3. Materials and Methods

The present study has been conducted at the Vision Performance Institute (VPI) of the College of Optometry, Pacific University in Forest Grove, Oregon, USA. The study was approved by the Pacific University Institutional Review Board (IRB) (see Appendix) and followed the World Medical Association (WMA) Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. Data collection was carried out by various research assistants with a background in either biology, vision science, or optometry and took place between March 3rd 2015 and June 21st 2015.

3.1. Subjects

Thirty-four subjects aged 19 to 28 have been recruited from the Forest Grove area, predominantly from the Pacific University campus. The 16 female and 18 male participants were screened to fulfill the following eligibility criteria:

- within the age range of 19 to 42 years
- able to read English at middle-school level
- normal near vision (e.g., >0.7 near-vision acuity in each eye)
- no eye nor systemic pathologies or abnormalities affecting the ocular surface, accommodation, or oculomotor system
- no photosensitivity
- no epilepsy

- no claustrophobia

Furthermore, subjects with binocular or accommodative anomalies regardless of these having been treated or not (i.e., vision therapy, eye muscle surgery etc.) have been excluded from the study.

The demographics shown in Table 3-1 suggest that there is no statistical significant difference in the age when the subjects are divided by gender (p = .612). This was verified by a 2-tailed t-test for independent samples.

Gender	N	Min. Age	Max. Age	Mean Age	SD Age
Female	16	19	28	23.3	2.6
Male	18	19	28	23.7	2.6
Male and female	35	19	28	23.5	2.6

Table 3-1 Subjects demographics

3.2. Protocol and Sequence

Even though this report focuses on changes of the oculomotor near-response-triad reflex (i.e., accommodation, vergence, and pupils), it was part of a bigger study measuring various aspects of visual fatigue. As interference between the different measurements cannot be excluded, all used tests are listed in the following test sequence for completeness. However, the relevant procedures for this report will be specified in more detail later and are printed in bold for easier identification.

3.2.1. Consent and Enrolment

At the beginning of the session the subject was informed about the study and written consent (see Appendix) was obtained. The participant was thereafter screened for the inclusion and exclusion criteria. Those satisfying the criteria have then been formally entered into the study.

3.2.2. Reading Materials

Afterwards those enrolled in the study could choose to read one of the following three books during the experiment: *The Brain That Changes Itself,* a scientific non-fiction book by Norman Doidge[210], *Brave New World* by Aldous Huxley, a science-fiction book[211], or the optometry textbook *Clinical Anatomy and Physiology of the Visual System* by LeAnn Remington[212].

3.2.3. Baseline

To establish a baseline as reference for the following measurements subject's initial **accommodation**, **vergence,** and stereopsis functions as well as dry eye status and **subjective rating of fatigue** was obtained prior to the first reading block.

3.2.4. Reading and Real-Time Measurements

Participants have been seated in a height-adjustable chair in front of a 31" high-definition LCD display (Sharp PNK321) with a resolution of 2014 × 1536 pixel and a luminance of 250 cd/m^2. A chin- and forehead-rest was used to maintain a viewing distance of 55 cm and the head was stabilized with a bandeau to minimize head movements. The height of the screen was adjusted to allow level viewing. Electromyography (EMG) electrodes were attached to the subject's forehead, right earlobe and right lower eyelid as shown in Figure 3-1.

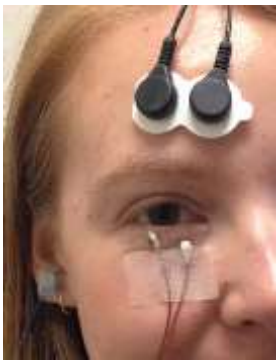

Figure 3-1 EMG electrodes attached to forehead, right earlobe and right lower eyelid.

Participants read the chosen book displayed at 11-point Verdana for about 55 minutes per block. The exact time depended on their actual reading speed. For the experiment design, a typical college student's reading speed of 280 words per minute was assumed.[213] Subjects read 4 to 5 blocks each one followed by the posttests described in Chapter 3.2.5.

