0, $\pm$5, $\pm$10, $\pm$15, and $\pm$20 degrees with the right eye, left eye, and both eyes. The patient was then asked to make binocular step vergence responses from distance to near. Lastly fixation at 0 degrees with both eyes was accomplished for 10 minutes. (To rule out asymmetric (a) periodic alternating nystagmus).

The types of waveforms present were classified according to the previously described 12 waveforms associated with horizontal INS.[15] Because of the sensitivity of these recording techniques, foveation periods and fast and slow phases could be identified during all recording sessions. All eye movement data were analyzed off line. Mathematical and statistical analysis was done on a computer spreadsheet.

• **EXPANDED NYSTAGMUS ACUITY FUNCTION (NAFX):** This measure is defined in the following way. The NAF, and later the NAFX, originated from the nystagmus foveation function (NFF).[24] The nystagmus acuity function (NAF) was developed to provide an objective measure of the quality of a nystagmus waveform, to predict best-corrected visual acuity in INS patients under benign conditions, and to assess the effects of treatments on the INS oscillation. The NAF is a function that predicts the best-corrected visual acuity possible in subjects with nystagmus, based on objective measurements from eye movement recordings of their waveform characteristics during fixation of a small light-emitting diode. It combines the foveation time/cycle and the standard deviations of both eye position and velocity during target foveation into a function that is linearly proportional to best-possible visual acuity. The NAFX is an attempt to mathematically predict optimum visual potential, and is a "theoretical" variable with only indirect clinical application.

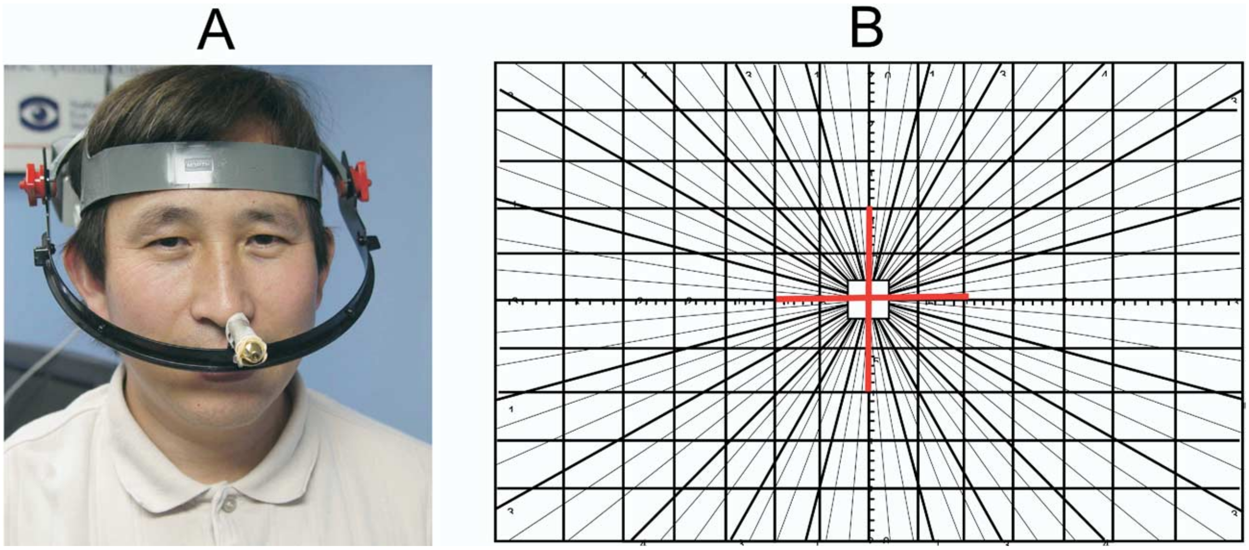

FIGURE. Laser-3 Dimensional Head Posture Measurement System. The system consists of two parts. A headband with a 2 mW red laser (projecting a cross) situated in the sagittal and axial center of rotation of the head (left). A screen positioned 1.5 m from the patient with variable size linear optotypes of 3 lines presented in the center of the screen (right). The periphery of the screen is marked in degrees by lines running vertically, horizontally and torsionally. With the patient's best correction in place they are seated 1.5 m from the screen and asked, under binocular conditions, to read the linear optotypes of decreasing size (increasing spatial frequency) in the center of the screen. The tester then reads directly off of the screen the laser cross position. This cross and the patient's resultant head posture are recorded on a preprinted report form.

