Date: 11 August 2022

INVESTIGATING EYE SHAPE AND ITS EFFECT ON FOCUSING IN DOWN'S SYNDROME

End of study report for the Down's Syndrome Association

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Study background

The main aim of this project was to further our understanding on the origin of accommodation deficits (poor near focusing) in Down's syndrome (DS), by studying the shape and size of different eye structures involved in the process of accommodation (near focusing) in this population.

Research has shown that a large proportion of individuals with DS struggle to focus at near, and that bifocal glasses are successful at improving this focusing ability (Woodhouse et al., 1993, 1996, 2000; Stewart et al., 2007; Nandakumar & Leat, 2009). However, the origin and mechanisms behind this deficit are still unknown. This project proposed to investigate possible differences in the characteristics of the ocular structures involved in the accommodative process, mainly the ciliary muscle (CM) in individuals with DS and without DS (i.e. control group) using non-invasive technology. Any differences found could explain the accommodation deficits widely found in DS and its mechanism.

Summary of methods and procedures

Prior to the imaging of the anterior segment of participants, visual acuity, refractive error and accommodation was assessed. The participants' visual acuity was measured with the Sonksen logMAR Crowded test while wearing their spectacle correction, if any. The participant's prescription was obtained from their spectacles and an objective over refraction with distance retinoscopy was also obtained. In addition, objective refraction was also obtained with the WAM autorefractor. Participants' accommodative abilities were clinically assessed using dynamic retinoscopy and the Ulster-Cardiff Accommodation Cube.

Following this, images of the CM were obtained using Anterior Segment Optical Coherence Tomography (AS-OCT) and an adaptation to the imaging protocol already developed and published by the Aston University Ophthalmic Research Group (Sheppard & Davies, 2010, 2011). Briefly, participants were asked to fixate an eccentrically located target, so that the AS-OCT was aligned with the temporal or nasal area of the eye allowing the imaging of the CM. The adaptation implemented in this study was because previous studies using AS-OCT to assess the CM in typical developing populations have required participants to wear soft contact lenses and fixate at a target through a Badal Optometer (Sheppard & Davies, 2010; Sheppard & Davies, 2011). However, this was not going to be possible in some of the participants with DS due to the invasive nature of the contact lens fitting. Hence, a pilot study was conducted at the beginning of the research project to investigate whether the planned measurements could be conducted without wearing contact lenses and requiring the participants to look at a distant light target.

The results of this pilot study conducted on a control group (n=10) showed that there were no statistically significant differences ($p>0.5$) between the CM measures obtained with contact lenses when fixating on a target through a Badal Optometer and without contact lenses when fixating on a non-accommodative distant light target. This pilot study was key to inform the final protocol and procedures for the study, and therefore CM imaging in all of the primary study participants was undertaken uncorrected while they were fixating on a distant eccentric non-accommodative light target (Figure 1).

Finally, to further understand the morphology of additional ocular structures involved in the accommodation process in DS and their relation to the CM morphology and accommodation abilities in this population, we also used the Aladdin Optical Biometer and Corneal Topographer to obtain Lens Thickness (LT), Anterior Chamber Depth (ACD), Axial Length (AL), corneal curvature (K1 and K2) and Central Corneal Thickness (CCT) for each participant.

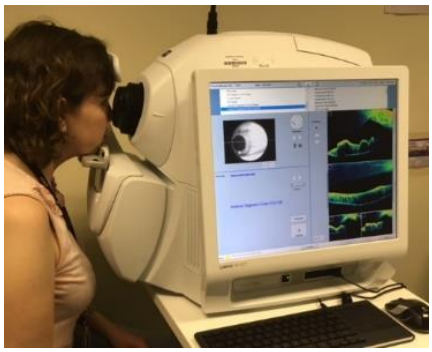

Figure 1. Imaging of the anterior segment and CM in a control participant taking part in the pilot study. The participant is uncorrected and eccentrically looking at a distance non-accommodative light target.

Study results

Participants: A total of 16 participants with DS (9 females, 7 males) with a mean age of 25.87±SD5.48 and 15 participants without DS (12 females, 4 males) with a mean age of 24.12±SD4.75 were recruited for the study.

