Ciliary Muscle and Sustained Accommodation

THESIS

Presented in Partial Fulfillment of the Requirements for the Degree Master of Science in the Graduate School of The Ohio State University

By
Amanda Ransdell, OD
Graduate Program in Vision Science

The Ohio State University
2015

Master's Examination Committee:
Melissa D. Bailey, OD, PhD, Advisor
Marjean Kulp, OD, PhD
Donald O. Mutti, OD, PhD
Copyright by
Amanda Ransdell
2015
Abstract

**Purpose:** to determine how the dimensions of the ciliary muscle are related to a subject’s ability to sustain accommodation by measuring accommodative lag and accommodative fatigue in school-age children and pre-presbyopic adults.

**Methods:** 117 subjects ages five to thirty years participated in the present study. Images of the nasal ciliary muscle of the relaxed right eye were obtained with the Zeiss Visante Anterior Segment Optical Coherence Tomographer. Autorefraction measurements of the right eye were performed at distance and near using the Grand Seiko Autorefractor, with habitual correction worn at near so the accommodative response, not refractive error, was found. Amplitude of accommodation was measured three times and averaged. Subjects were then asked to watch a 2 minute video at 40 centimeters while keeping vision clear out of alternating +2.50 diopter (D) and −2.50 D lenses over any habitual correction. Autorefraction at near was repeated after the accommodative fatigue task. Ciliary muscle images were analyzed and thickness was measured at multiple points along the length of the muscle, including the point of maximum thickness (CMTMAX) and at 1 mm (CMT1), 2 mm (CMT2), and 3 mm (CMT3) posterior to the scleral spur. The thickness of the ciliary muscle at the apex was also calculated (CMTMAX\textsubscript{Apical} and CMT1\textsubscript{Apical}). Accommodative lag was calculated for all subjects before and after the fatigue task using the subject’s accommodative response and refractive error. Stepwise linear regression
procedures were used to model the relationship between all accommodative measurements and each ciliary muscle thickness measurement (CMTMAX, CMT1, CMT2, CMT3, CMTMAXApical, and CMT1Apical) and paired t-tests were performed to demonstrate the change in accommodative lag before and after the fatigue task.

**Results:** Only age was significantly associated with the mean amplitude of accommodation for the analyses of all subjects, children, and adults. Although not statistically significantly, CMTMAX was found to be thinner in subjects with average amplitudes of accommodation below the age-expected average. Similar results were found for CMT2, and CMT3. When average amplitudes of accommodation were below the minimum based on age, CMT2 and CMT3 were found to be thinner, but the difference was not quite statistically significant. When accommodative lag was measured prior to the accommodative fatigue task, younger age was significantly associated with a larger accommodative lag for all models of ciliary muscle thickness. The more anterior regions of the muscle were significantly associated with refractive error. For the models including predictors for the apical region of the ciliary muscle, there was also a significant interaction between ciliary muscle thickness and refractive error, where more hyperopic refractive errors with thinner apical ciliary muscle thickness were associated with greater accommodative lag. For models including predictors for the posterior region of the muscle, the trend was the opposite, where more myopic refractive errors with thicker ciliary muscles were associated with greater accommodative lag. The results were similar when accommodative lag was measured after the accommodative fatigue task.
Some subjects may have been in an accommodative spasm post-fatigue task because their post-fatigue task accommodative lag was lower than their measured pre-fatigue task accommodative lag. The trend was for these subjects to have a thinner ciliary muscle than subjects whose accommodative lag was more positive post-fatigue task compared with pre-fatigue task, but the differences were not statistically significant.

Conclusions: Only age was significantly associated with the mean amplitude of accommodation for the analyses of all subjects, children, and adults. The more apical and posterior regions of the ciliary muscle and refractive error were associated with accommodative lag prior to and after an accommodative fatigue task.
This document is dedicated to my family for all of their love and support.
Acknowledgments

The work presented in this thesis would not have been possible without the help of Dr. Melissa Bailey. She has offered considerable knowledge, guidance, and inspiration as my research advisor. I also wish to thank Drs. Donald Mutti and Marjean Kulp for their work serving on my thesis committee. Finally, I would like to thank undergraduate research assistants, Libby Fisher and Tyler Dowdall, for their assistance in data collection.
Vita

2009 ................................................................. B.S. Biochemistry, University of Dayton

2013 ................................................................. O.D. The Ohio State University College of

Optometry

Fields of Study

Major Field: Vision Science
# Table of Contents

Abstract.............................................................................................................................................. ii

Acknowledgments............................................................................................................................ vi

Vita................................................................................................................................................... vii

List of Tables .................................................................................................................................... x

List of Figures ................................................................................................................................. xi

Chapter 1: Introduction.................................................................................................................... 1

1.1 Anatomy of the Ciliary Muscle................................................................................................. 1

1.2 Development of the Ciliary Muscle ......................................................................................... 3

1.3 Differences Based on Refractive Error ................................................................................... 6

1.4 Ciliary Muscle Function........................................................................................................... 7

1.5 Accommodative Deficiencies .................................................................................................. 9

1.6 Presbyopia ............................................................................................................................... 12

1.7 Present Study .......................................................................................................................... 13

Chapter 2: Methods........................................................................................................................ 15

2.1 Subjects ...................................................................................................................................... 15

2.2 Visual Acuity Measurements .................................................................................................. 16
2.3 Ciliary Muscle Imaging ........................................................................................................... 16
2.4 Autorefraction Measurement Pre-Fatigue Task ................................................................. 16
2.5 Accommodative Testing and Fatigue Task ........................................................................... 17
2.6 Autorefraction Measurement Post-Fatigue Task ............................................................... 18
2.7 Ciliary Muscle Image Analyses ........................................................................................... 18
2.8 Calculating Accommodative Lag ......................................................................................... 19
2.9 Statistical Analyses ............................................................................................................... 19

