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Marandi, Ramtin Zargari

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WORK, AGING, MENTAL FATIGUE, AND EYE MOVEMENT DYNAMICS

BY
RAMTIN ZARGARI MARANDI

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AALBORG UNIVERSITY
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Work, aging, mental fatigue, and eye movement dynamics

PhD Thesis

by

Ramtin Zargari Marandi

Communauté UNIVERSITÉ Grenoble Alpes

AALBORG UNIVERSITY DENMARK

Dissertation submitted

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PhD supervisors: Associate Professor Afshin Samani
Aalborg University

Associate Prof. Nicolas Vuillerme
Université Grenoble Alpes

Assistant PhD supervisors: Professor Pascal Madeleine,
Aalborg University

PhD committee: Associate Professor Hendrik Knoche (chairman)
Aalborg University

Associate Professor Dan Witzner Hansen
IT University of Copenhagen

Professor Edmund Wascher
Dortmund University of Technology

PhD Series: Faculty of Medicine, Aalborg University

Department: Department of Health Science and Technology

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CV

Ramtin was born in Tehran, Iran, in 1986. He received his B.Sc. degree in electrical engineering from Shahid Rajaee University, Iran, in 2008, and his M.Sc. degree in biomedical engineering from Iran University of Science and Technology, Iran, in 2013. He then enrolled as a Ph.D. Fellow at the Department of Health Science and Technology, Aalborg University (AAU), Denmark, jointly with the Université Grenoble Alpes, France. Since then, he has been a member of the Ergonomics and Work-related Disorders Laboratory, AAU. His current research interests include eye movements, cognitive ergonomics, and machine learning.

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- Ramtin Zargari Marandi

August 2019, Aalborg

English summary

Mental load and fatigue are important multidimensional phenomena concerning increasing involvement of elderly individuals in computer work. Fatigue may be associated with reduced cognitive resources and increased errors. Micro-breaks are strategic solutions to impede fatigue subject to design constraints, such as a timing plan. The present work aimed to use eye tracking as a promising technology to measure mental load and fatigue in young and elderly adults (Studies I and II), and to apply micro-breaks based on fatigue-related changes in eye movements to decelerate fatigue development (Study III).

The three studies involved 58 young and elderly participants. A novel task resembling computer work was developed to induce mental load (Study I). Gaze positions and pupillary responses were recorded during the task execution to detect ocular events (saccades, fixations, and blinks) and to quantify their characteristics as oculometrics. In Study I, the task was performed with three load levels across two days. In addition to measuring the load effects on performance, perceived workload, and oculometrics, the test-retest reliability of 19 oculometrics was assessed. In Study II, the effect of 40-min time-on-task was explored on oculometrics, perceived fatigue, and performance. Then, in Study III, a predictive model of fatigue was developed based on the data collected in Study II. Oculometrics-based biofeedback was implemented in real time to detect fatigue using the developed model, which triggered micro-breaks upon fatigue detection to impede it. Perceived fatigue and workload were compared between a session with the biofeedback and a control session with self-triggering micro-breaks.

A set of oculometrics were found to reflect mental load (Study I) and fatigue (Study II) in both age groups. Similar trends in oculometrics were observed with increased mental load and fatigue, implying shared neural systems for both conditions (Studies I and II). Age-related differences were exhibited in a few of the oculometrics (Study II), but age as a feature did not significantly contribute to fatigue detection (Study III). The biofeedback reduced workload and fatigue development, which suggests an improved strategy to design the timing plan of micro-breaks (Study III). All in all, the findings may support the viability of detecting the effects of fatigue and mental load on oculometrics to apply oculometrics-based biofeedback in computer work.

Dansk resumé

Computerarbejde, som er et udbredt erhverv, resulterer i forskellige niveauer af mental belastning og træthed med mulige negative påvirkninger af helbredet som følge. Grundet den aldrende befolkning, er seniorer også stærkt involveret i computer-arbejde i dag. Dette understreger behovet for udviklingen af psykofysiologisk overvågning og beskyttelsessystemer.

Mental belastning og træthed er multidimensionale psykofysiologiske fænomener. Ineffektive arbejdsrutiner fremskynder træthedsudvikling, hvilket kan associeres med nedsatte kognitive ressourcer og øgede arbejdsfejl. Mikropauser er strategiske løsninger som kan modvirke denne udvikling. Eye-tracking er en lovende teknologi til kvantificering af mental belastning og træthed. Dette ph.d.-projekt sigter mod at udnytte okulometri i forbindelse med mental belastning og træthed. Ny viden om mental belastning og træthed kunne f.eks. bruges til at udskyde udmattelse ved brug af relevante mikro-pauser som forebyggende tiltag af træthedsudvikling under computerarbejde.

