Static and Dynamic Measurements of Accommodation in Individuals with Down Syndrome

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Purpose. To identify whether static and dynamic aspects of accommodation other than accuracy are deficient in individuals with Down syndrome (DS) and whether poor accommodation is related to sensory or motor pathway deficits.

Methods. Static aspects of accommodation (maximum accommodative response and lag) were measured with an autorefractor for both proximal and minus lens demands. Dynamic aspects of accommodation (latency, peak velocity, microfluctuations) were recorded at 30 Hz with a custom-built photorefractor as subjects viewed a movie switching between 11 m and 50, 33, 25, or 20 cm. Thirty-six subjects with DS were recruited (age 3 to 39 years), and 24 (67%) had useable responses for at least one study measurement for comparison with 140 controls (3 to 40 years) from a previously published cohort.

Results. DS subjects had lower maximum accommodative responses (mean = 2.52 ± 1.66 D) and higher lags (1.81 ± 1.30 D for 33 cm demand) than controls for both proximal and minus lens stimuli. DS subjects had greater microfluctuations (one-way ANCOVA, $P < 0.001$), and a small percentage of the total number of latency measurements (17% accommodative and 16% disaccommodative) were longer than controls. Peak velocities of accommodation and disaccommodation were not different between groups (one-way ANCOVA, $P = 0.143$).

Conclusions. Peak velocities of accommodation and disaccommodation (primarily motor aspects) did not differ between controls and DS subjects; however, latencies (primarily sensory) and microfluctuations (combined motor and sensory) were poorer in DS subjects. These results suggest that poor accommodative accuracy in individuals with DS may be predominantly related to sensory deficits. (*Invest Ophthalmol Vis Sci.* 2011;52:310–317) DOI:10.1167/iovs.10-5301

Poor accommodative accuracy is a common finding in individuals with Down syndrome (DS).[1,2] Several studies have used dynamic retinoscopy to measure accommodative lag in subjects with DS,[2–10] and bifocal prescriptions have been evaluated as a treatment option.[11–13] However, the cause of poor accommodative accuracy is still unknown. One possible explanation is that poor accommodative accuracy is related to a mechanical deficit of the eye in which the accommodative mechanism is limited in its ability, such as with presbyopia. Another possibility is that deficits in the sensory pathway fail to detect changes in blur, such as would be seen in individuals with an increased depth of field.[1,5] A recent study supports the explanation of sensory deficits based on observed improvements of accommodative accuracy in young subjects with DS after a period of bifocal wear.[13] The authors of that study suggested that the improvement would not have occurred if accommodation were limited by mechanical deficits.[13]

Knowledge of accommodative dysfunction in individuals with DS is limited to lag. One previous study attempted to measure accommodative amplitudes in these subjects,[2] but a later publication by the same laboratory acknowledged that this goal may not have been met.[5] The purpose of the present study was to objectively measure both static (maximum accommodative response and lag) and dynamic (latencies, peak velocities, microfluctuations) aspects of accommodation in individuals with DS to enable a more complete assessment of accommodative function. Prior studies of accommodative deficiencies in subjects with DS have not included dynamic aspects of accommodation. Measurements of dynamic accommodation will address whether increased accommodative lag is related to a sensory or motor deficit by comparing measures that are assumed to be primarily reflexive and sensory driven (latencies) versus those that are primarily motor driven (peak velocities) to measurements from normal controls.

Methods

This study followed the tenets of the Declaration of Helsinki and was approved by the University of Houston Committee for the Protection of Human Subjects, and appropriate consent and assent was obtained from all subjects or parents of subjects.

Subjects

Subjects with DS were recruited from the University of Houston Eye Institute's patient population and the local Down Syndrome Association. Thirty-six subjects between the ages of 3 and 40 years (inclusive) were recruited (24 male, 12 female). Subjects with a history of surgery involving the crystalline lens were excluded. Subjects with strabismus, nystagmus, and amblyopia were included because of the high prevalence of these conditions in this population.[14–16]

Data from the subjects with DS were compared with a population of control subjects who were recruited for studies of age-related changes in accommodation during the same time frame. A large number of control subjects were tested to describe normative accommodative function with age. These results have been previously published.[17–19] Control subjects were recruited from staff, students, and patients from the University of Houston Eye Institute. Subjects were required to have no significant ocular history or history of taking medications that could impact accommodation because of a desire to define age norms unaffected by these conditions. One hundred and forty control subjects (81 females, 59 males; ages, 3–40) participated in at least one of the accommodative measures reported.

Vision Assessment

All subjects were screened with visual acuity measurements, a binocular vision assessment, noncycloplegic refraction, and slit-lamp exam-

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ination. Distance visual acuity was tested with the highest cognitive level acuity test the subject could perform. The tests used (in order of increasing difficulty) were the Cardiff Preferential Looking Acuity Test,[20] the Lea Symbols Test,[21] the HOTV letter chart, the Snellen letter chart, and the Bailey-Lovie acuity chart.[22] Near acuities were measured on those subjects who were cognitively able using either a LEA symbols or Snellen near card. Binocular vision was evaluated with distance and near prism neutralized cover test, and two stereoacuity tests (Lang I; Lang-Stereotest AG, Forch, Switzerland; and Randot; Stereo Optical Co., Chicago, IL). For subjects with DS and pre-school–aged control subjects, refractions were assessed by loose lens retinoscopy. A standard subjective refraction technique was used for older control subjects.