The NAFX incorporates the time intervals of foveation periods and their position and velocity standard deviations into a measure of the quality of an INS waveform (that is, how likely it was to allow good acuity). It assesses the upper limits of the acuities of individuals with poor foveation capabilities. Neither the NAFX nor the NAF, which it includes, are dependent on the methodology of data collection (for example, infrared, video, or magnetic search coil), the type of nystagmus (INS, latent/manifest latent nystagmus, and so on), or the particular nystagmus waveform. NAFX values are between 0 and 1 with a value of 1 = 20/20 Snellen Acuity and a value of 0 = no light perception.[24,25]

In this study, NAFX values calculated for fixation intervals from each recording session were averaged and it is those average NAFX values that appear in the data. All eye movement data were analyzed off-line by manual selection of fixation periods with computer assisted NAFX calculation on a computer spreadsheet.

• **FOVEATION TIME (FOV):** FOV was defined as the period of time during the slow phase immediately after a fast phase (or breaking saccade) during the nystagmus beat (cycle). The FOV is a relatively constant eye position that occurred during an oscillatory cycle usually followed a fast phase, and lasted for at least 20 ms. Those foveation periods present in the preferred eye during five minutes of primary position viewing under binocular conditions were included in data analysis. A minimum of 39 cycles that contained foveation periods was used to calculate the "average" foveation period for each patient. All eye movement data were analyzed off-line by manual selection of FOV periods and mathematical and statistical analysis accomplished on a computer spreadsheet.

• **NULL ZONE POSITION (NUZP):** The NUZP was defined oculographically under binocular viewing conditions, using data from the preferred eye during the eye movement protocol above, as the absolute position (in degrees of gaze) where the nystagmus intensity (amplitude × frequency) was least and foveation time best (those slow phases with velocity least and closest to the target position) over all tested positions of gaze. All eye movement data were analyzed off-line by manual selection of NUZP and mathematical and statistical analysis accomplished on a computer spreadsheet.

• **NULL ZONE WIDTH (NUZW):** The NUZW was defined oculographically, under binocular viewing conditions, using data from the preferred eye during the eye movement protocol above, as the expanse of gaze (in degrees) where the nystagmus intensity and foveation characteristics for any given patient were within 20% of the NUZP characteristics. The "20%" figure was chosen as a conservative estimate of NUZW and reflects ours and other authors' long-term analyses of eye movement data showing that nystagmus intensity, foveation, and best acuity are affected when increases greater than 20% to 25% are observed.[1,13,18,26,27] All eye movement data were analyzed off-line with computer assisted calculation. Mathematical and statistical analyses were done on a computer spreadsheet.

• **ANOMALOUS HEAD POSTURE (AHP) MEASUREMENTS:** Measurement of the patient's head position was recorded using a Laser 3-Dimensional Head Posture Measuring System (Figure). The system consists of two parts. A headband with a 2 mW red laser (projecting a cross) situated in the sagittal and axial center of rotation of the head. A screen positioned 1.5 m from the patient with variable size linear optotypes of 3 lines presented in the center of the screen. The periphery of the screen is marked in degrees by lines running vertically, horizontally, and torsionally. The laser/headband is positioned on the patient's head with the laser in the center of rotation of the head, without obstruction of the visual axis. With the patient's best correction in place, they are seated 1.5 m from the screen and asked, under binocular conditions, to read the linear optotypes of decreasing size (increasing spatial frequency) in the center of the screen. The tester then reads directly off of the screen the laser cross position. This cross and the patient's resultant head posture are recorded on a preprinted report form.