Dette ph.d. projekt er baseret på videnskabelige undersøgelser (I-III). I alt deltog 58 frivillige unge og ældre computerbrugere. En computeropgave som afspejler almindeligt computerarbejde, blev udviklet til at fremkalde mental belastning. Blik-positioner og pupillære responser blev registreret under computerarbejde for at detektere okulære hændelser (sakkader, fikseringer og blink) og derved beregne oklumetri, f.eks. fikseringsvarighed. I forsøg I blev opgaven udført i samme rækkefølge over to dage. Nitten Oklumetriske parametre blev beregnet til at vurdere disses pålidelighed over for mental belastning. Desuden blev der udført målinger af præstation og oplevet belastning, samt pålidelighed over test dagene. I forsøg II blev udmattelsesudvikling undersøgt i okulometri i løbet af 40 min. Der blev udført computer-arbejde, mens subjektiv træthed og præstationsevner blev registreret. En prædiktiv model af træthed blev udviklet baseret på de okulære data indsamlet i forsøg II. Ydermere blev et okulometri-baseret biofeedback-system implementeret i realtid for at detektere træthed ved hjælp af den udviklede model. Modellen udløste mikropauser for at modvirke træthedsudvikling under computerarbejdet. Systemets nyttevirkning og

robusthed blev sammenlignet med selvudløste mikropauser baseret på opfattet arbejdsbyrde og træthedstendenser.

En gruppe af Oklumetriske parametre blev fundet sensitive og pålidelige. Disse kunne afspejle mental belastning og træthed hos både unge og ældre computerarbejdere. Lignende tendenser i okulometri blev observeret med øget mental belastnings- og træthedsniveauer. Dette fortolkes som at både mental belastning og træthedsprocesser deler fælles neurale input. Selvom aldersrelaterede tendenser blev fundet for nogle Oklumetriske parametre, havde alder ikke en direkte indvirkning på forudsigelsesmodellen for mental træthed. Den oklumetri-baserede biofeedback førte til en forbedret timing af mikropauseudløsning. Dette kunne reducere den opfattede arbejdsbelastning og træthedsudvikling sammenlignet med selvudløste mikropauser. Effekten forblev stabil over daglige afvigelser. Okulometri-biofeedback-systemet kan vise sig til at sikre en produktiv og sund måde at arbejde med computer. Alt i alt kan resultaterne understøtte levedygtigheden af at registrere effekterne af træthed og mental belastning på Oklumetriske parametre.

Résumé français

Nous sommes de plus en plus nombreux, jeunes ou âgés, à travailler devant un écran en milieu professionnel. Cette activité de travail peut induire une charge mentale et une fatigue importante, qui peuvent à leur tour générer, chez les personnes âgées notamment, des problèmes de santé. Dans ce contexte, il est donc important de développer et de déployer des solutions de surveillance de l'état psychophysiologique et d'alerte du travailleur sur écran.

La charge mentale et la fatigue sont des phénomènes psychophysiologiques multidimensionnels. Des routines de travail inappropriées sont susceptibles d'accélérer le développement de la fatigue, qui peut s'accompagner d'une diminution des ressources cognitives disponibles et d'une augmentation des erreurs. Les micro-pauses font partie des solutions possibles pour retarder, si elles sont mises en place de manière appropriée, l'apparition de la fatigue et de ses effets corollaires. L'oculométrie est une technologie prometteuse permettant la quantification de la charge mentale et des niveaux de fatigue. Ce travail doctoral avait pour objectif principal d'évaluer si, et dans quelle mesure, l'oculométrie, en association avec la charge mentale et la fatigue, peut être utilisée comme outil de détection précoce de la fatigue (études I et II), et comme moyen de paramétrage de micro-pauses à mettre en œuvre afin de ralentir et/retarder le développement de la fatigue durant l'exécution d'un travail sur ordinateur (étude III).

Pour répondre à cet objectif, trois études (I-III) portant sur 58 individus jeunes et âgés ont été conduites. Une tâche expérimentale, se rapprochant de celle qu'un travailleur peut réaliser sur ordinateur, a été développée pour induire une charge mentale de trois niveaux d'intensités croissantes (étude I). Les positions du regard et les réponses pupillaires ont été enregistrées pendant l'exécution de cette tâche afin de détecter les événements oculaires (saccades, fixations et clignements des yeux) et de calculer des paramètres oculomoteurs tels que la durée de fixation par exemple.

Dans l'étude I, cette tâche a été effectuée à deux jours d'intervalle et dans un ordre contrebalancé. Les performances à la tâche et la charge de travail ont d'une part été mesurées. Dix-neuf paramètres oculomoteurs ont, par ailleurs été calculés pour évaluer leur sensibilité à la charge mentale, et leur fiabilité sur plusieurs jours.

Dans l'étude II, l’effet de l’exécution de la tâche sur ordinateur pendant 40 minutes sur des mesures oculométriques, de fatigue subjective et de performance a été exploré. Dans l’étude III, un modèle prédictif du développement de la fatigue a été développé sur la base des données d’oculomotricité recueillies dans l'étude II. Un système de biofeedback en temps réel basé sur l'oculométrie a été conçu et mis en œuvre. Son principe de fonctionnement repose sur la détection de la fatigue à l'aide du modèle développé, et le déclenchement de micro-pauses dès lors qu’un état de fatigue est détecté, afin de ralentir sa progression durant l’exécution de la tâche. L'efficacité et la robustesse de ce système de contrôle en boucle fermée ont été comparées à des micro-pauses déclenchées de manière automatique en termes de charge de travail perçue et de précision de la détection de la fatigue.