Chapter 3: Results ......................................................................................................................... 21
3.1 General Sample Characteristics ......................................................................................... 21
3.2 Mean Amplitudes of Accommodation ............................................................................... 21
3.3 Change from First to Last Amplitude of Accommodation Measurement ......................... 22
3.4 Accommodative Fatigue ....................................................................................................... 22
3.5 Lag of Accommodation ........................................................................................................ 22
3.6 Accommodative Spasm ........................................................................................................ 23

Chapter 4: Discussion ................................................................................................................... 24

References ..................................................................................................................................... 38
List of Tables

Table 1. Linear regression analyses of accommodative lag verses average amplitude of accommodation prior to the accommodative fatigue task in subjects of all ages. ............... 28

Table 2. Linear regression analyses of accommodative lag verses average amplitude of accommodation after the accommodative fatigue task in subjects of all ages.................. 29
List of Figures

Figure 1. Sample ciliary muscle outline. ................................................................. 30
Figure 2. Refractive error distribution among all subjects. ....................................... 31
Figure 3. Accommodative lag verses CMT2, before and after the accommodative fatigue task .......................................................................................................................... 32
Figure 4. Accommodative lag verses CMT3, before and after the accommodative fatigue task .......................................................................................................................... 33
Figure 5. Accommodative lag verses CMT1Apical based on refractive error before and after the accommodative fatigue task .......................................................................................................................... 34
Figure 6. Accommodative lag verses CMTMAXApical based on refractive error before and after the accommodative fatigue task .......................................................................................................................... 35
Figure 7. Accommodative lag verses CMT2 based on refractive error before and after the accommodative fatigue task .......................................................................................................................... 36
Figure 8. Accommodative lag verses CMT3 based on refractive error before and after the accommodative fatigue task .......................................................................................................................... 37
Chapter 1: Introduction

Accommodation refers to the ability of the eye to change power and bring near objects into focus on the retina by adjusting the power of the lens and is mainly controlled by the ciliary muscle.\(^1\) A recent study in our laboratory investigated ciliary muscle thickness and how it relates to academic achievement in third through fifth grade students.\(^2\) The data provided evidence suggesting that higher academic achievement is associated with a thicker anterior ciliary muscle.\(^2\) A hyperopic refractive error was also independently associated with poorer academic achievement.\(^2\) This study led to the question that we have only begun to address in the present study: Is ciliary muscle thickness an indicator of a child’s ability to sustain accommodation over longer periods of time than are typically measured clinically? The goal of the present study was to determine how the dimensions of the ciliary muscle were related to a subject’s ability to sustain accommodation by measuring accommodative lag and accommodative fatigue in school-age children and pre-presbyopic adults.

1.1 Anatomy of the Ciliary Muscle

To determine if the dimensions of the ciliary muscle are related to one’s ability to sustain accommodation, it is first necessary to understand the structure and development of the muscle.
The ciliary body is a structure in the eye that runs circumferentially behind the iris.\(^1\) The triangular shape has its base located anteriorly at the limit of the iris root and scleral spur and posterior limit at the ora serrata.\(^1\) The ciliary body consists of the pars plana (orbicularis ciliaris) and the pars plicata (corona ciliaris).\(^1\) The pars plana makes up approximately 2/3 of the tissue and extends from the ora serrata to the pars plicata.\(^1\) It is continuous with the pars plicata and the choroid.\(^3\) The pars plicata contains the ciliary processes (approximately 70 radially oriented projections) involved in aqueous humor production and assists in accommodation.\(^3\) The pars plicata makes up the anterior 2 millimeters of the ciliary body.\(^3\)

The ciliary muscle is comprised of 3 types of smooth muscle fibers which are named based on their orientation: longitudinal, radial, and circular.\(^1\) All muscle fibers originate at the scleral spur but have unique points of termination. The longitudinal fibers are the most external and lie parallel to the sclera.\(^1\) They have a narrow V shape with the apex terminating at the choroid.\(^1\) The radial muscle fibers are medial and terminate at the base of the ciliary processes\(^4\) and the circular muscle fibers are located the most internal and terminate into the top of the pars plicata.\(^1\) The ciliary body is covered with a dual layer of epithelium positioned apex to apex connected with gap junctions, desmosomes, and tight junctions.\(^1,4\) The outer layer contains desmosomes and gap junctions and is pigmented.\(^4,6\) This pigmented ciliary epithelium is continuous with the iris epithelium anteriorly and with the retinal pigment epithelium posteriorly.\(^1\) It is attached to the stroma with a basement membrane continuous with the basement membrane of the anterior iris epithelium and the inner basement membrane portion of Bruch’s membrane of the
The inner layer of the epithelium contains desmosomes, gap junctions, and zonula occludens to create a blood-aqueous barrier.\textsuperscript{5-7} This non-pigmented ciliary epithelium is continuous with the posterior iris epithelium and neural retina.\textsuperscript{1} The layer acts as a diffusion barrier between blood and aqueous and is involved in active secretion of aqueous humor components.\textsuperscript{1} The basement membrane for the non-pigmented ciliary epithelium is continuous with the internal limiting membrane of the retina.\textsuperscript{1}

The transition from the sclera to the ciliary body is known as the supraciliaris and creates a potential space to allow accommodation without tearing of ocular structures.\textsuperscript{1} This potential space also allows for separation of the ciliary body from the sclera in instances of trauma.\textsuperscript{1} The ciliary body stroma is located between the ciliary muscle and the epithelial layers as well as at the core of each ciliary process.\textsuperscript{1} It is highly vascularized and consists of loose connective tissue and melanocytes.\textsuperscript{1} The stroma contains fenestrated capillaries and receives its blood supply from the major arterial circle of the iris, which is located in the stroma near the iris root.\textsuperscript{1}

