Visual Acuity Deficits in Children With Nystagmus and Down Syndrome

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• PURPOSE: To investigate the association between visual acuity deficits and fixation instability in children with Down syndrome and nystagmus.
• DESIGN: Prospective cross-sectional study.
• METHODS: SETTING: Institutional. STUDY POPULATION: Sixteen children (aged 10 months-14 years) with Down syndrome and nystagmus, and a control group of 93 age-similar children with unassociated infantile nystagmus. OBSERVATION PROCEDURES: Binocular Teller acuity card testing and eye-movement recordings. Fixation stability was quantified using the nystagmus optimal fixation function (NOFF). An exponential model based on results from the control group with unassociated infantile nystagmus was used to relate fixation stability to age-corrected visual acuity deficits. MAIN OUTCOME MEASURES: Binocular grating visual acuity and NOFF.
• RESULTS: Visual acuity was 0.2-0.9 logMAR (20/30-20/174 Snellen equivalent) and corresponded to a 0.4 logMAR (4 lines) mean age-corrected visual acuity deficit. Fixation stability ranged from poor to mildly affected. Although visual acuity deficit was on average 0.17 logMAR larger ($P = .005$) than predicted by the model, most children had visual acuity deficit within the 95% predictive interval.
• CONCLUSIONS: There was a small mean difference between the measured visual acuity deficit and the prediction of the nystagmus model. Although other factors also contribute to visual acuity loss in Down syndrome, nystagmus alone could account for most of the visual acuity deficit in these children. (Am J Ophthalmol 2014;157:458–463. © 2014 by Elsevier Inc. All rights reserved.)

ABNORMALITIES OF VISUAL FUNCTIONING IN children with Down syndrome are caused by uncorrected refractive error, limited accommodation (including limited accommodative effort), strabismus, nystagmus, and possibly abnormal cortical morphology.[1–5] When wearing proper optical correction, these children usually have mild to moderate deficits in visual acuity,[5–8] which are presumably the cumulative result of nystagmus (fixational instability) and cortical abnormalities, including, perhaps, amblyopia. Accurate assessment of visual functioning in children with Down syndrome may be hampered by limitations in executive functioning and attention.[9,10]

Reportedly, up to 30% of patients with Down syndrome have nystagmus.[5,11,12] Recent advances in the understanding of the relation between the various waveforms of nystagmus eye movements and visual acuity in patients with unassociated infantile nystagmus (typically referred to as "idiopathic infantile nystagmus" or "congenital nystagmus," ie, infantile nystagmus in the absence of any other afferent visual system disease),[13,14] as well as progress in delineating the functional improvements after nystagmus surgery in children,[15,16] prompted us to investigate to what extent fixational instability may explain visual acuity deficits in children diagnosed with Down syndrome and nystagmus.

METHODS

THE RESEARCH PROTOCOL AND INFORMED CONSENT FORM for this cross-sectional study were approved by the Institutional Review Board of the University of Texas Southwestern Medical Center. Written informed consent was obtained from a parent or legal guardian for each participant. This study was performed in accordance with the US Health Insurance Portability and Accountability Act.

• PARTICIPANTS: Sixteen children (aged 10 months-14 years [median 3.5 years]) diagnosed with Down syndrome and nystagmus participated in this cross-sectional study carried out in the Visual Disorders and Eye Movements Laboratory at the Retina Foundation of the Southwest between August 2009 and July 2012. Children with cataracts or other apparent structural abnormalities in the eyes were excluded, as were children with *severe* developmental delay. The Table provides basic clinical data for this cohort. As can be seen from the Table, most children were myopic (and wore spectacle correction), while several had various amounts of (intermittent) strabismus. A group of 93 infants, children, and young adults with unassociated infantile nystagmus (aged 5 months-27 years [median 4.4 years]) from a previous study[14] formed a comparison group; the diagnosis of unassociated infantile nystagmus in these children was based on eye-movement recordings and a complete ophthalmologic examination by the referring pediatric ophthalmologist.

• VISUAL ACUITY: Binocular, spectacle-corrected grating visual acuity was assessed with the Teller visual acuity cards

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TABLE. Patient Characteristics (Including Visual Acuity, Refractive Error, Strabismus, and Nystagmus Charactteristics) of the 16 Children With Down Syndrome and Nystagmus Included in This Study