• **STATISTICAL ANALYSIS:** For the visual acuity measure, a change score was calculated for each patient as the difference between the postsurgery (three months) and presurgery score. The distribution of this change score was evaluated and a mean and 95% confidence interval for the mean was calculated. A Wilcoxon signed-rank test was performed to evaluate whether or not there was a significant shift in the distribution of visual acuity scores before vs after surgery. Because of the small sample sizes and the potential for outliers to produce large differences in means when comparing between two groups, and because of the unknown distribution of the underlying data, nonparametric statistical tests (which are based upon no assumption on the distribution of the data) were used. These test statistics evaluated whether or not there was a shift in the distribution of scores before vs after surgery (Wilcoxon signed rank test), or whether or not there was a shift in the distribution of change scores. These are analogous to the paired samples *t* test and independent samples *t* test, both of which were performed on the remaining outcome measures. These tests are based on ranks of the data and thus are not as sensitive to potential outliers that may affect the test statistic if we were to use statistics based on the mean. Outcome data reported in this study included preoperative (within 1 week) and postoperative 6 to 28 months for all data (Table 1), except acuity data that was performed at three months postoperatively to try and negate the age effect on acuity.

TABLE 2. Pre-operative and 3-Month Post-operative Binocular Best Optically Corrected LogMar Visual Acuity in all 15 Patients

PT No.	Pre-Op	Post-Op
1	0.6	0.6
2	0.7	0.5
3	0.7	0.6
4	0.9	0.7
5	0.98	0.7
6	0.6	0.4
7	0.6	0.5
8	0.8	0.6
9	0.6	0.4
10	1	0.7
11	1	0.9
12	0.9	0.6
13	0.5	0.3
14	0.6	0.5
15	0.7	0.4
AVE	0.7	0.6
SD	0.2	0.1
P =	.000001	

Shows the best corrected, binocular, LogMar acuity values pre- and post-operatively. LogMar = log of the minimum angle of resolution; Pre-Op = preoperatively; Post-Op = postoperatively; 1 = 20/200; .98 = 20/160; 0.8 = 20/125; 0.7 = 20/100; 0.6 = 20/80; 0.5 = 20/63; 0.4 = 20/50; 0.3 = 20/40; 0.2 = 20/32; 0.1 = 20/25; 0 = 20/20. AVE = average; SD = standard deviation; *P* = pre- and post operative group difference significantly at *P* = .000001.

RESULTS

FIFTEEN PATIENTS WITH TYPICAL CLINICALLY DIAGNOSED OCA are the subjects of this report. Patients included in the study ranged in age from 2.5 to 43 years, with an average age of 16 years. Eight patients were male. All patients had coexisting strabismus; nine had a clinically significant anomalous head posture (AHP) (Table 1). Surgery was performed for strabismus alone in three patients, for an eccentric null position alone in five patients, for strabismus plus an eccentric null position in four patients, and for the nystagmus only in three patients (Table 1). Variable amounts of resections and recessions were performed on all four horizontal recti (two in each eye) in the first three groups of patients, while in the "nystagmus" only group, all four horizontal recti (two in each eye) were cut at the tendon-scleral junction and immediately reattached at the original insertion (tenotomy). Follow-up for all patients was at least six months after surgery with a mean of 16.5 months for all patients. There were no postoperative complications. One patient in the strabismus surgery group required repeat extraocular muscle surgery after one year of follow up because of a consecutive strabismus.

TABLE 3. Effect of Surgery in Degrees at Maximum Follow-up on Head Position in the Nine Patients Who Had Head Postures

PT no.	Pre-Op AHP	Post-Op AHP
1	15	5
3	15	5
4	20	6
5	25	4
6	30	7
7	33	2
9	30	5
11	40	7
13	22	5
AVE	25.6	5.1
SD	7.6	1.4
P =	.0000684	

Shows the average preoperative (Pre-Op) and post-operative (Post-Op) change in anomalous head posture in degrees in 9 OCA patients in whom this was measured with the L3D before and at maximum follow up (See Figure) after extraocular muscle surgery.