While the participant was reading, real-time measurements of **accommodation** (with auto-refractor), **eye movements** and reading behavior (with eye-tracker), **pupil size** (with auto-refractor and eye-tracker), reading speed (with a custom-made program), eye muscle activity (with Noraxon wireless EMG, Noraxon U.S.A. Inc. Scottsdale, Arizona, USA; http://www.noraxon.com/products/emg-electromyography), heart rate and arterial oxygenation were recorded. A video recording of the participant's face was used to detect signs of fatigue (e.g., yawing, extended blinking, or falling asleep).

3.2.5. Posttests

After each block of reading, subjects took a series of clinical tests, including **accommodative amplitude and facility, vergence amplitude and facility**, stereopsis tests, and dry eye assessment (with LipiView). In addition, a **questioner** to subjectively measure the fatigue symptoms was administered.

3.2.6. Debriefing and Compensation

After 4 of 5 blocks of reading the posttests have been repeated one last time. Afterwards the participants have been debriefed about the study and have been compensated monetarily and/or with extra course credits towards there optometry degree if applicable.

3.3. Objective Measurements

Several objective measurements have been used to detect changes in the accommodation, vergence and pupillary system. The methods used can be categorized in two groups:

A. Real-time measurements

   have been recorded continuously while the subject was reading on screen.

B. Clinical Tests

   have been used sequentially after each reading block.

3.3.1. Real-time Measurements

To detect changes and fluctuations in the oculomotor near-response-triad reflex potentially due to visual fatigue, their functions were monitored in real-time while the subjects read. Shiomi et al.[214] have shown in 2013 that it was possible to simultaneously measure both accommodation and convergence when subjects gazed at an object. However, since a different eye tracking system was used in this study, we decided to interrupt the accommodation measurement twice for 10 minutes in each block in order to obtain uninfluenced eye tracking recordings.

3.3.1.1. Accommodation

The real-time eye focusing status (accommodation) of the dominant eye was measured with the Grand Seiko binocular auto refractor/keratometer WR-5100K (SHIGIYA MACHINERY WORKS LTD., GS Division, Hiroshima, Japan; http://www.grandseiko.com/english/WR-5100K.htm; Figure 3-2) to monitor the change in accommodative power over time as well as its accuracy and micro-fluctuations.

Figure 3-2 Grand Seiko WR-5100K from https://www.aitindustries.com/images/wr-5100k_binocular_autorefractor_keratometer.jpg

The WR-5100K provides an open binocular field of view while the subject is reading on a screen in 55 cm distance. The instrument was set to hi-speed recording, allowing a continuous data collection of the accommodative status at a temporal resolution of 5 Hz.

To collect data of high quality, accommodative function were recorded three times within each reading block. In each of this sequences data was recorded for 10 continued minutes followed by a 10-minute period during which only the eye movements have been recorded. This protocol resulted in three recordings (start, middle and end) for each reading block of about 50 minutes.

The software provided by the manufacturer records the time of each reading, the spherical equivalent refraction (SER) and pupil size in a comma separated data file. To enhance data quality, data points differing more than three standard deviations from the mean, calculated for each block and subject individually, have been filtered. This procedure has been repeated until no more values outside the three standard deviations interval were present. The data were then aggregated and descriptive statistical values for each block and subject were calculated. The first recording (start 10 min. of the first block) of each subject was used as baseline.

Evaluations of the WR-5100K have proven its reliability and accuracy. [215–218] It was used for continued monitoring of accommodation functions in investigation of eye strain and transient myopia[20; 219] as well as accommodative response under near work conditions and visual discomfort[19; 220]. Furthermore, Shiomi et al. have used this instrument in combination with an eye tracker to simultaneously measure the lens accommodation and convergence and have shown that the measurements are not influencing each other. [214]