Nos résultats ont mis en évidence la fiabilité et la sensibilité d’un ensemble de paramètres oculomoteurs permettant d’estimer la charge mentale et la fatigue chez les personnes jeunes et âgées. Des observations similaires en oculométrie ont été rapportées avec une augmentation de la charge mentale et des niveaux de fatigue, impliquant des systèmes neuronaux partagés pour les deux conditions. Le biofeedback basé sur l’oculométrie a permis la planification des micro-pauses, qui, en comparaison à des micro-pauses déclenchées de manière automatique, ont réduit de manière significative la charge de travail perçue et le développement de la fatigue.

Dans leur ensemble, les résultats suggèrent que le système de biofeedback oculométrique développé dans le cadre de ce travail doctoral peut représenter une solution prometteuse pouvant contribuer à un travail sur ordinateur productif et sain.

List of publications

The main studies involved in this PhD project have been published in the following peer-reviewed journals:

Study I)

Marandi RZ, Madeleine P, Omland Ø, Vuillerme N, Samani A. Reliability of oculometrics during a mentally demanding task in young and old adults. IEEE Access. 2018;6:17500-17.

Study II)

Marandi RZ, Madeleine P, Omland Ø, Vuillerme N, Samani A. Eye movement characteristics reflected fatigue development in both young and elderly individuals. Scientific Reports. 2018;8(1):13148.

Study III)

Marandi RZ, Madeleine P, Omland Ø, Vuillerme N, Samani A. An oculometrics-based biofeedback system to impede fatigue development during computer work: A proof-of-concept study. PloS One. 2019;14(5).

Abbreviation

BD	Blink Duration
BF	Blink Frequency
CI	Confidence Interval
CR	Corneal Reflection
DT	Decision Tree
DTG	Determinism of Gaze Trajectory
DTP	Determinism of Pupillary Response
FAS	Fatigue Assessment Scale
FD	Fixation Duration
FF	Fixation Frequency
FIS-FCM	Fuzzy Inference System (Fuzzy C-Means clustering)
FIS-SC	Fuzzy Inference System (subtractive clustering)
ICC	Intraclass Correlation Coefficient
kNN	k-Nearest Neighbors
LDA	Linear discriminant analysis
LoA	Limit of Agreement
MP	Memorization Period
MSaEn	Multivariate Sample Entropy of Gaze Trajectory
NASA-TLX	National Aeronautics and Space Administration Task
NB	Naive Bayes
NN	(Feedforward) Neural Network
OP	Overall Performance
PSaEn	Sample Entropy of Pupillary Response
RemT	Remaining Time
RMEP	Recurrence Map Entropy of Pupillary Response
RP	Replication Period
RRG	Recurrence Rate of Gaze Trajectory
RRP	Recurrence Rate of Pupillary Response
PDR	Pupil Dilation Range
SA	Saccade Amplitude
SAAI	Saccade Acceleration Asymmetry Index
SCD	Saccade Duration
SCR	Saccade Curvature
SF	Saccade Frequency

SPV	Saccade Peak Velocity
SVA	The slope of the line regressing SPV on SA
SVM	Support Vector Machines
ToT	Time-on-Task
TPDL	Task-Evoked Pupillary Peak Dilation Latency
VFS	Visual Fatigue Scale
WP	Washout Period

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Chapter 1. Introduction

1.1. Motivations of this PhD project

Today, long hours of daily life are dedicated to performing occupational or personal tasks on computers. A great body of research on computer workers is devoted to work-related musculoskeletal disorders (1–3), focusing mainly on physical aspects of computer work. A number of studies have also provided a broader picture beyond musculoskeletal disorders, including visual discomfort (4,5). However, these studies have mainly highlighted physical facets of computer work. Their findings may be complemented by studying cognitive and psychophysiological aspects of computer work (6,7), such as fatigue and mental load. Table 1-1 provides definitions of the main technical terms used in this thesis.

Table 1-1 A brief overview of the technical terms used in this PhD thesis

Terms	Definitions
Computer work	Occupations in which workers use computers. Here, a sitting model of a computer workstation is used.
Fatigue	“A multifaceted phenomenon, referring to an inhibiting feeling during a sustained task coincident with the body requirements for rest.”[1]
Mental load	The cognitive effort one makes to perform a task.
Oculometrics	Quantitative features characterizing eye movements and pupillary responses.
Time-on-task	The period of time spent performing a task.
Performance	Quantitative features of performing a task, here reflecting how fast and accurately it has been performed
Biofeedback	A cognitive intervention in which an individual’s biological information is fed back to notify him or her about ongoing processes in his or her body (e.g. fatigue development) to regulate one’s own behavior (e.g. to avoid overwork by taking work breaks).

1 –This definition was applied in the context of computer work and healthy individuals in (8).