The optometric parameters (visual acuity, objective refraction and accommodation) were successfully obtained from all participants. Participants with DS had visual acuities significantly lower than control participants ($p<0.001$) and their accommodative lags were also significantly larger ($p<0.001$). In contrast, participants from both groups were well matched for age ($F=1.103$; $p=0.343$) and spherical equivalent refractive error obtained with the WAM autorefractor ($F=0.514$; $p=0.432$).

Success rate: As expected, the success rate of the imaging was lower in participants with DS than in control participants. This is in line with lower success rates found in other vision studies involving participants with DS (Doyle et al., 2016). In our study, while 6 images (3 temporal and 3 nasal) of the CM were successfully obtained for 90% the control participants, this was only the case for 30% participants with Down's syndrome. However, at least 4 successful images (2 temporally and 2 nasally) were obtained for all control participants and most participants with Down's syndrome (68.75%). For data analysis purposes, an average of the CM measurements was obtained by averaging the parameters obtained across the successful images for each participant. For the situations where only one image was obtained (3 participants with DS), the CM measurement used in the analysis was the one obtained for that single image.

CM measures obtained for each participant (brief description and illustration in Figure 2):

- CM Anterior Length (CM Length): distance from the scleral spur to the point of CM maximum width. This measurement was made for the temporal and nasal CM (Temp_CM_Length and Nas_CM_Length).
- CM width at different points along the CM (CM25, CM50, CM75, CMT1, CMT2).
- CM thickness at 3mm posterior to the scleral spur (CMT3). This measurement was made for the temporal and nasal CM (Temp_CMT3 and Nas_CMT3).
- Maximum CM thickness (CMTMAX). This measurement was made for the temporal and nasal CM (Temp_CMTMAX and Nas_CMTMAX).

- Distance from the scleral spur to the inner apex. This measurement was made for the temporal and nasal CM (Temp_SS_IA and Nas_SS_IA).

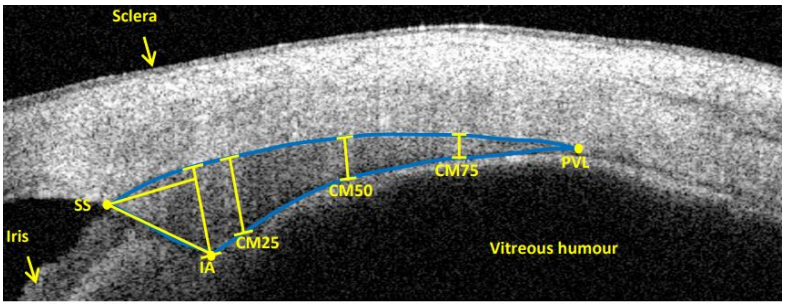

Figure2. Representation of the CM measurements obtained. The CM is outlined in blue and the thickness and width obtained are superimposed in yellow. PVL = posterior visible limit; SS = scleral spur; IA = inner apex; CM25, CM50, CM75 = thickness at 25%, 50% and 75% of total length (SS to PVL); maximum thickness = perpendicular distance from IA to sclera; anterior length = perpendicular distance from line of maximum thickness to SS.

Results: Table 1 presents all the average ciliary muscle measurements obtained from both groups indicating the p-values from the independent t-tests that were conducted to compare potential differences between the participant groups (participants with DS and without DS (Control)). It can be observed that most p-values are >0.05 indicating non-significant differences between the groups. Only two parameters have a p-value <0.05: Nas_CM_length (0.006) and Nas_CMT3 (0.046), but given the multiple comparisons conducted with the independent t-tests there is a risk that the chances of obtaining statistically significant results have been increased. For this reason, a Bonferroni correction was conducted to avoid false statistically significant results. Following this correction, the p value to indicate statistically significance was 0.002. After the Bonferroni correction, Nas_CM_length and Nas_CMT3, that were previously significant, do not remain significant.