3.3.1.2. Vergence

To analyze the functions of the vergence system, eye movements of both eyes have been recorded simultaneously and continuously during the reading task with the EyeLink II. The video-based dark pupil system of the instrument uses infrared light at wavelengths of 900 and 925 nm to track the center of the pupil and has the capacity to provide a spatial resolution (RMS) of 0.01° and an average accuracy of typically less than 0.5° (details provided by SR Research Ltd., Ottawa, Ontario, Canada; http://www.sr-research.com/eyelinkII.html). On their company website the manufacture claims that: "EyeLink eye trackers have been cited in over 3290 peer-reviewed publications, demonstrating the wide adoption of our eye trackers and the

success researchers have had using them."[221]. According to SR Research, all EyeLink eye trackers are intended for research purpose only and are not designed for diagnostic nor therapeutic use of any medical condition. The current study used this device accordingly. Usually the EyeLink II is used as a head mounted device. However, we did not use the helmet but the cameras were fixed at the chin and forehead rest of the Grand Seiko auto refractor used to monitor accommodation functions; see Figure 3-3. A headband was used to fix the subjects and minimize head movements. Prior to each recording, i.e. reading block, the system was newly calibrated using an algorithm provided by SR Research Ltd., and in addition drift control was used after every page. As in the subset of the study reported in this thesis, the vergence system in general and not the reading behavior is of interest, in contrast to other subsets of the vision fatigue study, all pages, including the ones showing graphs or pictures have been used for analysis.

Figure 3-3 EyeLink II mounted on Grand Seiko head rest.

3.3.1.2.1. Output Variables Eye-Tracking

The EyeLink Data Viewer (http://www.sr-research.com/dv.html) was used for a first visualization and data analyzation. With its help output variables including the following were calculated and exported into a spreadsheet.

EYE_USED

The eye used by the eye tracker as reference, not necessarily the dominant eye.

CURRENT_FIX_START

Time in milliseconds elapsed since the page turn, i.e. start of the recording until the start of the current fixation for the eye used.

CURRENT_FIX_START_OTHER

Same as CURRENT_FIX_START but for the opposite eye.

CURRENT_FIX_END

Time in milliseconds elapsed since the beginning of the recording, i.e. page change until the end of the fixation for the eye used.

CURRENT_FIX_END_OTHER

Same as CURRENT_FIX_END but for the opposite eye.

CURRENT_FIX_X

Horizontal positon (X coordinate) of the current fixation for the eye used in degrees of visual angle.

CURRENT_FIX_X_OTHER

Same as CURRENT_FIX_X but for the opposite eye.

CURRENT_FIX_Y

Vertical positon (Y coordinate) of the current fixation for the eye used in degrees of visual angle.

CURRENT_FIX_Y_OTHER

Same as CURRENT_FIX_Y but for the opposite eye.

NEXT_SAC_AMPLITUDE

Distance between the point of fixation prior and after the saccade, i.e. the length or amplitude of the saccade in degrees of visual angle.

NEXT_SAC_AVG_VELOCITY

Average speed of the saccade following the fixation in degrees of visual angle per second.

NEXT_SAC_PEAK_VELOCITY

Maximum speed of the saccade following the fixation in degrees of visual angle per second.

3.3.1.2.2. Target Variables Eye-Tracking

These output variables were then used to calculate the target variables listed below. The thus generated data were merged into one spreadsheet for each block and subject. They were then filtered with the same protocol as the real-time accommodation data (repeated filtering until all values within the three SD ranges). Afterwards the descriptive statistics have been calculated to aggregate the data.

3.3.1.2.2.1. Disparity of Fixation Points

The variable described in this paragraph might be regarded as a form of fixation disparity as it is understood in the English literature. This expression is, however, used differently in the German literature as described by London and Crelier[163]. Therefore, to prevent confusion, the term "fixation disparity" was not used for what has been calculated out of the eye-tracking recordings but the term disparity of fixation points was used instead.

The term disparity of fixation points refers to the difference between the fixation point of the right and left eye. It is reflecting the vergence status of the eyes. And was calculated for the

horizontal (using X coordinates), vertical (using Y coordinates) and diagonal (using X and Y coordinates) direction. The results were stored as Variables Fix_Disp_X, Fix_Disp_Y and Fix_Disp_XY. For the horizontal and diagonal disparity of fixation points a positive value reflects a crossed disparity, i.e. the visual axis cross prior to the display resulting in the fixation point of the right eye being left of the one of the left eye. Negative values reflected uncrossed disparity.