Subjects with no prior eye examination or those with a clinically significant change in refraction from their presenting correction received a complete eye examination, including cycloplegic refraction and dilated internal ocular health assessment. These subjects were prescribed spectacles if necessary and asked to return for completion of the study after adapting to the new correction for 1 month (one subject with DS did not return, leaving 35 subjects for analysis). Subjects who were not cyclopleged or dilated were able to complete the accommodative study measures on the initial visit while wearing their habitual correction.

Accommodative Measures

Accommodation was measured statically using an open-field autorefractor (Grand Seiko WR-5100K; RyuSyo Industrial Co., Kagawa, Japan)[23] and dynamically using a custom-built infrared photorefractor similar to that described by Schaeffel et al. (1993)[24] and used in several previous studies.[19,25–27] All measurements were performed on the right eye with the left eye occluded, except in cases of constant strabismus of the right eye, in which case the left eye was measured. Refractive errors were corrected with either spectacles or contact lenses for all study measurements. Spectacles were held up against the bridge of the nose to avoid surface reflections during autorefractor measurements. One subject with DS and 5 control subjects were included who had previously undergone refractive surgery.

Measurement of Maximum Accommodative Response

Subjects first viewed a distance target at 11 m through their habitual correction, and distance-corrected refraction was measured with the autorefractor. These measurements were used to ensure that uncorrected refractive error was minimal and were also used to calculate maximum accommodative responses. Near refraction was measured as subjects viewed an illuminated target with words and pictures that was suspended from the near-point rod on the autorefractor at 33.33 cm (3 D accommodative demand). Accommodation was further stimulated by placing minus lenses of increasing power in front of the unoccluded, viewing eye in −1 D increments until no further increase in accommodative response was elicited. This means that two different stimulus conditions were used to induce blur, a proximal target for the 3 D stimulus and minus lenses for higher stimulus amplitudes. Accommodative responses and effective stimulus demands were calculated using formulas for reconciling the effect of spectacle lenses on autorefractor readings.[28] Accommodative response was plotted as a function of stimulus demand (graphs not shown) and the maximum accommodative response identified as the point at which the stimulus-response function peaked or reached a plateau. The maximum response was then added to the distance-corrected refraction measurement to adjust for any measured uncorrected refractive error. This value is defined as the maximum accommodative response.

For subjects with DS, maximum accommodative response was also measured with the near target presented at distances of increasing proximity (termed a proximal stimulus to distinguish between this and minus lens–stimulated accommodation). Accommodative response to the proximal stimulus was measured to ensure that any reduced performance observed with the minus lens–stimulated technique was not due to an inability of subjects with DS to respond to minus lens blur. For this procedure the near target was suspended from the near-point rod of the autorefractor on a custom-built attachment that allowed the target to be moved incrementally closer for demands of 3 to 8 D. Because of the physical constraints of the beam splitter, 8 D was the greatest demand attainable. Because of the inability to present higher stimulus demands, the stimulus-response function for proximal stimuli failed to peak or plateau in some subjects, and thus the accommodative response for some subjects tested with this technique may not represent their true maximum ability.

Accommodative Lag

Accommodative lag was defined as the difference between the stimulus demand and accommodative response after adjustments were made for the effectivity of spectacles or loose lenses using the formulas mentioned previously.[28] Accommodative lag was calculated for all subjects for the 33 cm near target and the first five minus lens–stimulated demands.

Dynamic Measurements of Accommodation

Refraction was measured dynamically at 30 Hz with a custom-built infrared photorefractor as subjects viewed a cartoon movie alternating between a near and far monitor. The far monitor was positioned 6 m from the subject and viewed directly through a beam-splitter. The near monitor was positioned off to the side of the subject at a variable position of either 2, 3, 4, or 5 D demand, and the reflection of the movie viewed off the beam-splitter.[19] Both monitors were connected to a computer, and custom software displayed the movie in a media window on one monitor at a time. The switch between monitors occurred instantaneously, and an LED controlled by the computer's printer port illuminated when the movie played on the near monitor. The subject viewed the movie monocularly in primary gaze with the contralateral (right eye) covered with a 720 nm cutoff filter that transmits infrared light of longer wavelengths (89B Wratten filter; Eastman Kodak Company, Rochester, NY). The step stimulus was presented in cycles of distance to near and back to distance with pseudorandom timing controlled by the software to avoid anticipation. At least three cycles were presented for each near stimulus demand from 2 D up to 5 D.

Recorded images were analyzed off-line. The slope of the brightness profile in the pupil was determined from a linear fit to the average of two vertical sampling lines for each individual video frame. The slope was output to a file along with the image frame number, stimulus status, pupil diameter, and mean pupil brightness. The slope of the brightness profile was converted to refraction based on individual trial lens calibrations performed on each subject.[24] Accommodation was plotted as a function of time for each step stimulus cycle. For the calibration, subjects viewed the far stimulus with the right eye (so that accommodation remained relaxed) while the left eye was occluded with the Wratten filter. Trial lenses (−1 to +6 D) were introduced in front of the Wratten filter over the left eye in 1 D steps. Data were plotted with slope on the x-axis and lens power on the y-axis and regression analysis performed to convert slope to refraction for each individual subject. Calibrations were performed while subjects wore their habitual prescriptions.