Innervation of the ciliary muscle comes from both the sympathetic and parasympathetic systems of the autonomic nervous system.\textsuperscript{1} Parasympathetic stimulation causes contraction of the ciliary muscle to allow accommodation\textsuperscript{1} while sympathetic stimulation has a small inhibitory effect on the ciliary muscle.\textsuperscript{8,9}

1.2 Development of the Ciliary Muscle

The ciliary muscle begins to develop during the fifth month of gestation and aqueous humor production begins at 4 to 6 months.\textsuperscript{1}
At birth, the ciliary body is already of substantial length. It continues to grow through age 2 years and reaches up to 90% of its mature adult length by 6 years.¹⁰ Like many other ocular structures, the ciliary muscle will undergo certain changes with age. One marked and consistent change is a decrease in the total area of the ciliary muscle as measured on histological meridional sections.¹¹ The length of the muscle has also been shown to decrease, from approximately 4mm in the 4th decade to 2mm by the 8th decade of life, however the width of the muscle shows no significant change with age.¹¹ Strenk et al. found a significant decrease in ring diameter with age when the muscle is in its unaccommodated state.¹²

In studying the different types of muscle fibers that make up the ciliary muscle, it was found that the three types do not age in the same way.¹¹ Tamm et al. found a reduction in area of the longitudinal fibers that correlated with age but no significant reduction in the radial fibers were noted and the circular fibers actually demonstrated a significant increase in area with age. They also found a decrease in the distance between the inner apex of the muscle and its insertion to the sclera spur.¹¹

The ciliary muscle thickness has been measured in 1st through 5th grade students and found that it does increase with age in childhood.¹³ Pucker et al. measured the ciliary muscle in 270 subjects ages 6 to 14 years and found this increase in thickness at all locations.¹³ Other changes associated with age include an increase in intramuscular connective tissue, differing between the type of muscle fiber, and the loss of contractile elements.¹¹
Quite a bit of research has been done on age changes in non-human primates. In one such study, Lutjen-Drecoll et al. worked with the rhesus monkey from birth to 6 years. They found the rhesus monkey to be a good animal model for human accommodation, presbyopia, and cataract formation. In studying the muscle, it was determined that the newborn ciliary muscle was mainly composed of longitudinal fibers, but by age 1 year longitudinal, radial, and circular muscle fibers could all be identified. As the monkey continued to grow, through age 4, the muscle progressively grew into its familiar triangular shape. This study also looked at the muscle cells and differentiated them from other smooth muscle cells in the body. It is noted that the muscle’s capability of rapid contraction and relaxation, the parallel-like structure of the myofibrils, the extensions of the dark bands similar to Z-bands, and the dense innervations of the ciliary muscle cells are remarkably similar to striated skeletal muscles. A unique characteristic of the ciliary muscle cells appears to be the large number of mitochondria, which was not noted until the monkey reached age 1 or 2 years.

Pardue and Sivak studied age-related changes in human ciliary muscle by treating donor eyes (aged 1 to 107) with atropine or pilocarpine and examining muscle dimensions. They found the overall length of the ciliary muscle tended to decrease with age while the width tended to increase with age. They also found the proportion of muscle fiber types changed with age: radial fibers increased, longitudinal fibers decreased, and circular fibers remained stable with age. Strenk et al. examined MRI images of phakic and monocularly pseudophakic patients ages 22 to 91 years and found the ciliary muscle ring diameter decreased significantly with age.
1.3 Differences Based on Refractive Error

Ciliary muscle thickness is likely related to one’s ability to sustain accommodation, and differences in ciliary muscle thickness have been found based on refractive error.\textsuperscript{17,18,19} This suggests that a person’s refractive error will have an impact on his or her ability to perform extended near activities. In particular, the thickness of the ciliary muscle at its thickest point was found to be thinner in patients with larger values of both hyperopia and myopia when compared with the same point in patients with low to moderate amounts of myopia. The same study found that when comparing the thickness of the muscle located at 2 and 3 millimeters posterior to the sclera spur, a thicker muscle was associated with a more myopic refractive error.\textsuperscript{13} It was also determined that higher amounts of hyperopia were associated with greater apical ciliary muscle thickness, suggesting these fibers can change in response to increased workload.\textsuperscript{13} A study measuring microfluctuations, or small variations in the refractive power of the eye, in subjects aged 8 to 15 years found a negative correlation between refractive error and ciliary body thickness as well as a negative correlation between age and accommodative microfluctuations.\textsuperscript{20} This suggests that people with a thicker ciliary muscle and greater age have a smaller high frequency component of microfluctuations of accommodation than those who are younger or who have a thinner ciliary muscle.\textsuperscript{20} The high frequency component of microfluctuations also tended to be larger in subjects who are more hyperopic.\textsuperscript{20}
1.4 Ciliary Muscle Function

The ciliary body has several functions in the human eye. These include aqueous production, production of some vitreal components, and control of accommodation.¹

Aqueous production occurs in the ciliary body and involves the fenestrated capillaries facilitating the movement of substances into and out of the blood from the stroma through the epithelium.¹ The non-pigmented ciliary epithelium is involved in active secretion of the aqueous humor into the posterior chamber.⁴

The ciliary body may have a role in production and secretion of connective tissue macromolecules located in the vitreous.²¹

Like any muscle, the ciliary muscle contracts and relaxes in response to stimuli. Accommodation refers to the ability of the eye to change power and bring near objects into focus on the retina by adjusting the power of the lens.¹ This is achieved by contracting the longitudinal and circular muscle fibers of the ciliary muscle, pulling the choroid forward and inward and stretching the choroid and posterior zonules.²² This results in a more spherical shaped lens which increases refractive power.¹ The choroid and zonules are returned to their resting position when the muscle relaxes.²²