TABLE 4. Effect of Surgery at Maximum Follow-up on NAFX in the Ten Patients Who Had Their NAFX Measured

PT No.	Pre-NAFX	Post-NAFX
1	0.332	0.506
2	0.252	0.458
3	0.388	0.502
4	0.463	0.744
5	0.338	0.441
6	0.436	0.586
7	0.555	0.765
8	0.336	0.398
9	0.379	0.664
10	0.380	0.697
AVE	0.386	0.576
SD	0.076	0.121
P =	.00006	

Shows pre- and post-operative (at maximum follow-up, see Table 1) change in the expanded nystagmus acuity function (NAFX). PT no. = Patient number; NAFX = expanded nystagmus acuity function; Pre = preoperative; Post = postoperative (maximum follow-up); AVE = average; SD = standard deviation; P = significantly different at $P < .00006$. NAFX values are between 0 and 1 with a value of 1 = "potential" of 20/20 vision.

• **PRE- AND POSTOPERATIVE BINOCULAR BEST OPTICALLY CORRECTED (BBOC) ACUITY:** To reduce investigator bias all 15 patients had their visual acuity checked objectively by an acuity tester who was certified using the ETDRS and single surrounded HOTV optotype testing as part of separate multicenter clinical trials not directly related to this study.[23] Acuity outcome data reported in this study included preoperative (within one week) and postoperative (at three months after surgery) BBOC acuity. We used three month postsurgical acuity data to allow for complete healing postoperatively, and to avoid age related increase in acuity in the younger age group because of visual system maturation. Any change in acuity measured in this way was presumably attributable to the surgical intervention and not an age related change, a change in refraction, or learning effect. Acuity is reported as the log of the minimal angle of resolution (LogMar) so that statistical analysis is more easily performed. BBOC acuity is a more accurate representation of a nystagmus patient's visual acuity as a "person". As a group, monocular acuity is often worse than binocular acuity. This is attrbutable to the presence of both a "latent" component and increased nystagmus intensity (amplitude × frequency) under monocular conditions. Table 2 shows the absolute change in LogMar of each of the 15 patients after surgery. The average BBOC acuity as group was 0.7 (20/125) preoperatively and significantly different at 0.6 (20/100) postoperatively (Table 2, $P = .000001$). One patient had no improvement, 14 improved 0.1 LogMAR or greater, 10 patients improved 0.2 LogMar, and 4 patients improved 0.3 LogMar. There were no significant differences within the four surgical groups (that is, tenotomy, null zone, and strabismus plus null zone or strabismus alone (Table 2).

• **PRE- AND POSTOPERATIVE ANOMALOUS HEAD POSTURE (AHP):** Nine of 15 patients had an AHP with measurements made pre- and postoperatively using the Laser 3-Dimensional Head Posture Measuring System (Table 3). Six of these nine patients had a preoperative multiplanar (that is, face turn plus chin up/down) anomalous head posture. The only plane of deviation for which surgery was planned was the horizontal deviation. This was accomplished by operating on all four horizontal recti. The average position of the horizontal plane of deviation preoperatively was 25.6 degrees and this decreased 20.5 ± 7.6 degrees postoperatively to 5.1 ± 1.4 degrees ($P = .00006$, Table 3) Of the six patients with a multiplanar (face turn plus chin up/down) deviation preoperatively, one had a postoperative chin up/down deviation after the "horizontal" surgery. There were no differences within the four surgical groups.

• **PRE- AND POSTOPERATIVE EXPANDED NYSTAGMUS ACUITY FUNCTION (NAFX):** Ten of the 15 patients had their NAFX calculated preoperatively and at least six months postoperatively (Table 4). One patient in this group had tenotomy alone, three patients had null zone surgery alone, four had nystagmus plus strabismus surgery, and two patients had strabismus surgery alone. Each patient had his or her NAFX values calculated from their preferred eye during continuous fixation in primary posi-

TABLE 5. Effect of Surgery on Null Zone Position (NUZP) and Null Zone Width (NUZW) (Both in Degrees)

PT No.	NUZW Pre-Op	NUZW Post-Op	Age	PT No.	NUZP Pre-Op	NUZP Post-Op
1	6.0	29.0	13.0	1	15.0	5.0
2	8.0	36.0	15.0	2	11.0	6.0
3	10.0	35.0	6.0	3	7.0	4.0
4	7.0	28.0	5.0	4	28.0	4.0
5	5.0	15.0	2.5	5	15.0	5.0
6	12.0	29.0	8.5	6	28.0	10.0
7	8.0	16.0	4.0	7	35.0	7.0
8	6.0	20.0	15.0	8	22.0	5.0
9	6.0	18.0	4.0	9	23.0	8.0
10	4.0	14.0	46.0	10	4.0	4.0
AVE	7.2	24.0	11.9		18.8	5.8
SD	2.4	8.4	13.2		10.0	2.0
P =	.00004			*P* =	.00143	