Accommodative responses were analyzed (Excel; Microsoft, Redmond, WA) to calculate dynamic measurements. Measures of accommodative and disaccommodative latencies were calculated as the time from stimulus onset to the initiation of the accommodative or disaccommodative response. The magnitude of the accommodative microfluctuations was the RMS deviation of a 2 second portion of the sustained accommodative response beginning 1 second after the stimulus switch to near with visual confirmation that the response had reached its peak by one second. Peak velocities of accommodative and disaccommodative responses were determined from first-order exponential functions fit to the responses.[19,25]

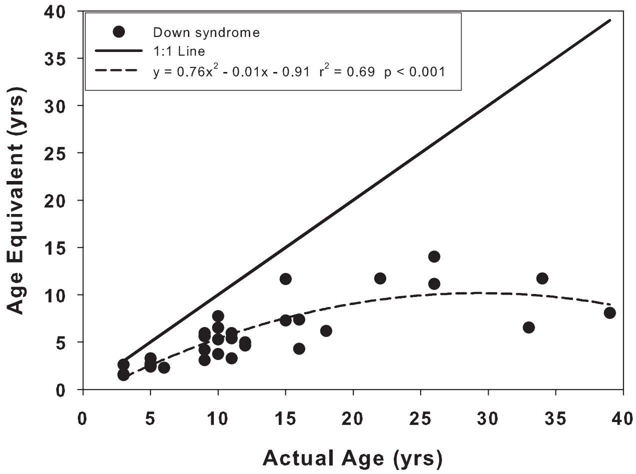

FIGURE 1. The *dashed line* fit to the data shows a significant curvilinear relationship between chronological age and age equivalent as determined from the survey used for subjects with DS. The *solid line* indicates the 1:1 line.

Adaptive Abilities Assessment

The parent or guardian of each subject with DS was asked to complete a survey of adaptive behavior skills (Vineland II; AGS Publishing, Circle Pines, MN). This is an extensive survey that evaluates communication, daily living skills, socialization, and motor skills and is appropriate for all ages. The assessment provides age-equivalent scores and not only is used to identify individuals with cognitive deficits, but also has been shown to have high reliability and validity to distinguish the functional level of individuals with mental retardation.[29] For the present study, the age equivalents from all categories were averaged for each subject to provide an overall age equivalent. This assessment allowed comparisons between accommodative measurements based on adaptive ability (age equivalent) as well as actual age. Parents of 33 subjects with DS completed the survey.

RESULTS

Vision Assessment

Of the 35 subjects with DS, 9 had strabismus and 5 had nystagmus, one of whom had both. Best corrected visual acuities for the tested eye averaged 20/45 at distance (range = 20/25 to 20/100) and was similar in the fellow eye. Near visual acuities were measured in 29 subjects and averaged 20/60 at 40 cm through the habitual distance correction (range = 20/25 to 20/125). Control subjects had best corrected monocular distance acuities of 20/20 or better, except for a few of the youngest subjects who were testable only to 20/25, which is within the expected range for typical young children.[30,31]

The distribution of refractive errors for subjects with DS was 22 (63%) with hyperopia (mean = +3.54 D ± 1.81, range = +1.25 to +8.50 D), 5 (14%) with myopia (mean = −6.90 D ± 3.61, range = −3.00 to −11.50 D), 4 (11.5%) with mixed astigmatism, and 4 (11.5%) with emmetropia (−0.16 to +0.37 D). Mean astigmatism was 1.72 D (range = 0.25 to 5.00 D). All nonemmetropes wore spectacles except for one 36-year-old subject whose myopia had been corrected with LASIK.

Control subjects included 65 (46.5%) with myopia (mean = −3.54 D ± 2.10, range = −0.75 to −10.25 D), 3 (2%) with hyperopia (mean = +1.08 D ± 0.14, range = +1.00 to +1.25 D), 68 (48.5%) with emmetropia (−0.50 to +0.50 D), and 4 (3%) with mixed astigmatism. Nonemmetropes were corrected with spectacles or contact lenses, except five myopic adult subjects who had been corrected with LASIK.

Age-Equivalent Scores

Age-equivalent scores determined from the survey of adaptive behavior scales used here are shown in Figure 1. As expected, subjects with DS had age equivalents several years younger than their chronological age because of cognitive deficits (age equivalent, 1.5 to 14 years, versus actual age, 3 to 39 years).

Minus Lens–Stimulated Maximum Accommodative Response

Measurements were attempted on 30 subjects with DS, and 19 completed the measures. There was a statistically significant difference in age between subjects who could and could not complete the measurements ($t_{(26)} = 3.10$, $P < 0.01$). Subjects who could cooperate were older (mean = 17.6 years, range = 9 to 39) than subjects who could not (mean = 7 years, range = 3 to 14), and age equivalents also differed significantly (mean = 7 years versus 4 years, $t_{(26)} = 2.16$, $P = 0.02$).

Mean maximum accommodative response to minus lens blur was 2.52 ± 1.66 D in these 19 subjects with DS. No significant relationships between maximum accommodative response and age, age-equivalent, or distance visual acuity were found ($P \geq 0.19$). Minus lens–stimulated maximum accommodative response for subjects with DS and controls are shown in Figure 2. Only one subject with DS falls along the mean curve of the control subjects (age = 26, max response = 5.94 D). All remaining 18 subjects fall below the mean predicted curve with only 5 (26%) falling within −2 standard deviations of the mean. The mean actual age of the 5 subjects who fell within −2 standard deviations was similar to the actual age of the other 14 subjects with DS ($t_{(17)} = 1.21$, $P = 0.2$); however, these subjects had mean age equivalents significantly greater than the rest of the subjects with DS (mean age equivalent = 11.0 vs. 5.8 years, $t_{(17)} = 3.99$, $P < 0.01$), suggesting they were more advanced cognitively.