Humans are able to accommodate at birth and the system continues to mature with the child. Some studies have suggested accommodation is relatively fixed during the first month of life and progresses towards adult behavior over the next few months.²³,²⁴ Stachs et al. performed investigations showing that the ciliary muscle is active in humans of all ages.³ They examined the ciliary muscle in a 34 year old and a 71 year old for changes during an accommodative stimulus and found that although the muscle contour changes
were greater in the younger eye, the response was present in the older presbyopic eye as well.³ This same effect was seen by Strenk et al. when they found that in 25 subjects ages 22 through 83, the ciliary muscle continues to contract with accommodative effort.¹² They found only a slight reduction in ciliary muscle contractile activity with age.¹² Gwiazda et al. studied 64 children to determine changes in accommodative response based on refractive error.²⁵ They found that myopic children accommodated less to a near target and experienced more blur than emmetropic children.²⁵

The AC/A is the ratio of the accommodative convergence (measured in prism diopters) to the stimulus to accommodation (measured in diopters).²⁶ Strenk et al. found that this ratio can only be reliably measured in subjects under the age of 45 years due to the small accommodative response after this age.¹² They also demonstrated that the response AC/A ratio increases by approximately 0.1 prism diopters per year from age 30 to 45 years of age.¹² A study by Ciuffreda et al. agrees that the AC/A cannot be reliably assessed in subjects aged 45 years and older and there is a gradual increase of the response AC/A ratio up to age 40-45 years.²⁷ Similarly, Bruce et al. found the response AC/A ratio increases from age 20 to 40 years.²⁸

As a primary function of the ciliary muscle, it is important to note there are several disorders that can cause deficiencies with the control of accommodation. Several such deficiencies are: accommodative insufficiency, accommodative infacility, accommodative excess, ill sustained accommodation, paralysis of accommodation, unequal accommodation, and accommodative lag in myopia development.²⁶ Unfortunately, few studies have determined the prevalence of accommodative
dysfunction in the general population, perhaps because it is widely under-diagnosed. The data that are available will be discussed below.

1.5 Accommodative Deficiencies

The action of the ciliary muscle has been of recent interest when researching deficiencies in the accommodative system. In a group of subjects ages 6 to 13 years without a diagnosed accommodative dysfunction (accommodative insufficiency, accommodative infacility, or accommodative excess)\(^{26}\), thickening of the anterior portion of the ciliary muscle and thinning of the posterior portion of the ciliary muscle was repeatedly found during an accommodative task.\(^{29}\) In another recent study, Thiagarajan and Ciuffreda evaluated asymptomatic individuals to determine if the accommodative system can be fatigued and if there is a different response of the accommodative system when a subject performs a task when the accommodative and vergence stimuli were the same (congruent) verses a task when the vergence stimulus remained constant but the accommodative stimulus was altered (noncongruent).\(^{30}\) They found no significant difference in the initial response amplitude, peak velocity, and time constant of accommodation after either task but did discover a trend for a reduction in peak velocity after the noncongruent task.\(^{30}\) They also found that while none of the subjects reported fatigue after the congruent task, 60% reported fatigue after the noncongruent task, suggesting the accommodative system can be fatigued in subjects without symptoms or a diagnosed vergence or accommodative dysfunction.\(^{30}\)
Several researchers have found that among accommodative deficiencies, accommodative insufficiency is the most common. These studies claim the prevalence is 55% to 84% in subjects diagnosed with accommodative disorders.\textsuperscript{31,32} Still, in a pediatric population, Scheiman et al. found the prevalence of accommodative insufficiency comparable to accommodative excess and accommodative infacility.\textsuperscript{33} Accommodative insufficiency is defined as a condition in which the ability of a patient to stimulate accommodation is not present.\textsuperscript{26} In diagnosing accommodative insufficiency, it is recommended to compare a patient’s amplitude of accommodation to the minimum expected amplitude according to Hofstetter’s formula \[15 - \frac{1}{4}(\text{age})\].\textsuperscript{34} If the patient’s amplitude is 2 diopters or more below this value, it is considered abnormal.\textsuperscript{26} Other valuable findings in a patient with accommodative insufficiency include low findings on the positive relative accommodation, difficulty clearing minus lenses with both monocular accommodative facility and binocular accommodative facility testing, and more plus than expected with monocular estimation method retinoscopy and the fused cross-cylinder test.\textsuperscript{26} Accommodative insufficiency is often associated with a binocular vision problem, especially a small esophoria, and common patient complaints include blur, headaches, eyestrain, double vision, reading problems, fatigue, difficulty changing focus from one distance to another, and sensitivity to light.\textsuperscript{26,32} Patients who are found to have accommodative insufficiency will likely respond well to vision therapy and/or added plus lenses.\textsuperscript{26}

Accommodative infacility is a condition in which the patient experiences difficulty switching focus from distance to near.\textsuperscript{26} In this disorder, amplitude of accommodation is
normal, and symptoms are often associated with near work. Patients report blurred vision, difficulty changing focus from one distance to another, headaches, eyestrain, difficulty sustaining and attending to reading and other close work, and fatigue.\textsuperscript{26,32} In office testing will reveal poor performance with monocular accommodative facility and binocular accommodative facility and reduced negative relative accommodation and positive relative accommodation.\textsuperscript{26} These patients will likely respond well to vision therapy.\textsuperscript{26}