Computer work may require low physical demands, but it can be mentally demanding. Nonetheless, little research has investigated mental aspects of computer work. In the last few decades, computer work has been quickly and widely extended to various fields of work. However, cognitive and psychological effects of this work are less known concerning preventive actions to avoid potential risk factors. Computer work dealing with enormous amounts of data handling and exploration in long periods without proper work pauses may lead to problems such as mental overload or fatigue-related errors. Fatigue alone has been estimated to cost $136 billion annually in health-related lost productivity in the United States (9).

A conventional view in ergonomics to study fatigue or mental load is to objectively quantify them using noninvasive and potentially unobtrusive technologies (e.g. eye tracking) to benchmark safe regions with low probability of human errors. Eye movement characteristics may present new opportunities to investigate fatigue. This view has been applied in the literature mainly for safety issues and prevention of accidents in various applications, including driving (10,11), aviation (12), and surgery (13). However, in the context of computer work, fatigue and mental load, among others, are less explored, especially concerning the prevalence of fatigue among elderly individuals (14). Computer work may involve a broad spectrum of mostly mental activities (e.g. reading, monitoring, and data analysis) during work hours, which may require sustained attention. Varying levels of mental load may be experienced during a day of computer work with additive temporal demands to meet deadlines (15). The ubiquity of computer work (16) and the limited number of studies on fatigue in tasks with low physical demands (17) may require further investigation of fatigue in computer work.

Mental load and fatigue development may have intensified impacts on the elderly, as the geriatrics literature reports that they may have a decline in cognitive capacity (18). This is also of social and political importance, since the proportion of individuals aged 50 years and over is growing globally (19). For example, in Denmark the retirement age has been increased to 69 years old. There are similar trends in population aging around the world – not only in developed countries, but also in developing ones (20). This indicates that more and more elderly people will be working in the coming decades.

The motivation behind this PhD project is to identify mental load and fatigue traces noninvasively via eye tracking, and to use this information to develop a strategy to reduce possible risks of computer work in relation to mental load and fatigue. This work also aims to investigate the age-related differences in the manifestation of fatigue and mental load during computer work between young and elderly adults. With an application-based mindset, a biofeedback framework using eye tracking should be developed to promote productive and healthy interaction with computers. Such a framework may provide pragmatic solutions to avoid excessive fatigue. Thus, the final aim of this PhD project is to implement a biofeedback system based on eye tracking to reduce fatigue development.

1.2. Aims of this PhD project

The scope of this PhD project is briefly outlined here and discussed in detail with the background information in Chapter 2. In general, the aim of this study is to examine the behavior of eye movements in a task resembling computer work, and to investigate conventional and novel oculometrics in relation to fatigue and mental load related to computer work in healthy young and elderly individuals. This PhD project is divided into three studies, as summarized in Figure 1-1.

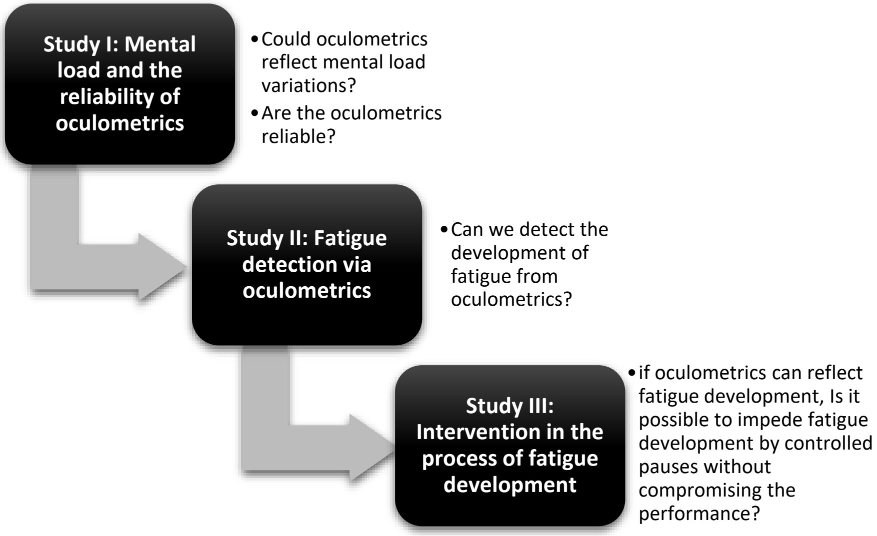

Figure 1-1 An overview of the structure of the main studies involved in this PhD project along with the research questions addressed in each study. Studies I, II, and III are described in detail in (21), (8), and (22), respectively.

1.2.1. Study I: Mental load and the reliability of oculometrics

Research question i: Could oculometrics reflect mental load variations?

Based on the majority of the findings in the literature, significant changes were expected in most of the oculometrics in association with mental load variation. Hence, the following was posited:

Hypothesis: The mental load induced by a cognitive task can be reflected by oculometrics.