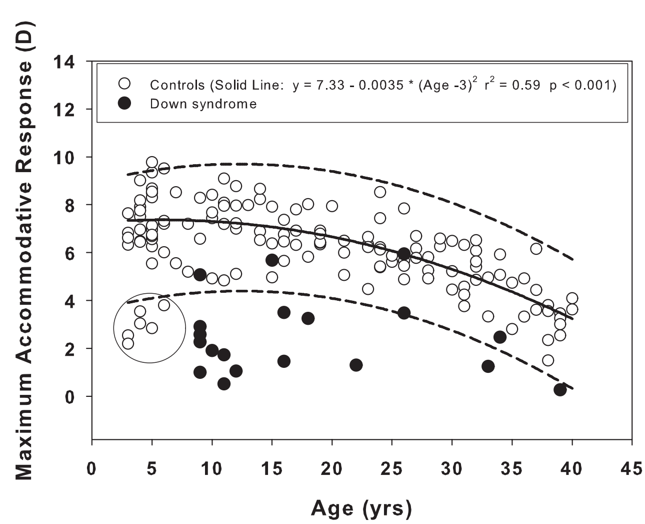

FIGURE 2. Minus lens–stimulated maximum accommodative responses measured with the autorefractor. The control data (*open symbols*) had a significant curvilinear relationship with age (*solid line*) ± 2 SD (*dashed lines*). Only six subjects with DS fell within −2 standard deviations of the control subjects. The *circled* data points are control subjects with maximum responses more than −2 standard deviations away from the mean of the other control subjects and were identified as outliers and excluded from the regression fit. A possible explanation for the reduced performance of these young subjects is poor response to minus lens blur.

Maximum Accommodative Response to the Proximal Stimulus

The subjects with DS who fell below the mean predicted curve of controls show similar maximal accommodative responses to six young control subjects who performed below the range of their peers (circled data points in Fig. 2). The poor performance of these young control subjects was previously attributed to a poor response to minus lens–stimulated blur that improved when they were tested with the proximal stimulus.[19] To investigate the effect of stimulating accommodation with a proximal stimulus rather than minus lenses in the subjects with DS, maximum accommodative responses were measured to a target of increasing proximity from 33.33 cm (3 D) to 12.5 cm (8 D). Of the 19 subjects tested, 7 did not reach a definitive peak or plateau in their stimulus-response curves. The data from these subjects are still presented here, although their maximum accommodative amplitudes may potentially be greater.

Table 1 shows each individual subject's maximum accommodative responses to both the minus lenses and proximal stimulus. Maximum accommodative responses were significantly greater with the proximal stimulus (mean = 3.30 D ± 1.54 vs. 2.52 D ± 1.66, $t_{(17)} = -2.69$, $P = 0.02$), but the mean improvement was <1 D and did not occur for all subjects. Ten out of 19 subjects had a significant increase in maximum accommodative response with the proximal stimulus. The criterion for a significant increase in response was defined as 0.67 D, which is equal to the SE of the group multiplied by the *z*-score for a significance level of 0.05 when using a one-tailed *t*-test. The 10 subjects with significant improvements are identified in bold italic text in Table 1, and their improvements ranged from 1.05 to 4.17 D. Even though improvement was observed in about half of the subjects with the proximal stimulus, only two additional subjects fell within −2 standard deviations of the group mean for controls shown in Figure 2.

Accommodative Lag Measurements

Accommodative lags are presented in Figure 3 for the subjects with DS who completed maximum accommodative response measurements ($n = 19$). With the target at 33.33 cm and no trial lens present, stimulus demand ranged from 2.28 to 3.50 D (because of habitual spectacle lens effectivity), and accommodative lag averaged 1.81 ± 1.30 D for these subjects. No significant linear relationships were observed between lag at 33.33 cm and age, or between lag and age equivalent for subjects with DS ($r^2 \leq 0.01$, $P \geq 0.69$). This is contrary to the trend observed in the control subjects, who demonstrated a linear decrease in accommodative lag from age 3 to 20 years.[19]

Because no relationship between lag and age was observed in the subjects with DS, all responses were binned together to compare minus lens–induced accommodative lags between subjects with DS and controls for each demand. All the control subjects for these measurements were either emmetropic or were corrected with contact lenses, and thus stimulus demands were the same across subjects and allowed for direct comparison. In the subjects with DS, spectacle lenses produced large differences in stimulus demand across subjects, and thus a direct comparison of accommodative lag for each added minus lens could not be made. To compare between the two populations, effective accommodative demands were first calculated based on each subject's spectacle power. The accommodative lag data were then grouped into the same five demand bins ±0.25 D as controls. This strategy meant that not all subjects with DS were included in each stimulus demand bin (number of subjects ranged from 9 to 14 for each bin). After correcting for differences in effective stimulus demand, mean accommodative lags for subjects with DS were significantly larger than mean accommodative lags of all control subjects (irrespective of age) at all stimulus demand bins (one-way ANOVA with post-hoc Tukey testing, $P < 0.05$) (Fig. 3).