To prevent a leveling effect, the disparity data have been aggregated in four different ways:

1. Using all data, i.e. crossed and uncrossed disparity. This might result in means that are "too" close to zero to have a levelling effect (Fix_Disp).
2. Using absolute values analyzing the amplitude of the disparity, regardless of whether crossed or uncrossed (Fix_Disp_ABS).
3. Aggregating only the uncrossed disparity data (Fix_Disp_Uncross).
4. Only the data of crossed disparity was aggregated (Fix_Disp_Cross).

A similar method was used by Jaschinski et. al.[222]

3.3.1.2.2.2. Fixation Duration

By subtracting the CURRENT_FIX_START from CURRENT_FIX_END the duration of the fixation was calculated for the eye used and in the same way for the other eye. Depending of the EYE_USED the result was stored in the variable Fix_DURATION_R or Fix_DURATION_L, respectively.

3.3.1.2.2.3. Saccades

The variables NEXT_SAC_AMPLITUDE, NEXT_SAC_AVG_VELOCITY and NEXT_SAC_PEAK_VELOCITY describing saccadic eye movements have not been further transformed and were used as calculated by the Data Viewer software.

3.3.1.3. Pupils

Both instruments used for the real-time recordings have the capacity to capture pupil size and have been used to monitor pupillary functions. However, as the WR-5100K has a smaller range, a sealing effect was expected and data captured by the EyeLink II were used to analyse the pupillary functions. These have been evaluated using the SR Data Viewer and recorded in the variable CURRENT_FIX_PUPIL. Filtering and aggregation was executed analogously to the other real-time data.

3.3.2. Clinical Tests

In addition to the real-time measurements, functions of the accommodative and vergence system were tested at baseline and after each block of reading by diagnostic tests widely used in everyday optometric praxis and recorded into an excel file.

3.3.2.1. Accommodation

To prevent a potential influence of the vergence system on the accommodative function during the measurements, all testing of the accommodative system was carried out monocularly. To allow a comparison with the real-time measurements only the dominant eye was measured.

3.3.2.1.1. Accommodative Amplitude

The accommodative amplitude was measured to determine the maximum refractive power the system could achieve when fully accommodating. The push-up technic was used in order to identify the closest point to the eye that a 20/30 (~0.6) target could be focused. Based on the protocol suggested by Scheiman and Wick[223] the following test protocol was used:

Test:	**Accommodation Amplitude**
Cover:	**Cover the non-dominant eye**
Target:	PUCO Reduced Snellen #2 20/30 @ 40cm
Distance:	Start at 40 cm and bring in
Endpoint(s):	Blur out (= too blurry to read)
Record:	Endpoints distance from corneal plane / cantus to target in cm

Protocols similar to this one have been used in numbers of previous studies.[224; 117; 85]

3.3.2.1.2. Accommodative Facility

The endurance and speed of the accommodative system was examined by measuring the accommodative facility with the lens flipper method. To greatest possible stress the normal and healthy accommodative system of our test subjects a ±2.0 dpt. lens flipper was used for 60 s and cycles per minute (cpm) have been recorded. One cycle was defined as two lens flips, with each flip the required accommodation changed by 4 diopters. The used test protocol was based on the one suggested by Scheimann and Wick[223]. Similar protocols have been used by several studies.[225; 226] However, in contrast to their suggestion the test distance was set to 55 cm, the distance used as viewing distance during the real-time measurements. Since none of

the included subjects was older than 30 years no age-related adjustment was made and all participants have been tested with the same protocol.

Test:	**Monocular Plus / Minus Lens Flipper**
Cover:	**Cover the non-dominant eye**
Lenses:	± 2.0 dpt. flipper (be sure the pt. can clear each side before starting the test)
Target:	20/40 (@ 40 cm)
Distance:	55 cm
Start with:	Plus lens
Flip:	Each time a letter is clear, call it out and flip the lenses
Endpoint(s):	After 1 min.
Record:	Number of completed cycles (one cycle = two flips) in one minute

3.3.2.2. Vergence

In contrast to the accommodative system there is no clinical feasible technique to isolate the vergence system during testing. Therefore, the following tests are not solely testing for changes in the vergence system but might potentially be influenced by changes in the accommodative system or the coordination of the two. Since vergence is a binocular function, all tests have been carried out binocularly.