Independent variables: the mental load (according to the three levels of task difficulty – low, medium, and high; see Section 3.2.1) and the two age groups (young and elderly, aged 18-30 and 50-70 years, respectively)

Dependent variables: the oculometrics (Section 3.4), the perceived workload (section 3.6), and the performance metrics (Section 3.5)

Research question ii: Are oculometrics reliable?

An equally important issue to address was the variability of oculometrics across days in the young and elderly individuals.

Independent variables*:* the two experimental days (sessions) and the age groups

Dependent variables: the oculometrics

As outlined in Figure 1-2, Study I aimed to address the first two research questions (i and ii). The absolute and relative reliability of oculometrics was assessed, with a focus on the oculometrics quantifying different levels of mental load in computer work. Nonlinear features, such as sample entropy and recurrent map analysis, were utilized to extend the understanding of nonlinear dynamics underlying eye movements and pupillary responses. Two experimental sessions were conducted in two days with healthy volunteers in the young and elderly groups. The recruitment of the two groups provided the possibility to investigate age-related differences in oculometrics.

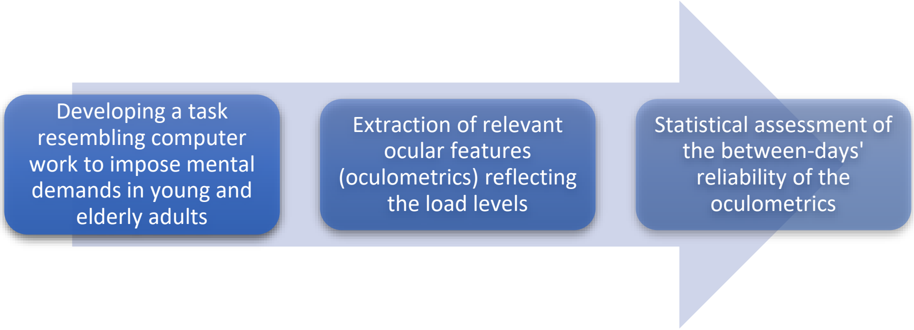

Figure 1-2 An overview of the main steps in Study I.

1.2.2. Study II: Fatigue detection via oculometrics

Research question iii: Can the development of fatigue be detected from eye movement dynamics?

Based upon findings associating fatigue and eye movements, increasing time-on-task to 40 min was expected to lead to gradual change in the oculometrics.

Hypothesis: Fatigue development can be reflected in oculometrics, and the effects are different across age groups.

Independent variable: time-on-task and the age groups

Dependent variables: the oculometrics, the perceived fatigue and workload, and the performance metrics

The aim of Study II was to test the hypothesis formulated for research question iii. The study, as outlined in Figure 1-3, was designed to explore the temporal evolution of the oculometrics in prolonged computer work. The experiments were performed on the same group of volunteers who participated in Study I. The study of the changes in oculometrics with time-on-task made it possible to better determine the challenges and possibilities for benchmarking fatigue in oculometrics using reliable features.

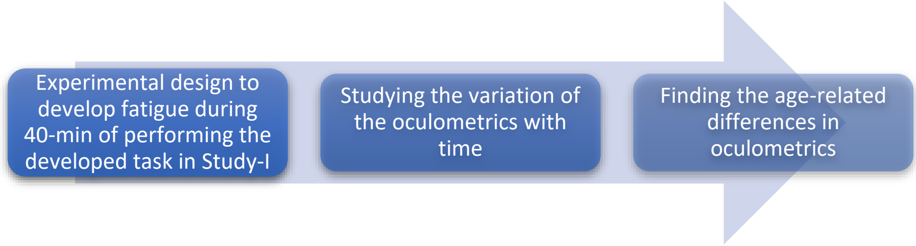

Figure 1-3 An overview of the main steps in Study II.

1.2.3. Study III: Intervention in the process of fatigue development

Research question iv: Is it possible to impede fatigue development by introducing controlled pauses without compromising performance?

Hypothesis: Controlled pauses (micro-breaks) mitigate fatigue.

Independent variable: exertion of micro-breaks in two sessions: 1) using oculometrics-based biofeedback and 2) a manual session (control)

Dependent variable: the oculometrics, the perceived fatigue and workload, and the performance metrics

To answer research question iv, Study III (Figure 1-4) addressed the possibility of intervening in the process of fatigue development by providing a biofeedback system based on reliable oculometrics during computer work. The first and second studies were designed to benchmark the applicable oculometrics for the biofeedback system. Study III investigated the utilization of the biofeedback system to decelerate fatigue development in comparison with participants having autonomy in taking micro-breaks.