There is some disagreement about an appropriate definition of accommodative excess. Because of this, published prevalence estimates for accommodative excess in the population vary greatly.\textsuperscript{32,35} In its broadest sense, accommodative excess is a disorder in which the patient has difficulty with relaxing his or her accommodation.\textsuperscript{26} Patient’s symptoms are usually associated with near work and include blurred vision, eyestrain, headaches, photophobia, diplopia, and difficulty concentrating.\textsuperscript{26} A patient with accommodative excess will have difficulty clearing plus lenses on monocular accommodative facility and binocular accommodative facility, along with difficulty with negative relative accommodation. Commonly, a binocular vision disorder is found along with accommodative excess. Vision therapy is often the best treatment for these patients.\textsuperscript{26}

Ill-sustained accommodation is a condition in which standard test conditions reveal normal amplitude of accommodation but the amplitude decreases over time. It is often categorized as a subcategory of accommodative insufficiency.\textsuperscript{26} Patients with ill-sustained accommodation will likely respond well to vision therapy and/or added plus lenses.
Paralysis of accommodation is a condition in which a patient is not able to stimulate accommodation in one or both eyes. Like ill-sustained accommodation, paralysis of accommodation is often considered a subcategory of accommodative insufficiency.\textsuperscript{26} It is considered very rare and can be associated with infections, glaucoma, trauma, lead poisoning, and diabetes.\textsuperscript{26}

When there is a difference in accommodation between the two eyes of at least 0.50 diopters, unequal accommodation is diagnosed.\textsuperscript{22} Unilateral paralysis of accommodation, trauma, and functional amblyopia can lead to unequal accommodation.\textsuperscript{22,26}

High accommodative lag has been suggested to cause high myopia progression in children similar to hyperopic defocus inducing eyeball growth.\textsuperscript{36} However, it is unclear if the accommodative lag is elevated before or after myopia onset. Several recent studies have determined there is no association between accommodative lag and myopia progression in children.\textsuperscript{36,37}

1.6 Presbyopia

Presbyopia is the age-related progressive loss of the ability to accommodate that occurs universally.\textsuperscript{1} It is irreversible and results in a situation where a patient can no longer maintain clear vision at the near point.\textsuperscript{22,26} Presbyopia usually occurs between the ages of 40 and 45 years.\textsuperscript{22,26} Patient-identified symptoms are identical to those of accommodative insufficiency: blur and discomfort with near work.\textsuperscript{22} Many possible factors contribute to presbyopia, including the elasticity of the lens capsule, a change in the refractive index of the lens, and changes to the structure of the ciliary body.\textsuperscript{11} In the
rhesus monkey, it has been shown that degenerative changes begin in the ciliary muscle as young as 6 years of age. In humans, it is thought that the remodeling of the ciliary muscle might result in the muscle being shifted to a more favorable position to induce accommodation as well as overcome factors in the lens that may deter accommodation.

1.7 Present Study

In order to determine how the dimensions of the ciliary muscle are related to a subject’s ability to sustain accommodation, accommodative lag and accommodative fatigue were measured in school-age children and pre-presbyopic adults. While limited research has been performed on children, there may be evidence that accommodative stress can influence sustained attention in adults. Without a universally accepted method for measuring ciliary muscle dimensions, we used a procedure developed in our laboratory which measures the nasal ciliary muscle of the right eye with the Visante Anterior Segment Optical Coherence Tomographer by having the subject look to the right of fixation. This is a brief and non-invasive procedure which we have used with great success.

A recent study in our lab investigated the ciliary muscle thickness and how it relates to academic achievement in third through fifth grade students. Ciliary muscle images of 97 children were taken and measured along with refractive error. Standardized test scores for two academic achievement tests were obtained from the schools. The data provide evidence of higher academic achievement associated with a thicker anterior ciliary muscle (at its thickest point). A hyperopic refractive error was independently
associated with poorer academic achievement. This study led to the question we have begun to address in the present study: Is ciliary muscle thickness an indicator of a child’s ability to sustain accommodation over longer periods of time than are typically measured clinically?
Chapter 2: Methods

2.1 Subjects

Subjects were recruited from the guest population visiting the Center of Science and Industry (COSI), a large and popular attraction for children and adults in Columbus. Guests who were interested in participating in research approached the research pods in the Labs in Life exhibit at COSI during normal business hours. If they could speak English, we asked if they were between the ages of five and 30 years and then explained the purpose of the study.

One hundred seventeen subjects ages five to 30 years (mean = 13.97 years, SD = 6.5 years) participated in the study. In our analysis, “children” is defined as those less than 18 years of age and “adults” is defined as ages 18 to 30 years. Exclusion criteria consisted of any subject who was unable or unwilling to complete study testing procedures for any reason and any subject who did not have visual acuity in each eye better than 20/40. After discussion of the purpose and procedures, written informed consent was obtained from each subject age 18 years and older and from a parent or guardian of each subject under age 18 years. Written assent was obtained from each subject under age 18 years. The study was approved by the Institutional Review Board of The Ohio State University.
2.2 Visual Acuity Measurements

All measurements with the exception of visual acuity and accommodative fatigue were made on right eyes only. Visual acuity was measured with habitual correction using a Bailey-Lovie acuity chart under normal examination room illumination. Habitual correction was determined by what the subject was wearing at the time of testing: spectacles, contact lenses, or neither. The spectacle prescription of every subject wearing them was read with a lensometer. The chart was located at a distance of 20 feet, was high contrast, and testing was performed monocularly. Visual acuity was recorded as the line where the subject had identified three or more of the letters correctly. Guessing was encouraged.

2.3 Ciliary Muscle Imaging

The nasal ciliary muscle of the relaxed right eye was imaged with the Zeiss Visante Anterior Segment Optical Coherence Tomographer (OCT) by methods previously described by our lab. Habitual correction was removed for ciliary muscle imaging. The subject viewed a target at a distance of 20 feet, slightly to the right of the machine, while three images of the ciliary muscle were obtained. The target was a large letter, approximately 20/200 Snellen.