Dynamic Measurements

Dynamic measurements of accommodation were attempted on 33 of the 35 subjects with DS. Nine of 33 (27%) were unable to complete the measurements because of poor cooperation, and images from 6 of 33 (18%) were too poor to be analyzed

Table 1. Maximum Accommodative Responses Measured with Minus Lens Blur and Then with a Proximal Target

Subject Age (y)	Age Equivalent	RE	Distance VA Tested Eye	Near VA OU	BV	Maximum Lens Stimulus Response (D)	Maximum Proximal Stimulus Response (D)
9	5.95	H	20/25	20/25		5.07	3.77
9	5.63	E	20/40	20/30		2.91	***7.08****
9	4.17	H	20/40	20/30		2.52	***4.01****
9	3.08	H	20/80	20/50	S&N	2.58	2.00
9	6.51	H	20/40	20/50		1	***3.35***
10	3.73	H	20/32	20/61		1.91	1.45
11	5.39	E	20/32	20/30		0.52	***1.57***
11	3.29	M	20/100	20/80	S	1.73	1.97
12	4.97	H	20/25	20/50		1.05	***2.69***
15	11.66	H	20/30	20/65	S	5.68	4.8
16	4.29	H	20/32	20/48	S	1.46	***2.82****
16	7.38	H	20/50	20/50	S	3.50	2.75*
18	6.17	M	20/50	20/60	N	3.25	2.94
22	11.71	MA	20/40	20/48		1.3	***2.78***
26	11.15	M	20/40	20/32		5.94	5.91*
26	14.02	H	20/50	20/53		3.47	***4.84****
33	6.53	MA	20/30	20/50		1.25	***4.23***
34	11.71	H	20/50	20/80	S	2.47	1.92
39	8.09	H	20/40	20/80		0.27	***1.82****
Mean maximum accommodative response (±SD)						2.52 (±1.66)	3.30 (±1.54)

Gray shading indicates subjects whose minus lens responses fell within −2 SD of the mean response curve of control subjects. Asterisks indicate subjects whose accommodative responses had not reached a peak by the 8 D demand. Bold italic values indicate a significant increase in maximum responses when measured with the proximal stimulus. RE indicates refractive error of hyperopia (H), myopia (M), or mixed astigmatism (MA). BV indicates binocular vision findings of strabismus (S) or nystagmus (N).

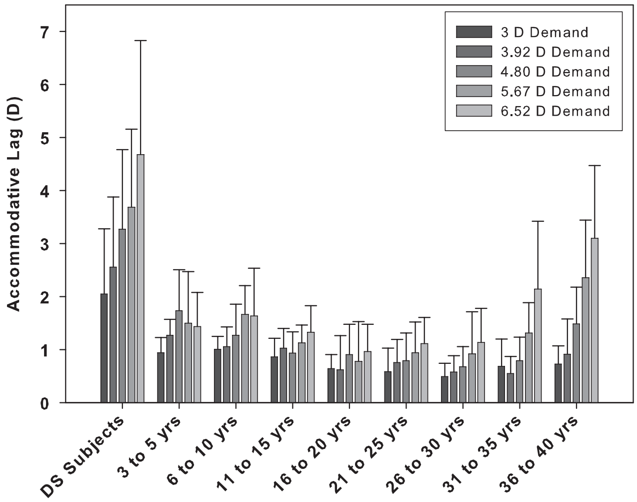

FIGURE 3. Mean accommodative lags (± 1 SD) measured with the autorefractor while subjects viewed a target placed at 33.33 cm through increasing powered minus lenses. All subjects with DS (age 3 to 39 years) were binned together because of the lack of a significant age-related trend in accommodative lags.

because of nystagmus, or downward pointing eyelashes. Eighteen subjects (55%) were able to cooperate for the recording session and had good-quality photorefraction images. The mean age of these 18 subjects was significantly greater than that of the 9 subjects who could not complete the task (14.8 vs. 5.5 years, $t = 2.77_{(25)}$, $P = 0.01$).

Dynamically recorded accommodative responses were analyzed and categorized as typical response (increased accommodation that persists the full duration of near stimulus presentation), early terminated response (increased accommodation that decreased before the near stimulus terminated), other atypical response (variable changes in accommodation uncorrelated to the stimulus), or no accommodative response. Examples of these response types are shown in Figure 4. In total, 319 stimulus cycles (far/near/far) were extracted from the videotaped sessions. Of those, 43 (13.5%) responses were typical, 74 (23.1%) were terminated early, 27 (8.5%) were atypical, and 175 (54.9%) showed no response. This distribution is in contrast to the control subjects who had 90.8% typical responses, 1% early terminated, 5.7% atypical, and 2.5% no identifiable response.[19]

Of the 18 subjects with DS included in the analysis, three had no systematic response to any of the stimulus demands, and only eight subjects had at least one or more typical response(s). This is in contrast to control subjects who all demonstrated one or more typical responses.[19] Although many of the responses from the subjects with DS were atypical, analysis for select measurements could still be performed on many of the responses. For example, accommodative latencies, peak velocities, mean response amplitudes, and RMS deviations could be calculated for the early terminated response, provided the sustained response lasted at least 2 seconds. In total 15 subjects had usable responses for at least part of or all the dynamic analysis. Although responses were collected from these subjects for four different stimulus demands, few subjects demonstrated responses to the smallest stimulus demand (2 D), and thus the majority of the responses analyzed were from the 3, 4, and 5 D stimulus demands.

Latencies

Figure 5 shows accommodative and disaccommodative latencies pooled as a function of age for both controls and subjects with DS. Both accommodative and disaccommodative latencies decreased linearly with age in controls.[19] The majority of measured latencies from subjects with DS were similar to those of controls, although 17% of accommodative latencies and 16% of disaccommodative latencies did fall above the 95% prediction interval of controls, which suggests some potential differences between the groups (Figs. 5A and 5B, respectively).