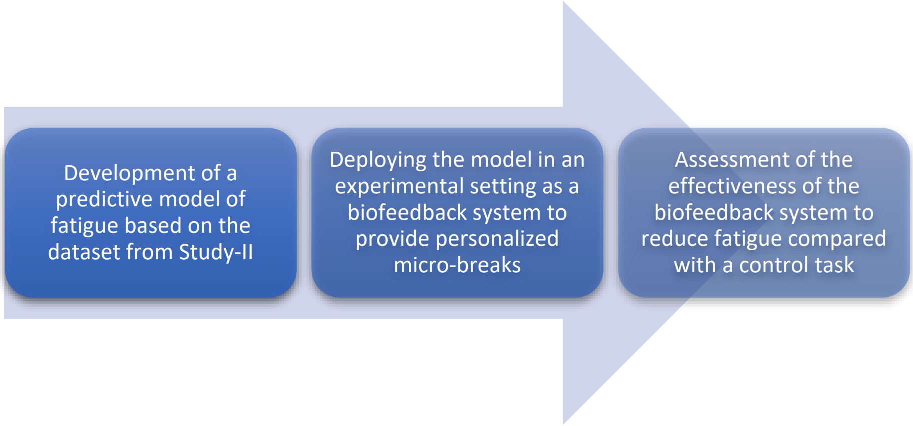

Figure 1-4 An overview of the main steps in Study III.

1.3. Organization of this PhD thesis

In this chapter, the aims and motivation of the project, as well as the PhD studies are overviewed. Chapter 2 presents main theories and findings about fatigue and mental load. It follows with background information about eye movements and their relevance to fatigue and mental load. Age-related changes in eye movements are also presented in Chapter 2. It is followed by Chapter 3, where a concise overview of the experimental approach and methods used in this project for each study are provided. Chapter 4 briefly presents an overview of the main results of each study in connection with each other. In the end, Chapter 5 provides discussions about the main findings of each study, and concluding remarks, including implications for workplaces, limitations, and perspectives according to the presented findings.

Chapter 2. Theoretical framework

The current PhD project is based upon four concepts:

1) Mental load and fatigue due to the cognitive demands of computer work,

2) Oculometrics, which are the characterizing features of eye movements and pupillary responses,

3) Aging, and addressing the age-related changes affecting the association between fatigue and oculometrics, and

4) Interventions in the process of fatigue development, which could be beneficial in computer work.

This chapter describes these concepts within the context of computer work.

2.1. Fatigue

Fatigue during computer work may appear as a gradual loss of the desire to perform a task (23). In its acute form, fatigue can be caused by prolonged mental load (24,25). Moreover, fatigue is hypothetically dependent on internal (personal), external (environmental), and task-dependent factors (26), as outlined in Figure 2-1. Fatigue is often attributed to the nature of the fatiguing factors; for example, “mental fatigue” is a term used to underline the role of mental load in causing fatigue in a given task. However, in the present PhD thesis, the multidimensional nature of fatigue is emphasized (27–31). Furthermore, in this work fatigue has been studied in healthy participants, and not in connection with pathological states (e.g. chronic fatigue disorder).

Besides mental fatigue, one may find similar terms in the literature to specify the fatiguing factor. For example, central fatigue has been used to underline the deficit in certain neurotransmitters (32), and peripheral fatigue has been used to point out the lack or accumulation of certain metabolites in muscles (33). “Mental fatigue” in a common term in psychology and “central fatigue" is more common in medicine, but both refer to the same concept, which may seem confusing (26).

Drowsiness and sleepiness are semantically similar but technically different from fatigue (34,35). Although these terms have some signs in common (34), they are distinguishable. Sleep deprivation may lead to drowsiness and sleepiness, whereas fatigue may develop while performing a task even after enough sleep (36). In addition, one can become fatigued in a short period, such as 20 min (36). In such a situation, a short break may be helpful to reinstitute cognitive capacity and counteract fatigue, in contrast to the sleepiness caused by sleep deprivation.

Fatigue has been studied in relation to several causal factors (Figure 2-1); these can be categorized into internal and personal factors, external and environmental factors, and task-dependent factors. Internal and personal factors underlie the differences between individuals under the same work conditions. These factors have been shown to explain some inter-individual differences in relation to fatigue, such as personality (37). On the other hand, external and environmental factors are related to workstation design – for instance, lighting conditions, social interactions, and plans for rest pauses. These factors are more flexible than internal and personal factors in relation to fatigue, since they can be easily changed to observe their effect on fatigue (38). Finally, task-dependent factors are any factors related to the nature of the task, and they may be designed to improve productivity and reduce health risks. These factors have been less explored in relation to fatigue during computer work.