2.4 Autorefraction Measurement Pre-Fatigue Task

Autorefraction measurements of the right eye were performed at distance and at near using the Grand Seiko Autorefractor. To measure distance autorefraction, subjects
first looked at the large letters of a letter chart (20/200 or 20/100 Snellen equivalent) more than 20 feet across the room for approximately one minute without any correction. At least five measurements were taken and the mean was used in analysis. Subjects wore any habitual correction and looked at a card set at 40 centimeters (a 2.50 diopter accommodative stimulus) with 20/25 letters that read “Keep these words clear” for near autorefraction. Habitual correction was worn so the accommodative response, not refractive error, was found. The mean of at least five measurements was used in analysis.

2.5 Accommodative Testing and Fatigue Task

The amplitude of accommodation was measured three times in the right eye of each subject. With the left eye occluded and habitual correction worn, a single 20/20 size letter was brought slowly towards the subject until the subject reported blur. The dioptric value was recorded and the mean of three values taken. Only a subjective measurement of amplitude of accommodation was measured. A recent study measured amplitudes of accommodation in subjects aged 3 to 64 years with both objective and subjective means and found that the subjective push-up technique consistently over estimates accommodative amplitudes in all ages, particularly in young children.41

No previous studies have attempted to fatigue the accommodative system in a group of subjects younger than age 7 years.38,42-44 In recent sustained accommodation studies, various tasks were used to attempt to fatigue the ciliary muscle. These tasks include viewing a computer screen for 15 minutes with −2.00D lenses,38 reading a passage of text from a computer screen for 30 minutes,43 and looking at a color cartoon
on a LCD monitor for 20 minutes. In an effort to make the protocol brief and still induce stress on the accommodative system, we attempted to induce some accommodative fatigue by alternating +2.50D and −2.50D lenses in front of each subject’s habitual correction while the subject watched a Disney video on an iPad for two minutes. This will be referred to as the fatigue task. The iPad was placed 40 centimeters from the subject. The subject was asked to report when the movie became clear at which point the lenses were flipped. Facility was recorded as the number of cycles completed in two minutes. One cycle consisted of the subject reporting clear vision through both the +2.50D and −2.50D lenses.

2.6 Autorefraction Measurement Post-Fatigue Task

Autorefraction at near only was repeated after the accommodative fatigue task again using the Grand Seiko Autorefractor and the same card containing 20/25 size letters at 40 centimeters. Habitual correction was worn and the mean of at least five measurements was used in analysis.

2.7 Ciliary Muscle Image Analyses

The images of the ciliary muscle were analyzed by a masked examiner. Ciliary muscle thickness measurements were obtained from each image at multiple points along the length of the ciliary muscle including at the point of maximum thickness (CMTMAX) and at 1 mm (CMT1), 2 mm (CMT2) and 3 mm (CMT3) posterior to the scleral spur. The
thickness of the ciliary muscle at the apex was also calculated in a manner similar to previous reports from our laboratory:\textsuperscript{13,45}:

\begin{align*}
\text{ApicalCMTMAX} & = \text{CMTMAX} - \text{CMT2} \\
\text{ApicalCMT1} & = \text{CMT1} - \text{CMT2}
\end{align*}

Figure 1 shows the muscle outline, scleral spur position, and all thickness measurements.

2.8 Calculating Accommodative Lag

Accommodative lag was calculated for all subjects before and after the fatigue task. The calculation as performed as previously described\textsuperscript{19} using the subject’s accommodative response (NAR), the spherical refractive error if glasses were worn (SP), and the amount of uncorrected refractive error if the subject was not wearing correction (DAR). The formula used is as follows:

\[
\text{Lag} = \left\{ \left[ \left( \frac{1}{NAR} + 0.015 \right)^{-1} + SP \right]^{-1} - 0.015 \right\}^{-1} - (DAR - SP)
\]

\[
- \left[ \left\{ -4 \left( 1 - \left[ 4 \left( \frac{1}{0.015} + SP \right)^{-1} \right] \right\}^{-1} + SP \right\}^{-1} - 0.015 \right]^{-1} - (DAR - SP)
\]

2.9 Statistical Analyses

To determine how the dimensions of the ciliary muscle are related to a subject’s ability to sustain accommodation in school-aged children and adults, stepwise linear regression procedures were used to model the relationship between all accommodative
measurements and each ciliary muscle thickness measurement (CMTMAX, CMT1, CMT2, CMT3, ApicalCMTMAX, and ApicalCMT1). Paired t-tests were also performed to compare accommodative lag before and after the accommodative fatigue task (Table 3).
Chapter 3: Results

3.1 General Sample Characteristics

This study includes 117 subjects ages five to thirty years (mean = 13.97 years, SD = 6.5 years). Based on non-cycloplegic distance autorefraction data, 59 were emmetropes (spherical equivalent of −0.50 DS to +0.50 DS), 26 were hyperopes (spherical equivalent of greater than +0.50 DS) and 32 were myopes (spherical equivalent of more than −0.50 DS) (Figure 2). Eighty one subjects were 18 years or younger and 24 subjects were older than 18 years.

3.2 Mean Amplitudes of Accommodation

Only age was significantly associated with the mean amplitude of accommodation for the analyses of all subjects (β = −0.18, p < 0.00002), for children (β = −0.39, p < 0.002), and for adults (β = −0.37, P < 0.003). Although not statistically significantly, CMTMAX was found to be thinner (p = 0.5) in subjects with average amplitudes of accommodation below the age-expected average based on Hofstetter’s formula \[18.5 - \frac{1}{3}(age)\]. Similar results were found for CMT2 (p = 0.2), and CMT3 (p = 0.2).
When average amplitudes of accommodation were below the minimum based on age according to Hofstetter’s formula \[15 - \frac{1}{4}(age)^2\], CMT2 (p = 0.06) and CMT3 (p = 0.11) were found to be thinner, but the difference was not quite statistically significant.