Patient No.	Age (y)/Sex	Visual Acuity (logMAR)	Refractive Error [OD; OS] (D)	Strabismus	Nystagmus Type	NOFF (logits)	Foveation Fraction
1	0.8/M	0.63	N/A	Ortho	INS	−1.00	0.27
2	0.9/M	0.53	N/A	Small-angle ET	INS	1.07	0.75
3	2.1/F	0.76	+0.25; +0.25	Ortho	INS	−0.73	0.32
4	2.4/M	0.83	−1.00; −1.00	Ortho	INS	−2.57	0.07
5	2.8/M	0.65	−7.00; −5.00	8 ET, post-op	INS	−1.34	0.21
6	2.8/M	0.89	−7.00+1.25×70deg; −7.00+1.25×100deg	12 E(T)	INS	−2.05	0.11
7	3.1/F	0.88	−1.50+1.50×80deg; −1.50+1.50×100deg	Ortho	INS	0.22	0.56
8	3.4/F	0.43	−1.00+1.00×60deg; −1.00+1.00×100deg	10 E(T), post-op	FMNS	−0.44	0.39
9	3.7/M	0.94	−8.50+1.00×90deg; −7.50+2.50×90deg	Ortho, post-op	FMNS	−2.93	0.05
10	4.1/M	0.46	−12.00; −10.50	Ortho	INS	−0.18	0.46
11	4.3/M	0.51	+2.50+1.00×70deg; +2.50+2.50×110deg	25 E(T)	INS	1.34	0.79
12	5.9/F	0.45	−1.75+2.25×80deg; −2.00+2.50×110deg	Ortho, post-op	INS	−1.77	0.15
13	5.9/F	0.35	−12.50+4.50×75deg; −12.50+6.00×100deg	25 ET, post-op	INS	−3.07	0.04
14	7.3/M	0.18	−4.00+3.75×100deg; −2.50+2.50×75deg	3 X(T)	INS	0.23	0.56
15	8.9/F	0.69	−3.50; −2.50	Ortho	INS	−4.59	0.01
16	14/M	0.46	−3.00+2.50×100deg; −3.00+2.50×80deg	Ortho	INS	0.99	0.73

D = diopter; deg = degrees; ET = esotropia; E(T) = intermittent esotropia; FMNS = fusion maldevelopment nystagmus syndrome (manifest latent nystagmus); INS = infantile nystagmus syndrome; N/A = not available; NOFF = nystagmus optimal fixation function; Ortho = orthotropia; Post-op = postoperative; X(T) = intermittent exotropia.

(Stereo Optical, Chicago, Illinois, USA) using a staircase procedure and a forced-choice paradigm using either preferential looking or pointing, depending on the individual child's abilities.[17] Thus, this grating detection task poses minimal requirements on cognitive abilities of the child tested. Visual acuity was defined as the mean of the last 6 of 8 total staircase reversals on a logMAR scale. Because the mean normal visual acuity improves with age in early childhood, the visual acuity measurements were converted to visual acuity *deficits* (ie, logMAR units relative to published age-corrected mean normal values[18–20]) for part of the analysis. For clinical reference, the logMAR visual acuities were also given in Snellen-equivalent values using the formula: $Snellen\ denominator = 20 \times 10^{(logMAR)}$.

• **EYE MOVEMENTS:** Nystagmus eye movements were recorded using a remote high-speed video system (EyeLink 1000; SR Research Ltd, Kanata, Ontario, Canada) while the child performed a simple fixation task for 20-30 seconds under binocular viewing. Children requiring refractive correction wore their spectacles. The recordings were low-pass filtered off-line and differentiated to obtain eye velocity information. Further details of instrumentation, calibration, and test protocol were published previously.[14]

Quantification of nystagmus eye movements centers around foveation periods: brief amounts of time (typically >20 ms duration; 1 during each oscillation of the nystagmus waveform) when the eyes are moving with sufficiently low velocity while the visual axis is in or near the direction of the target.[13,21,22] The gold standard for quantifying foveation periods is the expanded nystagmus acuity function (commonly referred to as "NAFX"),[13] a mathematical algorithm that applies simultaneous criteria on eye position and eye velocity in order to determine which portion of each oscillation corresponds to an event of fixation or "foveation." Here, a somewhat less stringent algorithm was used, the nystagmus optimal fixation function (or "NOFF"),[14,16] which was

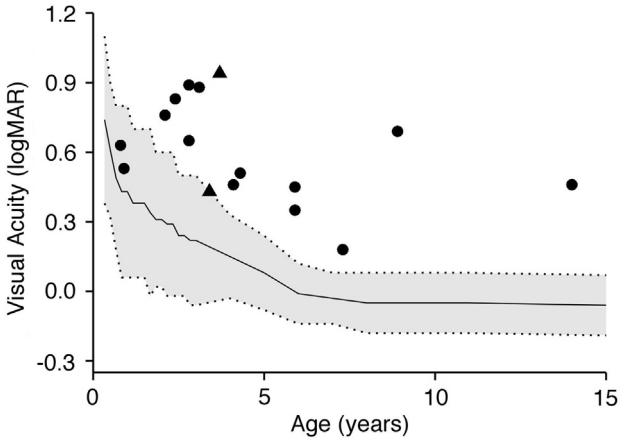

FIGURE 1. Scatterplot showing binocular visual acuity as a function of age in children with Down syndrome and nystagmus. Symbols correspond to the nystagmus waveform types: infantile nystagmus (solid circles); manifest latent nystagmus (solid triangles). Most of these patients fell outside of the normal limits indicated by the shaded area. (Solid line and shaded area: mean normative values and 95% confidence limits as published in the literature.[18–20])