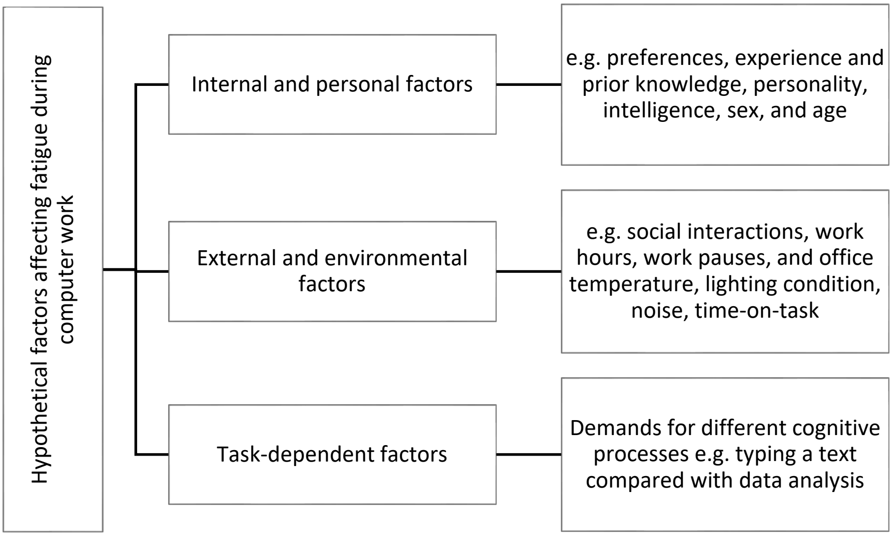

Figure 2-1 A list of hypothetical factors that may affect the manifestation and development of fatigue during computer work based on (37–44).

Another concept in association with fatigue is fatigability: namely, "how fast a person gets tired" (45–48). Fatigability is related to contextual information, such as the type and intensity of a task as well as task performance, in fatigue perception. In this concept, homeostatic and psychological factors are both important in the perception of fatigue (46). For example, fatigue may develop fast with increased stress and effort, and low control (49–51). This highlights the multidimensionality of fatigue (35,52,53).

2.1.1. Theoretical basis of Fatigue

A traditional and prevailing view of fatigue is that it is a result of an excessive amount of work, leading to the depletion of energy resources in the body (49). This view may have originated from the industrial revolution, when fatigue development in the human body resembled the lack of energy resources for machines in the process of production (54). In another common view, fatigue is seen as a negative sign and a byproduct of work (49). However, these views may not explain fatigue thoroughly, since no significant difference has been reported in the overall energy consumption of the brain during mental tasks compared to rest states (no task) (49). Thus, a rather subjective view on fatigue based on motivation has also been proposed

(49): In brief, the motivational control theory of fatigue suggests that fatigue can be viewed as an emotion with an adaptive and goal-oriented function to decide on alternative actions based on one's own motivation (49).

Fatigue has also been proposed to follow a self-regulatory mechanism that has physiological indications and is partially dependent on the subjective feeling of fatigue (55). This self-regulation can be impaired by the depletion of resources after mentally effortful work (56). This is thus a multidimensional view of fatigue, suggesting that more factors may mediate fatigue along with motivation (57).

The lack of energy resources may be perceived from involuntary physiological reactions, such as yawning, visual discomfort, and pain, which may lead to prioritizing another option (rest) over doing a task (e.g. playing a computer game), even if that task might be desirable. The overall energy level of the brain, as measured by deoxygenation and glucose metabolism in the blood flow, may not be significantly different between a resting state (no activity) and the performance of a mental task, but functional differences and shifts of blood toward different brain areas have been reported in a variety of mental tasks (58,59). In addition, neurotransmitters, including noradrenaline, dopamine, and adenosine, have an important role in the feeling of fatigue with time-on-task in mental tasks (60), further indicating that fatigue has physiological representations.

Based on the different views and theoretical backgrounds partly discussed here, various definitions of fatigue have been proposed in the literature. They are outlined in Figure 2-2.