3.3 Change from First to Last Amplitude of Accommodation Measurement

Nothing was significantly associated with the difference between first and last amplitude measurements. There was no significant difference between ciliary muscle thickness when comparing subjects whose amplitude of accommodation increased from the first to last measurement to subjects whose amplitude of accommodation remained stable or decreased.

3.4 Accommodative Fatigue

No accommodative measurements were significantly associated with cycles completed in 2 minutes during the accommodative fatigue task and accommodative lag before or after the fatigue task. There were also no significant associations between CMTMAX, CMT1, CMT2, or CMT3 and cycles completed in 2 minutes.

3.5 Lag of Accommodation

When accommodative lag was measured prior to the accommodative fatigue task (Table 1), younger age was significantly associated with a larger accommodative lag for all models of ciliary muscle thickness. The more anterior regions of the muscle (CMTMAX, CMT1, CMT2, and CMTMAXApical, and CMT1Apical) were significantly
associated with refractive error. For the models including predictors for the apical region of the ciliary muscle (CMTMAX\textsubscript{Apical} and CMT1\textsubscript{Apical}), there was also a significant interaction between ciliary muscle thickness and refractive error, where more hyperopic refractive errors with thinner apical ciliary muscle thickness were associated with greater accommodative lag. For models including predictors for the posterior region on the muscle (CMT2 and CMT3), the trend was the opposite, where more myopic refractive errors with thicker ciliary muscles were associated with greater accommodative lag. The results were similar when accommodative lag was measured after the accommodative fatigue task (Table 2). Figures 3 and 4 show accommodative lag verses CMT2 and CMT3, respectively, both before and after the fatigue task. Figures 5 through 8 show the association of ciliary muscle thickness with refractive error and accommodative lag.

3.6 Accommodative Spasm

Some subjects may have been in an accommodative spasm after the fatigue task because their post-fatigue task accommodative lag was higher than their measured pre-fatigue task accommodative lag. The trend was for these subjects to have a thinner ciliary muscle (CMTMAX, CMT1, CMT2, and CMT3) than subjects whose accommodative lag was more positive post-fatigue task compared with pre-fatigue task, but the differences were not statistically significant (p = 0.46, p = 0.18, p = 0.7, p = 0.7, respectively).
Chapter 4: Discussion

The goal of the present study was to determine how the dimensions of the ciliary muscle were related to a subject’s ability to sustain accommodation by measuring accommodative lag and accommodative fatigue in school-age children and pre-presbyopic adults. We found that CMTMAX is thinner in subjects with average amplitudes of accommodation below the age-expected average, but not statistically significant. Similarly, CMT2 and CMT3 were thinner in subjects with average amplitudes below the age-expected, but not statistically significant. When average amplitudes of accommodation were below the minimum based on age, CMT2 and CMT3 were found to be thinner than in subjects whose average amplitudes of accommodation were above the minimum, but these results were not statistically significant. Increasing age was significantly associated with a decreasing mean amplitude of accommodation for the analyses of all subjects, children, and adults.

Age, refractive error, and ciliary muscle thickness were not significantly associated with the difference between first and last amplitude measurements when comparing subjects whose amplitude of accommodation increased from the first to last measurement to subjects whose amplitude of accommodation remained stable or decreased. There was also no significant difference between CMTMAX found.
Again, age, refractive error, and ciliary muscle thickness were not significantly associated with the number of cycles completed in 2 minutes during the accommodative fatigue task. There was also no significant association between CMTMAX, CMT1, CMT2, or CMT3 and cycles completed.

Accommodative lag was related to age and refractive error in models that included various ciliary muscle thickness measurements, with differing effects of refractive error and interactions with ciliary muscle thickness at the various thickness points. The results likely represent the dichotomy of accommodative lag in children, where both hyperopic and myopic children are known to have higher accommodative lag.41

Some subjects may have been in an accommodative spasm after the fatigue task because their post-fatigue task accommodative lag was higher than their measured pre-fatigue task accommodative lag. These subjects were found to have a thinner ciliary muscle (CMTMAX, CMT1, CMT2, and CMT3) than subjects whose accommodative lag was more positive post-fatigue task compared with pre-fatigue task, but the results were not statistically significant.

Although we have found that amplitudes of accommodation are not significantly correlated with ciliary muscle thickness, the results may have been significant if we had used an objective measure of amplitudes. Anderson and Stuebing found that, especially in children, objective measurements of accommodation will yield a lower value than that measured by the subjective push-up technique.41 As many of our subjects were children and their amplitudes of accommodation were measured by the push-up method, we
wonder if even more subjects would have fallen below the expected or minimum values for their age had we used a different method. This should be considered in future studies.

A recent study claims that when wearing spectacle lenses, lag of accommodation is underestimated with an autorefractor. This may have occurred in the present study, however Kimura et al. performed measurements on a cyclopleged eye and found that the degree of underestimation was 0.3 D at most in myopic eyes so the difference may not be clinically meaningful in the non-cyclopleged eye.

Kulp and Schmidt performed a study on visual predictors of reading performance in kindergarten and first grade children and, although accommodative lag was not measured, accommodative facility was found to be significantly associated with successful reading performance in this group. They found that the relationship between accommodative facility and reading performance became more significant with increased age. Accommodative facility was not measured in the present study; however, we did measure number of cycles completed in 2 minutes during our fatigue task. In our study, cycles completed during the fatigue task was a subjective variable based on subject response of “clear,” so future studies should consider a different method which may be more effective.

The method of ciliary muscle imaging used in the present study has been successfully used previously in several studies from our laboratory and we are confident in the in vivo measurement of ciliary muscle thickness.