PT No. = patient number; age = age of patient in years; Pre-Op = preoperative; Post-Op = postoperative (maximum follow-up, see Table 1); NUZP = null zone position in degrees; NUZW = null zone width in horizontal degrees; AVE = average; SD = standard deviation; *P* = significantly different at *P* = value.

tion. Table 4 shows the average NAFX values pre- and postoperatively for the 10 patients in whom the NAFX was calculated. All but one patient showed an immediate, persistent and significant rise in the NAFX. The average NAFX values as a group increased significantly (P = .00006) from 0.386 SD 0.076 to 0.576 SD 0.121 (a potential increase of 2 Snellen lines) for the group. There were no statistical differences within the four surgical groups.

• **PRE- AND POSTOPERATIVE NULL ZONE POSITION NUZP AND NULL ZONE WIDTH (NUZW):** Ten of the 15 patients had their NUZP and NUZW measured and calculated from eye movement recordings preoperatively and at least six months postoperatively (Table 5). The age ranged from 2.5 to 43 years with an average of 11.9 ± 13.2 years. The average, largest direction, gaze NUZP was 18.8 ± 10 degrees from primary position preoperatively and this significantly improved (P = .00143) postoperatively in all patients to an average of 5.8 ± 2.0 degrees from primary position. The average, largest NUZW was 7.2 ± 2.4 degrees preoperatively and this significantly increased (P = .00004) to 24 ± 8.4 degrees postoperatively (Table 5). There were no statistically significant differences within the four surgical groups.

• **PRE- AND POSTOPERATIVE FOVEATION TIME (FOV):** Nine of the 15 patients had their FOV measured and calculated from eye movement recordings preoperatively and at 12 months postoperatively (Table 6). The average FOV was 225 ms ± 64 ms preoperatively and this significantly improved (P = .001) in all patients averaging of 442 ms ± 92 ms postoperatively (Table 6). There were no statistical differences within the four surgical groups.

DISCUSSION

WE CHOSE TO STUDY THE PATIENTS WITH OCA ALONE AS part of this report in an attempt to show that their unique

TABLE 6. Surgical Effect of Surgery on Foveation Time (in Milliseconds)

PT No.	Pre-Op FOV	Post-Op FOV
1	220.0	380.0
2	230.0	440.0
3	70.0	150.0
4	40.0	90.0
5	70.0	90.0
6	30.0	70.0
7	30.0	120.0
8	90.0	180.0
9	40.0	70.0
AVE	91.1	176.7
SD	78.7	138.0
P =	.00359	

Shows foveation times in milliseconds (see text) measured before and at least six months after extraocular muscle surgery in patients 1–9. PT no. = patient number; msec = milliseconds; Pre-Op = pre-operative; FOV = foveation time; Post-Op = postoperative. AVE = average; SD = standard deviation; *P* = significantly different at *P* = value.

visual sensory system could respond (in a positive way) to treatment of their ocular motor disorder (nystagmus). The results presented above, specifically regarding those patients with INS and associated OCA, may be summarized as follows: binocular, best-corrected LogMar visual acuity increased 0.1 LogMar or greater in 14 of 15 patients. All outcome measures showed a significant improvement after surgery. There were no significant differences among the varied indications for extraocular muscle surgery (null, tenotomy, strabismus, or strabismus and null) for any of the outcome measures in those outcome measures that were statistically tested. Patients 11 to 15 did not have their NAFX, NUZP, or NUZW studied, and patients 10 to 15 did not have their foveation times studied. The authors found that these first 9 to 10 patients were all that was necessary to statistically show that the respective measurements were effected in the OCA population.