3.3.2.2.1. Vergence Amplitude

To determine the reserves of the vergence system the fusional vergence amplitude was measured using the step vergence testing. This technique does not require the use of a phoropter and can easily be administered by research assistants with limited optometric

training. A multi-level prism bar was placed in front of the dominant eye and the break and recovery points were recorded in prism diopter (cm/m) for the negative (base-in) and positive (base-out) fusional vergence reserves. Again the protocol was based on the suggestions made by Scheiman and Wick[223] and was used in a similar way by Chen and Abidin[226].

Test:	**Step Vergence Testing (base-in and base-out break and recovery)**
Cover:	**Do not cover**
Lenses:	Prism bar in front dominant eye start with base-in
Target:	20/40 (@ 40 cm)
Distance:	55 cm
Start with:	Base-in
Increase:	By about 2 cm/m per second
Endpoint(s):	Break (= pt. reports seeing double) increase by approx. 5 more cm/m then reduce until pt. reports single vision again (= recovery)
Record:	Break point record first prism level that pt. cannot fuse this means sees double
	Recovery point record first prism level that pt. sees single again

3.3.2.2.2. Vergence Facility

To measure how quickly the vergence system could adapt to new situations, vergence facility was measured with a loose vergence facility prism with 12 cm/m base-out and 3 cm/m base-in. In a study by Gall et. al.[227], this prism amount has shown to be the most diagnostic and was used in various studies[45; 226]. The following protocol was inspired by the one recommended by Scheiman and Wick[223].

Test:	**Vergence Facility**
Cover:	**Do not cover**
Lenses:	12BO/3BI prism in front of dominant eye (be sure the pt. can fuse both)
Target:	Vertical letters 20/40 (@ 40 cm)
Distance:	55 cm
Start with:	Base-out prism
Flip:	Each time the letters are single and clear
Endpoint(s):	If 12 letters single
Endpoint(s):	After 1 min.
Record:	Number of completed cycles (one cycle = two flips) in one minute

3.4. Subjective Measurements

To assess the subjective symptoms, a viewing symptom survey was used to measure the severity of viewing discomfort and visual fatigue.

The use of questionnaires to assess the presence of symptoms for fatigue and discomfort is well established. In 1993 Kennedy et al.[228] developed the simulator sickness questionnaire (SSQ) as one of the first verified questioners to include visual symptoms and general discomfort. Kim et al recorded in there study in 2005 a good correlation of the subjective ratings on the SSQ with objective measurements.[229] This questionnaire was used by many authors[230–232].

As visual fatigue, visual discomfort, and simulator sickness share common symptoms, the SSQ has soon been adapted by Howarth and Costello for a more general use[233].

However, questionnaires to rate the severity of symptoms are not only used in vision science research but are also commonly used in optometric practice to help classifying and diagnosing conditions such as convergence insufficiency[234], visual fatigue[30; 235], and visual discomfort in general[20; 27; 220; 237; 238]. As Hjollund et al. show in their review paper, a large number of fatigue scales are used in the assessment of fatigue due to different chronic diseases and no consensus on which fatigue measuring scales are most appropriate is reached[239].

The survey used in this study is an advancement of the one used in a previous study at the VPI[240]. Subjects rated a total of 25 items on a linear scale at baseline and after every reading block. Each scale was a 10 cm line with descriptors at both ends as well as at each quartile. The subjects indicated magnitude by placing a specially designed mouse curser on the scale, see Figure 3-4.

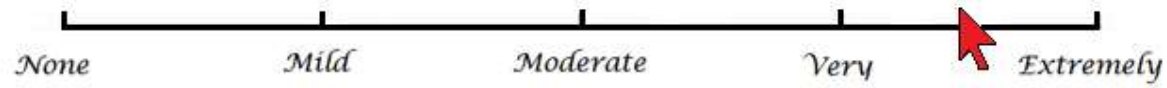

Figure 3-4 Linear scale with descriptors and special mouse curser.