There are several limitations to the present study. As discussed above, subjective amplitudes of accommodation were measured but it has been recently determined that
objective methods are much more accurate.\textsuperscript{41} Also mentioned above, our method of accommodative fatigue was based on subject recognition of blur which may have been difficult for certain subjects, especially the younger children. In addition, we cannot be sure the accommodative system was fatigued sufficiently or equally among all subjects with the current method.

Another limitation of the present study may be that cycloplegic measurements were not taken. While we assume the ciliary muscle was at rest during imaging of the ciliary muscle and refractive error measurements, we cannot be sure. In addition, all of our measurements were of very short duration. None of the current clinical tests that were used in this study can assess whether or not a child or adult can sustain accommodative effort for 10, 20, or even 30 minutes. The trends noted for many standard clinical measurements in this study suggest that thinner ciliary muscles may be associated with more accommodative dysfunction if either a larger sample size is used, if subjects with specific accommodative symptoms and diagnoses are recruited, or if the duration of the accommodative task was increased.

Finally, no assessment of binocular vision status was taken. Although most measurements were monocular and made on right eyes only, the accommodative fatigue task was performed binocularly. It is possible a subject had an undiagnosed binocular vision issue (such as convergence insufficiency or suppression) that caused difficulty clearing the image through the ±2.50 D lenses and is unrelated to ciliary muscle function.
<table>
<thead>
<tr>
<th>Effect</th>
<th>Anterior Region</th>
<th>Posterior Region</th>
<th>Apical Region</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CMTMAX</td>
<td>CMT1</td>
<td>CMT2</td>
</tr>
<tr>
<td>Intercept</td>
<td>4.14</td>
<td>4.17</td>
<td>3.01</td>
</tr>
<tr>
<td>Age (years)</td>
<td>−0.03 (p = 0.01)</td>
<td>−0.03 (p = 0.02)</td>
<td>−0.03 (p = 0.015)</td>
</tr>
<tr>
<td>Refractive Error (D)</td>
<td>0.18 (p &lt; 0.0001)</td>
<td>0.17 (p &lt; 0.0001)</td>
<td>−1.03 (p &lt; 0.001)</td>
</tr>
<tr>
<td>Ciliary Muscle Thickness</td>
<td>−0.001 (p = 0.3)</td>
<td>−0.002 (p = 0.2)</td>
<td>−0.00008 (p = 0.9)</td>
</tr>
<tr>
<td>RE X CMT Interaction</td>
<td>NS</td>
<td>NS</td>
<td>0.002 (p &lt; 0.001)</td>
</tr>
</tbody>
</table>

Table 1. Linear regression analyses of accommodative lag verses average amplitude of accommodation prior to the accommodative fatigue task in subjects of all ages.
<table>
<thead>
<tr>
<th>Effect</th>
<th>CMTMAX</th>
<th>CMT1</th>
<th>CMT2</th>
<th>CMT3</th>
<th>CMTMAXapical</th>
<th>CMT1apical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>4.23</td>
<td>3.97</td>
<td>2.92</td>
<td>2.66</td>
<td>2.37</td>
<td>2.76</td>
</tr>
<tr>
<td>Age (years)</td>
<td>−0.02</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>−0.02</td>
</tr>
<tr>
<td></td>
<td>(p = 0.04)</td>
<td></td>
<td></td>
<td></td>
<td>(p = 0.05)</td>
<td></td>
</tr>
<tr>
<td>Refractive Error (D)</td>
<td>0.18</td>
<td>0.19</td>
<td>−1.16</td>
<td>−0.32</td>
<td>0.83</td>
<td>0.93</td>
</tr>
<tr>
<td></td>
<td>(p &lt; 0.001)</td>
<td>(p &lt; 0.0001)</td>
<td>(p &lt; 0.001)</td>
<td>(p = 0.08)</td>
<td>(p &lt; 0.0001)</td>
<td>(p &lt; 0.00001)</td>
</tr>
<tr>
<td>Ciliary Muscle Thickness</td>
<td>−0.002</td>
<td>−0.002</td>
<td>−0.0009</td>
<td>−0.0007</td>
<td>0.0004</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>(p = 0.2)</td>
<td>(p = 0.2)</td>
<td>(p = 0.4)</td>
<td>(p = 0.6)</td>
<td>(p = 0.6)</td>
<td>(p = 0.9)</td>
</tr>
<tr>
<td>RE X CMT Interaction</td>
<td>NS</td>
<td>NS</td>
<td>0.0024</td>
<td>0.0016</td>
<td>−0.0023</td>
<td>−0.0003</td>
</tr>
<tr>
<td></td>
<td>(p &lt; 0.0001)</td>
<td>(p = 0.007)</td>
<td>(p &lt; 0.001)</td>
<td>(p &lt; 0.001)</td>
<td>(p &lt; 0.0001)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Linear regression analyses of accommodative lag verses average amplitude of accommodation after the accommodative fatigue task in subjects of all ages.
Figure 1. Sample ciliary muscle outline.
Figure 2. Refractive error distribution among all subjects.
Figure 3. Accommodative lag versus CMT2, before and after the accommodative fatigue task
Figure 4. Accommodative lag verses CMT3, before and after the accommodative fatigue task.
Figure 5. Accommodative lag versus CMT1Apical based on refractive error before and after the accommodative fatigue task.
Figure 6. Accommodative lag versus CMTMAX\textsubscript{Apical} based on refractive error before and after the accommodative fatigue task.
Figure 7. Accommodative lag verses CMT2 based on refractive error before and after the accommodative fatigue task.
Figure 8. Accommodative lag verses CMT3 based on refractive error before and after the accommodative fatigue task
References


46. Kimura S, Hasebe S, Ohtsuki H. Systematic measurement errors involved in over-refraction using an autorefractor (Grand-Seiko WV-500): is measurement of