Peak Velocities

Accommodative and disaccommodative peak velocities (V_{max}) were determined from the response amplitude (a) and time

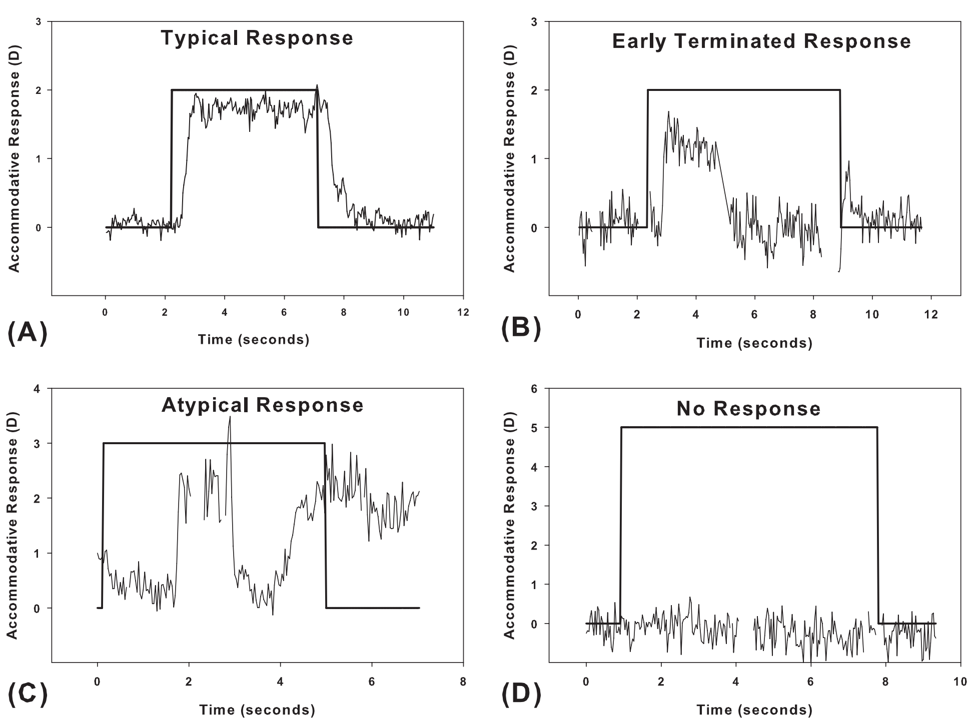

FIGURE 4. Examples of dynamically recorded accommodative responses to the step stimulus for a control subject (typical response) (**A**) versus subjects with DS (early terminated [**B**], atypical [**C**], and no response [**D**]).

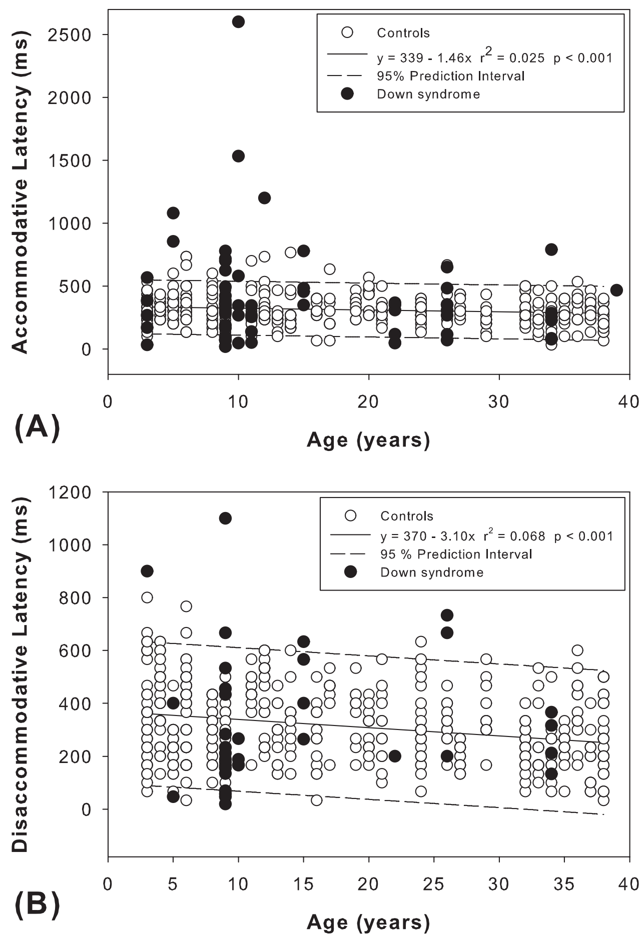

FIGURE 5. Accommodative (**A**) and disaccommodative (**B**) latencies for subjects with and without DS.

constant (τ) obtained from first-order exponential fits to the accommodative and disaccommodative responses using the formula $V_{\max} = a/\tau$.[19,25] Of the subjects with DS, 14 had accommodative and 11 had disaccommodative responses that could be analyzed for peak velocities. Fewer disaccommodative responses could be analyzed because of the tendency for subjects with DS not to sustain a response throughout the entire near stimulus duration. Overall, the magnitude of the accommodative responses were smaller in subjects with DS than control subjects as would be expected from measurements of maximum accommodative responses (Fig. 1) and measurements of accommodative lag (Fig. 3). As a result, the range of accommodative responses for which peak velocities were calculated was smaller for subjects with DS than controls (approximately 0.5 to 2.0 D vs. 0.5 to 4.0 D).

Figure 6 shows a comparison of accommodative and disaccommodative peak velocities in subjects with and without DS. For accommodative peak velocities, control data are shown with predicted fits from a previously reported age-related analysis of control data that demonstrate lower peak velocities in the older subjects for accommodative responses greater than 1.75 D. Peak velocities of subjects with DS showed a significant linear increase with response amplitude ($P = 0.02$, $r^2 = 0.068$). Peak velocities between subjects with DS and controls of similar age were not significantly different by one-way ANCOVA ($F = 2.16$, $df = 1271$ $P = 0.143$). For disaccommodation, peak velocities increased linearly with response amplitude for controls and did not differ with age. Subjects with DS had few responses for analysis, and thus a significant linear relationship was not observed. However, almost all measures were within the 95% prediction interval of the control data and were evenly distributed around the linear fit, suggesting that peak velocities of disaccommodation did not differ between controls and subjects with DS.