Upon clicking the mouse position was recorded and the next question appeared on the screen. Figure 3-5 shows an example for the questions and scale displayed digital.

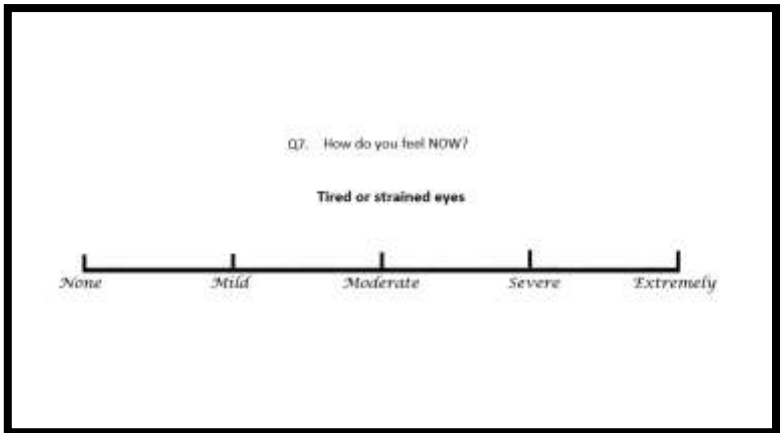

Figure 3-5 Question number 7 including scale as displayed on screen.

The survey consisted of the following three main types of questions:

A. Positive formulated questions

   would be rated on the right end of the scale by a non-symptomatic subject.

B. Negative formulated questions

   in contrast would be rated on the left end of the scale by a non-symptomatic subject while the rating would shift towards the right as symptoms and fatigue increases.

C. Neutral formulated questions

   or opinion questions are formulated in a way that a rating in the middle of the scale reflects full satisfaction while a rating toward the left end of the scale stands for too little or too small and a rating to the right for too much or too big, respectively.

D. The final question

   asking for overall fatigue was a type B question, however, as shown in Figure 3-6 in order to recalibrate the judgment of the subjects figures showing different degrees of fatigue have been used in addition to the categorizing adjectives.

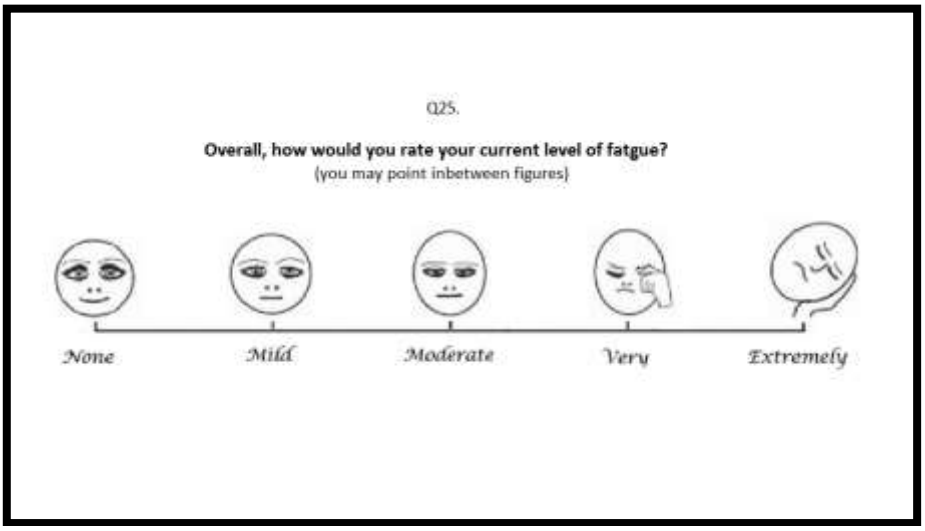

Figure 3-6 Question 25 asking for overall fatigue including figures showing different degrees of fatigue.

Table 3-3 shows the different questions, their tip as well as the descriptive adjectives used. The expression printed in bold is used to refer to the question in the further text.

In addition to the 25 questions with a linear scale, two open formulated questions that allowed the subjects to type their answer were asked, see the following Table 3-2 for details:

#	Question
26	Overall, what is your main symptom of fatigue? (if not fatigue, type "none")
27	Overall, what do you believe is most directly contributing to your fatigue during reading?