CM Measurements (µm)	CONTROL				DS				P value
	Mean	SD	Max	Min	Mean	SD	Max	Min	
Temp_CM_Length	471.80	65.35	627.11	347.44	435.66	67.56	559.64	320.82	0.13
Temp_CMT1	89.47	16.02	110.16	57.49	88.92	15.19	107.31	60.63	0.92
Temp_CMT2	57.88	15.00	84.56	35.27	57.58	14.02	81.14	33.71	0.95
Temp_CMT3	33.91	12.40	59.35	16.38	32.98	11.52	58.24	13.45	0.82
Temp_CM25	82.81	15.42	104.89	55.48	85.92	15.29	110.24	51.90	0.57
Temp_CM50	48.78	12.98	71.30	31.63	53.94	12.93	75.49	27.48	0.26
Temp_CM75	23.75	7.32	37.82	13.36	27.38	8.46	43.60	16.08	0.20
Temp_CM_Max	93.74	17.55	119.09	58.24	92.49	16.06	117.63	58.68	0.83
Temp_SS_IA	124.51	12.99	152.47	105.83	125.57	15.27	145.48	97.27	0.83
Nas_CM_Length	457.43	60.43	605.43	382.64	394.28	55.89	464.15	266.53	0.00
Nas_CMT1	81.83	14.11	99.68	56.78	79.56	15.89	106.72	52.01	0.68
Nas_CMT2	52.91	11.33	66.89	34.10	47.17	13.04	66.74	18.61	0.20
Nas_CMT3	28.58	9.42	43.20	15.06	22.15	7.10	36.39	11.74	0.04
Nas_CM25	77.28	12.06	95.84	55.20	80.50	14.86	100.99	50.59	0.51
Nas_CM50	45.37	8.16	60.61	32.20	49.27	11.47	68.26	26.64	0.28
Nas_CM75	21.02	4.98	32.24	14.70	22.45	7.19	34.76	11.96	0.52

Nas_CM_Max	91.18	17.73	116.69	57.57	87.01	16.46	116.13	55.45	0.31
Nas_SS_IA	113.72	9.60	135.83	102.57	113.76	13.14	133.05	95.32	0.99

Table 1. Results of the CM measurements obtained from participants with DS and Control participants.

The same statistical analysis was conducted for the other ocular measurements that were obtained with the Aladdin Optical Biometer and Corneal Topographer to further understand the morphology of additional ocular structures involved in the accommodation process in DS (Table 2).

	CONTROL				**DS**				**P value**
	Mean	**SD**	**Max**	**Min**	**Mean**	**SD**	**Max**	**Min**	
AL (mm)	23.8	1.38	26.04	21.28	22.54	1.60	25.93	20.01	0.01
ACD (mm)	3.63	0.27	4.10	3.13	3.46	0.49	4.14	2.23	0.17
Lens Thickness (mm)	3.57	0.19	3.90	3.27	3.63	0.98	5.81	0.92	0.81
K1 (mm)	7.95	0.25	8.41	7.44	7.55	0.54	836	6.61	0.003
K2 (mm)	7.61	0.21	7.92	7.11	7.16	0.35	7.65	6.50	<0.001
CCT (µm)	526.60	29.7	58	469	506.92	39.29	583	415	0.13

Table 2. Results of the Lens Thickness (LT), Anterior Chamber Depth (ACD), Axial Length (AL), corneal curvature (K1 and K2) and Central Corneal Thickness (CCT) measurements obtained from participants with DS and Control participants.

We can observe that there are some p-values that are <0.05 suggesting that there are statistically significant differences between groups (AL (0.01), K1 (0.003) and K2 (<0.001)). Given the multiple comparisons conducted with the independent t-tests, we also corrected the p-value using a Bonferroni correction. Following this, the p-value to indicate statistically significance was 0.008 and only K1 and K2 remain statistically different between groups after such correction.

Main conclusions

1. Our study results suggest that the CM structure does not significantly differ between participants with and without DS, and therefore it is unlikely that the CM morphology plays a role in the accommodative deficit found in people with DS. This is in line with very recently published findings. (Anderson et al., 2022)
2. These findings support the view that a mechanical deficit is unlikely to be the main contributor to the accommodative deficit found in DS and that such deficit is more likely to be a result of a sensory deficit of the accommodative system and/or an abnormal near triad coupling or relationship as suggested by Doyle et al., (2016 and 2017).
3. The results found from other ocular structures are in line with those previously published that indicate that the corneal curvature is steeper in the population with DS (Doyle et al., 1998; Haugen et al., 2001; Little at al., 2009).

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