Although numerous studies have described INS pathophysiology and its effect on the visual system, its etiology remains elusive. Defects involving the saccadic, optokinetic, smooth pursuit, and fixation systems as well as the neural integrator for conjugate horizontal gaze have been proposed.[1,4,10,28] Including genetic predisposition, many clinical conditions are associated with the INS oscillation, such as the OCA patients in this report. Regardless of the clinical association of OCA, nearly all patients with INS have infantile onset in common; we can deduce that this oscillation most likely to occurs in an immature ocular motor system.[3,13,29]

The relationship between Snellen visual acuity, nystagmus, and other sensory visual functions is complex in patients with OCA. The effect on vision of changing an OCA patient's nystagmus is related to a number of unknown, unpredictable variables including, but not limited to: patient age, underlying retina, optic nerve and optic pathway integrity, associated strabismus, amblyopia, uncorrected refractive errors, and associated central nervous system disease.[1,30–32]

Other aspects of visual functions have been reported to be affected in patients with OCA and INS, both with and without diagnosed sensory system deficits. These include contrast sensitivity, color vision, motion perception, temporal luminance, contour interaction, smooth pursuit, and OKN.[3,13]

The integrity of the afferent visual system may ultimately determine the mature clinical characteristics and waveform quality in any one patient.[27,33] One of the most common features of the INS waveforms is the presence of "foveation periods" segments of the slow phase wherein the eyes remain at or close to the point of desired fixation with little or no movement. Longer and more regular foveation periods have been shown to enhance visual acuity.[1,13,18,26,27] The accuracy and duration of foveation can be directly linked to visual acuity, especially in those INS patients in whom no other sensory system disease can be found. The NAFX is one such measure.[24,25]

Numerous treatments have been described for the ocular oscillations associated with INS with and without OCA. These include dietary manipulation, drugs, contact lenses, prisms, biofeedback, intermittent photic stimulation, acupuncture, transcutaneous vibratory or electronic stimulation of the face and neck, injection of botulinum toxin, and a variety of surgical procedures.[34] Excepting those treatments that directly improve visual acuity (spectacle and contact lens correction of refractive errors), all these treatments have in common a desired effect of reducing the nystagmus intensity directly or indirectly, allowing an increase in visual acuity. In a review of a total of 361 patients undergoing surgical repositioning of the eyes for congenital nystagmus from 21 reports in which vision was measured both preoperatively and postoperatively, 273 (76%) had improved vision after the surgery.[34] Most of these studies were retrospective reviews and did not use consistent or objective acuity measures before and after treatment of the nystagmus. The present study, showing an improvement in 0.1 or greater LogMar in this group of OCA patients after EOM surgery, is new data.

Surgery is usually indicated in patients with INS and an anomalous head posture because of an eccentric gaze null position, strabismus, or those who have good binocular function and whose nystagmus decreases and vision improves during convergence (convergence "damping" or "nystagmus blockage"). Those INS patients who have good binocular function, do not damp with convergence, or exhibit no eccentric null position are not normally surgical candidates. In 1953 Kestenbaum recommended surgery for an AHP on one eye, with surgery on the second eye after a period of stabilization.[20,21] Anderson, about this time, presented four patients with an AHP in whom he recessed the recti muscles in the direction of the slow phase of the nystagmus.[22] In both sets of patients, the head position and vision improved. Many authors have reported on series of patients on whom surgical repositioning of the extraocular muscles has improved head positioning, nystagmus intensity and vision.[4,16,17,30,35–38]

Artificial divergence surgery (bimedial rectus recession for convergence damping) combined with Anderson-Kestenbaum may simultaneously improve visual acuity and anomalous head posture and may result in fewer recurrences of head postures as compared with the Anderson-Kestenbaum surgery alone.[4,16,22,38,39] The surgical principles that guided treatment in the patients in this study were the following. All four horizontal recti were surgical addressed with combinations of resections and recessions in standard fashion to correct horizontal strabismus alone, an anomalous head posturing alone, or a combination of an AHP and strabismus. All four horizontal recti were addressed with insertion tenotomy and immediate reattachment at the original insertion (the Dell'Osso procedure) on those patients in whom there was no strabismus (deviation $\geq$8 prism diopters), AHP ($\geq$8 degrees), or eccentric gaze null position (≥10 degrees).[32,36,40]

Possible sources of error in this report, and the explanation of the results include chance, although all measures showed statistically significant changes. There was a chance that the patients selected are not representative of the population; in that the patients selected to complete measures on were different than those who do not have measures. Since there is no control group, it can never be certain how much of this improvement was because of surgery; however, from clinical experience, these measures do not usually improve acutely, on their own, thus likely improvement was as a result of the surgery.