Table 3-2 Open formulated questions

#	Question	Type	Left end	Left	Middle	Right	Right end
1	How do you feel NOW? **Physically energetic** / active	A	Not at all	Somewhat	Moderate	Very	Extremely
2	How do you feel NOW? **Mentally attentive**	A	Not at all	Somewhat	Moderate	Very	Extremely
3	How do you feel NOW? **Clear vision**	A	Not at all	Somewhat	Moderate	Very	Extremely
4	How do you feel NOW? **Physically tired**	B	Not at all	Somewhat	Moderate	Very	Extremely
5	How do you feel NOW? Sluggish or **slow to respond**	B	Not at all	Somewhat	Moderate	Very	Extremely
6	How do you feel NOW? **Headache**	B	Not at all	Somewhat	Moderate	Very	Extremely
7	How do you feel NOW? **Tired** or strained **eyes**	B	Not at all	Somewhat	Moderate	Very	Extremely
8	How do you feel NOW? Sore or **pain inside** the eye	B	Not at all	Somewhat	Moderate	Very	Extremely
9	How do you feel NOW? **Dry**, gritty or watery **eye**	B	Not at all	Somewhat	Moderate	Very	Extremely
10	How do you feel NOW? **Mentally drowsy**	B	Not at all	Somewhat	Moderate	Very	Extremely
11	How do you feel NOW? **Cloudy mind** / brain fog	B	Not at all	Somewhat	Moderate	Very	Extremely
12	How do you feel NOW? **Stressed** or worn out, overall	B	Not at all	Somewhat	Moderate	Very	Extremely
13	How do you feel NOW? Dozy / **Sleepy**	B	Not at all	Somewhat	Moderate	Very	Extremely
14	How do you feel NOW? **Loss of interest** to continue reading	B	Not at all	Somewhat	Moderate	Very	Extremely
15	How do you feel during reading? **Inability to see** the **text**	B	Not at all	Somewhat	Moderate	Very	Extremely
16	How do you feel during reading? Need to **re-read** the text	B	Not at all	Somewhat	Moderate	Very	Extremely
17	How do you feel during reading? Feel **words moving** or floating	B	Not at all	Somewhat	Moderate	Very	Extremely
18	How do you feel during reading? The **text** was **blurry**	B	Not at all	Somewhat	Moderate	Very	Extremely
19	How do you feel during reading? **Seeing double** or multiple image of the text	B	Not at all	Somewhat	Moderate	Very	Extremely
20	How do you feel during reading? Inability to concentrate or to **think critically**	B	Not at all	Somewhat	Moderate	Very	Extremely
21	How do you feel during reading? Inability to **remember** the **information**	B	Not at all	Somewhat	Moderate	Very	Extremely
22	How do you feel during reading? The **brightness** of the computer display was	C	Too dim		Just Right		Too Bright
23	How do you feel during reading? The **contrast** of the computer display was	C	Too Low		Just Right		Too High
24	How do you feel during reading? The **font size** of the txt was	C	Too Small		Just Right		Too Big
25	**Overall**, how would you rate your current level of **fatigue**?	D	None	Mild	Moderate	Very	Extremely

Table 3-3 Survey questions

3.4.1. Survey Data Transformation

In a first step the recorded mouse position (by pixel) was transferred to a 101-point scale using RStudio 0.99.484 (R 3.2.2) and the script FS_Survey_Calc_Rating.R (see Appendix). In concurrence with most clinically used rating systems a score of 0 reflected no symptoms present. Hence for questions type A the 100 score was at the left while for questions of type B and D it was at the right. For questions of the C type the center reflected a 0 score and both ends (left and right) were given a score of 100.

The analysis of the z-scores for cumulative frequency for linearity and normal distribution as suggested by Massof[241; 242] revealed a step-like distribution.

Therefore, using the R script FS_Survey_5p_Scale.R (see Appendix) the ratings were further transformed to a 5-point scale ranging from 0 to 4 according to the following Figure 3-7.