Accommodative Microfluctuations

RMS deviations of accommodative microfluctuations were calculated for 15 subjects with DS for each accommodative response lasting 2 seconds or more in duration. The magnitude of the accommodative microfluctuations was calculated as the RMS deviation of a 2 second portion of the sustained accommodative response beginning 1 second after the stimulus switch to near with visual confirmation that the response had reached its peak at 1 second. RMS deviation was pooled for all subjects (age range = 3 to 39 years) and plotted as a function of response amplitude to compare with controls (age range = 3 to 38 years) (Fig. 7). RMS deviation showed a significant linear increase with response amplitude for both groups (DS: $P = 0.001$, $r^2 = 0.11$; controls: $P < 0.001$, $r^2 = 0.22$). The RMS deviations of subjects with DS were significantly larger than controls by one-way ANCOVA ($F = 30.11$, $df = 1520$, $P < 0.001$). These differences are not due to poor fixation in sub-

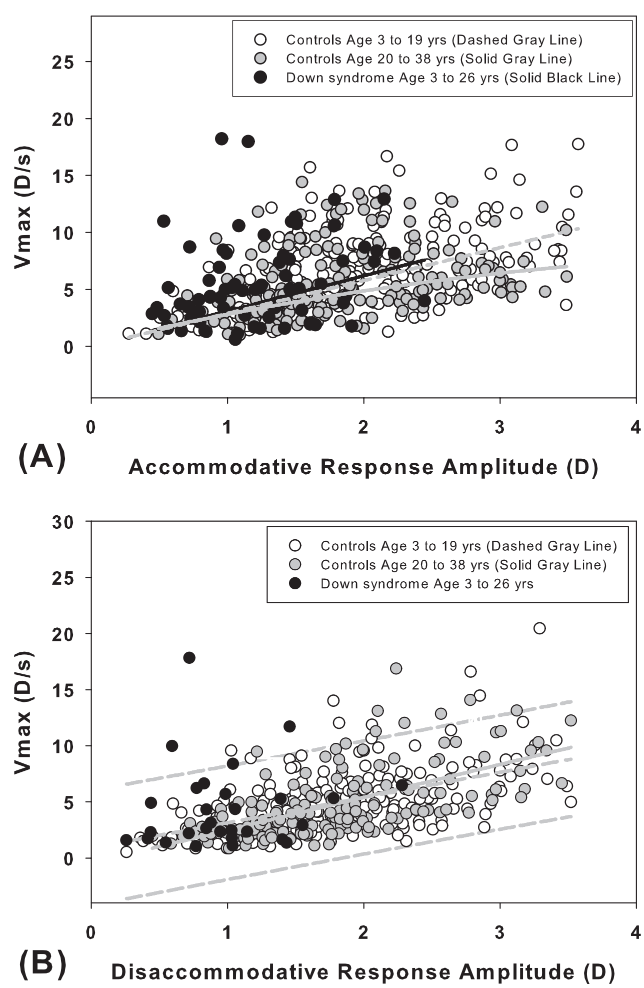

FIGURE 6. Peak velocities of accommodation (**A**) and disaccommodation (**B**) for subjects with and without DS. Accommodative peak velocities were not significantly different for subjects with DS and similarly aged controls. For disaccommodation, the majority of peak velocities for subjects with DS fell within the 95% prediction interval of similarly aged controls.

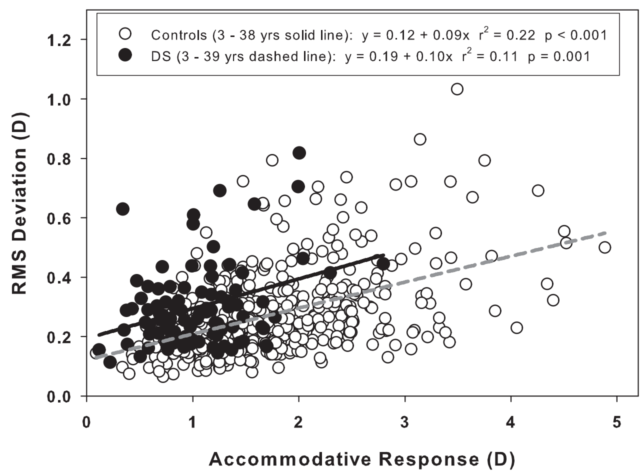

FIGURE 7. The magnitude of accommodative microfluctuations (RMS deviation) showed a significant linear increase with increasing response for both groups. Microfluctuations were significantly larger in subjects with DS (one-way ANCOVA, $F = 30.11$, $df = 1520$, $P < 0.001$).

jects with DS, because only two subjects with small amplitude nystagmus were included in this group, and the results were the same when analysis was performed without these two subjects.

DISCUSSION

In addition to the reduced accommodative accuracy shown previously in individuals with DS,[1–5] this study identifies multiple deficits in accommodative function that can now be further evaluated to identify the likely etiology of the deficits. One new finding reported here is that a large portion of the subjects with DS had atypical accommodative responses to the dynamic step stimulus (Fig. 4). Many subjects had initial responses that were not sustained, while others showed no response. Particularly for the latter case, this may suggest a lack of sensory pathway signaling for an accommodative response to the near stimulus.