The relationship between age and improvement could be confounded by the fact that younger patients may differ from older patients in some characteristics that may be related to improvement. We can never control this since this is not a randomized trial/scenario. The data collected on these patients support the hypothesis that surgical manipulation of the extraocular muscles in patients with oculographically diagnosed OCA and INS "improves" the oscillation and visual functions. There are measured increases in foveation periods and the NAFX. The subjective consequences of changing the nystagmus cannot be measured solely by high spatial frequency vision. Although patients will have absolute improvement in visual acuity, this is in the range of 1 to 3 Snellen lines. In many patients with low vision, this can make the difference between driving and not driving. Other "measures" of visual function are improved after surgery, and probably contribute to the visual "well-being" these patients report. These include vision in eccentric gaze, absolute recognition time, and improved binocular field (because of a more normal head posture). Other factors make relatively small changes, postoperatively hard to interpret, and include the normal variability of INS from day to day, and at different times of the day, as well as the effect emotional and psychological conditions have on its intensity.

Although physiology of the nystagmus reduction is not completely understood, recently discovered and possibly proprioceptive nerve endings in the extraocular muscles at the tendino-scleral interface (its "enthesis") may shed light on a further mechanism of action of eye muscle surgery in reducing nystagmus.[41] Given this information, it may be likely that afferent information from the extraocular muscles (either as proprioceptive signals or as other sensory information) serves as a continuous calibration. The clinical and electrophysiologic consequences of extraocular muscle surgery in patients with OCA and INS may be attributable to interruption of the afferent proprioceptive loop, producing a damped peripheral ocular motor response to the nystagmus signal. This report adds to the evidence that surgery on the extraocular muscles in patients with OCA and INS has distinct ocular motor and visual results.

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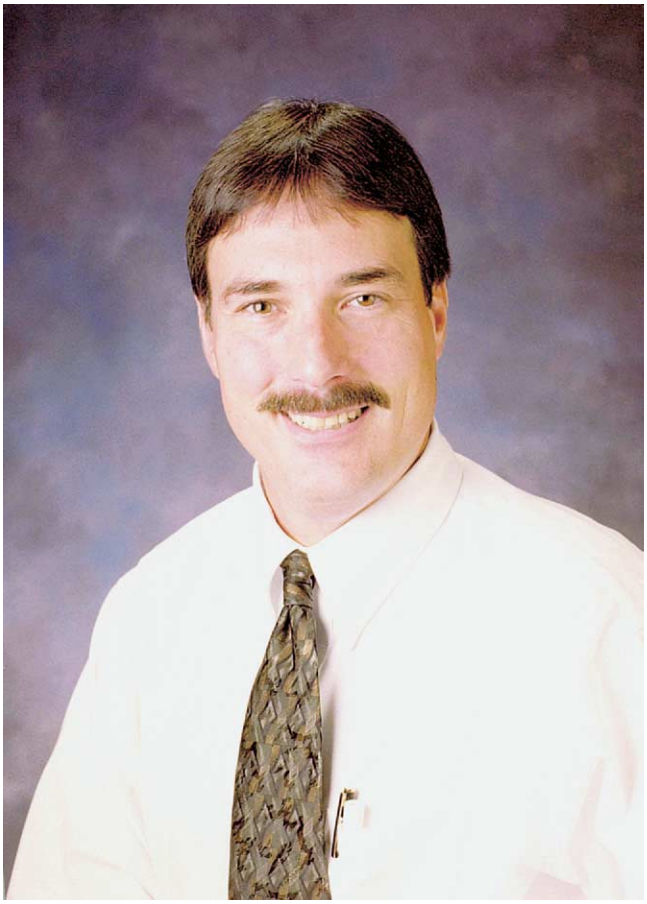

Biosketch

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