Figure 3-7 Transfromation from 101 pt. to 5 pt. scale

This transformation resulted in a more appropriate distribution allowing further data analyses with factor analyses and parametric statistic. Figure 3-8 shows the z-scores for cumulative frequency of question number one. The graph on the left uses a 101 pt. score (0 to 100), the 5 pt. score (0 to 4) is used for the right graph.

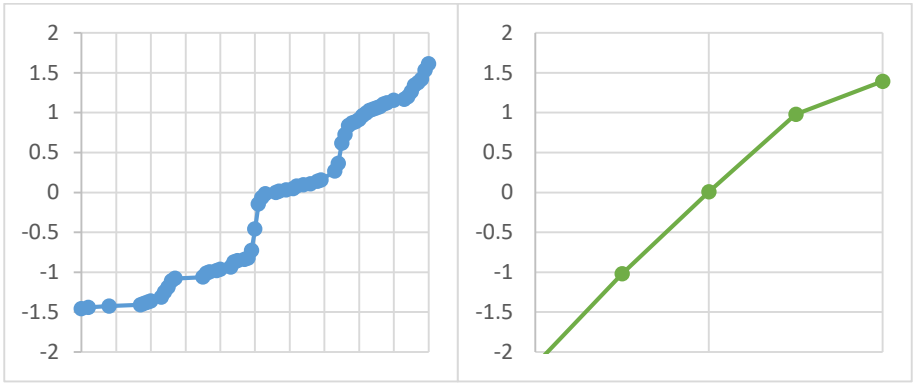

Figure 3-8 Cumulative frequency of ratings for question #1 (right: 101 pt. score; left: 5 pt. score) z-score on z axis.

3.4.2. Underlying Factors

Exploratory factor analysis of a random subset of the data using methods described by Kim et al.[243; 244] and Werner[245] revealed the following four factors that were then confirmed by confirmatory factor analysis.

1. Mental & Physical Fatigue focusing on typical symptoms of tiredness and consisting of the items

   physically energetic (Q1),
   mentally attentive (Q2),
   physically tired (Q4),
   slow to respond (Q5),
   headache (Q6),
   mentally drowsy (Q10),
   cloudy mind (Q11),
   stressed (Q12),
   sleepy (Q13),
   loss of interest (Q14),
   think critically (Q20),
   remember information (Q21) and
   overall fatigue (Q25).

2. Eye Discomfort mainly reflecting the stage of physical eye comfort and including

   clear vision (Q3),
   tired eyes (Q7),
   pain inside [the eye] (Q8) and
   dry eye (Q9).

3. Text Perception dealing with symptoms more related to the perceptive and mental part of vision or rather how subjects perceived the text including

   inability to see text (Q15),
   re-read (Q16),
   words moving (Q17),
   text blurry (Q18) and
   seeing double (Q19).

4. Display Setting reflecting how satisfied subjects were with the

   brightness (Q22),
   contrast (Q23) and
   font size (Q24).

For further analyses the average rating of each of the factors was calculated for baseline and each reading block for each subject.

3.5. Data Analysis and Statistics

As a repeated measurement study design was used and the occasional appearance of missing data points was assumed, a mixed model was used for the statistical analyses. After the data preparation and aggregation as described in the previous subchapters, IBM SPSS Statistics 23 was used to fit linear mixed models to analyze the effect of time (block) on the monitored

functions. The model specifics are listed in Table 3-4 below. In addition to the mean that was analyzed for all recorded variables, the standard deviation was analyzed for the real-time measurements as an indication for changes in the micro fluctuations.

Model	**Linear mixed model**
Subjects	Subject ID
Repeated	Block *(and Sequence for real-time accommodation)*
Repeated Covariance Type	Compound Symmetry
Dependent Variables	Mean of filtered data *(and SD for the real-time measurements)*
Factor	Block *(representing time)*
Covariate	Baseline
Fixed effects	Block, Baseline, Baseline*Block
Estimated Marginal Mean	Displayed for Block
Compare main effects	Pairwise
Confidence Interval Adjustment	Least significant difference (LSD)
Confidence Interval	95%
Significance Level	.05
Sum of squares	Type III

Table 3-4 Specifics ot the linear mixed models