The reduced maximum accommodative responses in subjects with DS could support the hypothesis of a mechanical deficit. Studies of in vivo lens biometrics reported thinner lenses (3.27 mm vs. 3.49 mm) with greater optical density and weaker calculated power (17.70 D vs. 19.48 D) in subjects with DS, which could account for reduced maximum accommodative responses.[8] Despite this logical prediction, no relationship was observed between crystalline lens properties and accommodative accuracy as measured with dynamic retinoscopy for subjects with DS in the previous study, which suggests that these structural differences do not impact accommodative function.[8] One caution about these conclusions is that accommodative accuracy was limited to a categorization of "weak" versus "accurate" rather than a quantitative measure in that study.

Conversely, reduced maximum accommodative responses could be due to sensory pathway deficits. Reduced responses are observed in amblyopic subjects, a population with reduced visual acuity due to sensory deficits. Accommodative responses were reduced by >2 D in the amblyopic eye (VA range of 20/25 to 20/137), with improvement when response was measured consensually while stimulating the nonamblyopic eye.[32] In addition, increased depth of field secondary to decreased visual acuity has been proposed to result in increased accommodative lags in amblyopes.[33] Measurements of accommodation and subjective depth of field in individual amblyopic subjects support this model.[33]

Decreased visual acuity is often present in individuals with DS[34] and could contribute to lower accommodative responses and increased lags, much as in amblyopes without DS. The average best corrected visual acuities in this study were 20/45 (range = 20/25 to 20/100) and are in agreement with previous studies.[3,34] As shown in amblyopes, even a visual acuity reduction to 20/25 (comparable to the best acuity in these subjects with DS) may be enough to impact accommodative performance.[32] For subjects with DS, there was not a significant relationship between level of acuity and accommodative measures. However, a limitation of this analysis is that visual acuity measures were obtained using a variety of tests (dependent on the cognitive ability of the subject), and thus analysis combining these different measures cannot be used to determine definitely if acuity impacted accommodation in the present study.

The results from the dynamic measurements also suggest that the primary deficit lies in the sensory pathway rather than the motor pathway. Both accommodative and disaccommodative peak velocities, which are driven by dynamic changes of the ciliary muscle, crystalline lens, and zonular fibers, did not differ between subjects with and without DS (Fig. 6). One limitation to this interpretation is that these observations may be biased by the sample, as perhaps those subjects whose responses were adequate for analysis were also the subjects who had better overall accommodative function. It should be noted, however, that accommodative microfluctuations were significantly elevated in these same subjects (Fig. 7). Increased accommodative microfluctuations could be suggestive of a more flexible crystalline lens in subjects with DS, although previous studies suggest the opposite.[8] Haugen et al.[8] report greater optical density in the crystalline lens of subjects with DS and suggest this could indicate decreased lens flexibility, although the relationship between optical density and lens stiffness is unclear. Conversely, increased accommodative microfluctuations may indicate that subjects have an increased depth of field. An increased depth of field is consistent with sensory pathway deficits and thus consistent with the lack of motor deficits as evidenced by normal peak velocities.

These findings of accommodative function suggest that accommodative inaccuracy is primarily related to a sensory pathway deficit in individuals with DS. However, the source of this deficit is still in question, especially given the large variability in accommodative performance between individual subjects with DS. One major source of variability between subjects may be refractive error and binocular status. Greater accommodative inaccuracy has been reported in subjects with DS with large amounts of hyperopia or strabismus,[10] whereas more accurate accommodative responses were found in subjects with DS with stable, low amounts of hyperopia.[7] The number of subjects in the present study is smaller than these previous studies, which may have masked significant differences related to refractive error or strabismus. However, subjects in this study with large amounts of hyperopia (exceeding +3.00 DS) and strabismus were among those who demonstrated adequate maximum accommodative responses (Table 1).

Refractive error and binocular status also differed between subjects with DS and the controls. These differences represent a potential limitation to this study. Subjects with DS had a similar range of myopic refractive error compared with controls, but a much greater range of hyperopia. In addition, 40% of subjects with DS had strabismus, nystagmus, or both. These differences between the two populations may contribute to some of the differences in accommodative measures observed in this study, although as noted above, some subjects with strabismus were among those with maximum accommodative responses similar to controls.

Another source of variability in the subjects with DS is their level of cognitive functioning. Cognitive functioning may be suggestive of the overall level of neural deficits and thus linked to accommodative function. The subjects with adequate accommodative responses in this study ($n = 5$) had significantly higher age equivalent scores, despite there being no difference in mean actual age from the subjects with poor responses. Several of these 5 subjects also had lower lags of accommodation and were among the few individuals to have at least one typical accommodative response. Only one previous study of accommodative function in individuals with DS known to the authors looked at the relationship of developmental ability with accommodative performance. That study did not find a relationship between accommodative accuracy and developmental quotient, but the developmental test used was intended for assessing mental and motor development in infants between the ages of 1 and 30 months.[4] Use of this test in subjects older than the intended age range (actual age range of subjects = 4.7 to 84.7 months) may have created a ceiling effect that limited the maximum score the subjects could attain, thereby creating an age equivalent range too small to observe differences in developmental ability among the subjects.

Further study is needed to identify the sensory deficits that may account for the large variability in accommodative function observed among subjects with DS. It would be useful to conduct future studies with more hyperopic controls as well as controls with strabismus, nystagmus, and amblyopia so that the effects of binocular vision anomalies on accommodation can be isolated from the cognitive impairment associated with DS.

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