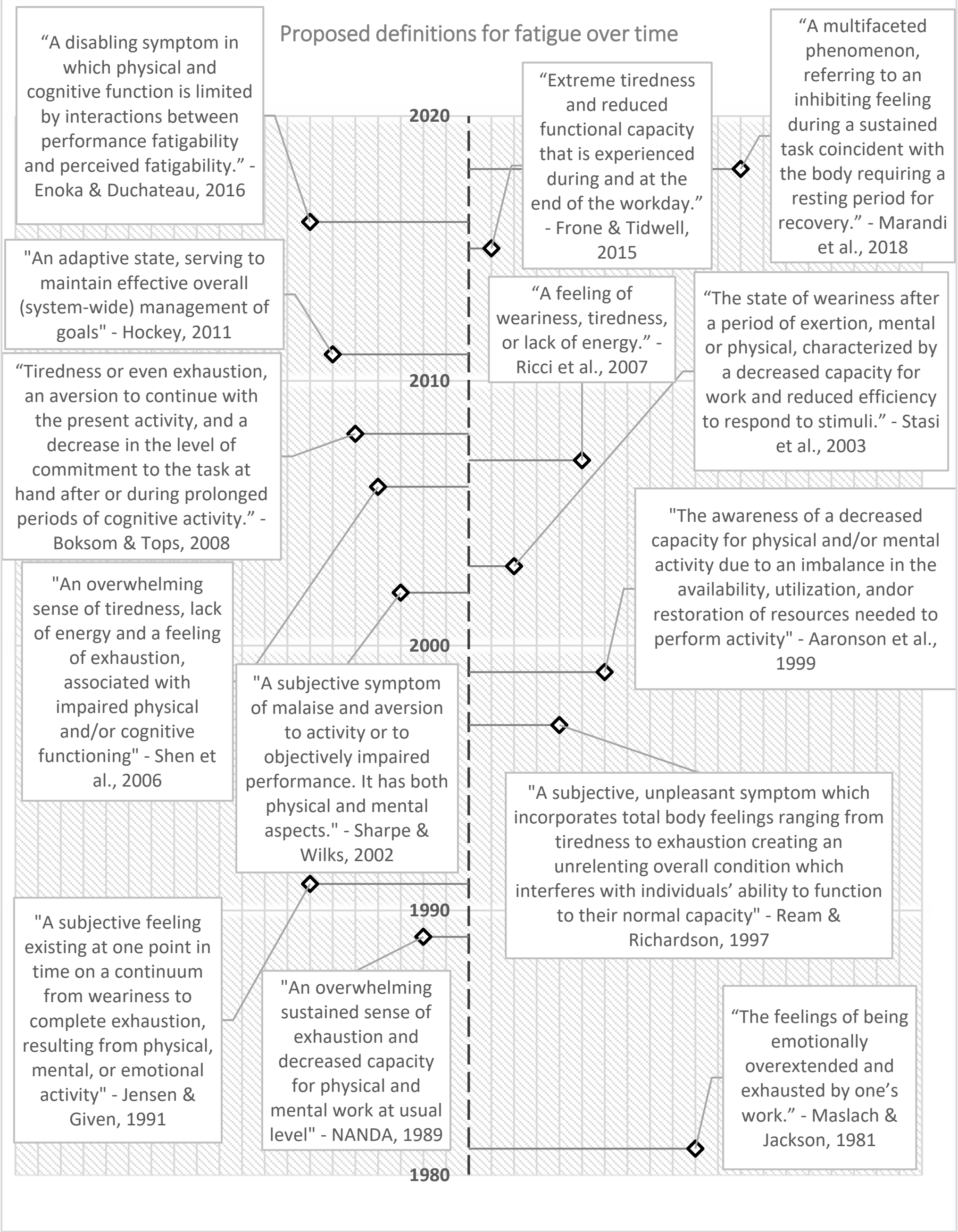

Figure 2-2 An illustrative timeline of the definitions of fatigue proposed in the literature over the last 40 years, i.e. (8,9,30,61–69).

A framework based on neural evidence has been proposed to explain (mental) fatigue (64). The authors have argued that the feeling of fatigue is modulated by subconscious assessments of costs and benefits of doing a task. In other words, one continues to perform a task while the predicted rewards of the current actions are greater than the costs (in terms of energy) of the actions. In this evolutionary view, some brain areas (e.g. insula) are involved in the perception of fatigue, and these are relayed by other brain areas (e.g. basolateral amygdala) that are involved in the reward system of the brain. This theory may partially explain human behavior in relation to fatigue based on self-evaluations of costs and benefits. Together with other studies, this theory highlights the importance of motivation and incentives in fatigability (70,71). Hence, social and monetary incentives were provided in the experimental designs used to study fatigue in this PhD project, as described in Chapter 3.

Task properties are the one of the main causal factors of fatigue with overload (active fatigue) or underload (passive fatigue) (10). Active fatigue may appear in tasks that are mentally demanding, whereas passive fatigue may occur in boring and monotonous tasks (72). Passive fatigue is related to the mindlessness and goal-habituation theories that posit that task disengagement due to underload may occur due to monotony, leading to decreased performance (72,73). In contrast, active fatigue has been related to the resource theory, which suggests that performance decreases with time-on-task are attributable to the depletion of (mental) resources (74–76). These theories have been developed to explain human behavior in vigilance (sustained attention (77)) tasks that require individuals to stay attentive and responsive to stimuli over long periods (78).

It has been found that different subjective feelings, including tiredness, may have a distinguishing physiological (objective) representation (79,80). Thus, viewing fatigue as an emotion (81), may not rule out its physiological representations. Furthermore, fatigue may be expressed subjectively due to the potential need for physiological reorganization in the brain (82–84). For example, the functional connectivity among brain regions may change with fatigue development (83,84). Hence, fatigue can be referred to as a multidimensional phenomenon that inhibits healthy individuals from continuing to perform a task.

This brief overview of the theories on fatigue in connection with the presently proposed definition (Table 1-1) may provide an operational view on the concept. The following sections discuss physiological reflections of fatigue with a focus on eye movements, involved brain regions, and performance. Assuming that fatigue can be objectively detected, implementation of a biofeedback system to intervene in the process of fatigue development is plausible.

2.1.2. Fatigue and performance

Though it may seem intuitive, performance may not necessarily decrease as fatigue develops (49). While this reduction seems to be a natural result of fatigue in a physical task, in a rather mentally demanding task, such as computer work, the pattern of fatigue may not necessarily correlate with performance.

The pattern of performance responses with fatigue may vary across tasks and conditions (49). Some aspects of physical performance (e.g. endurance but not maximal strength) may be reduced by fatigue as a result of prolonged cognitive tasks (60). Especially in the context of computer work, as defined in Table 1-1, performance is multidimensional. Fatigue can be a factor that influences performance, but some other causal factors also make a difference, especially on the individual level, including cognitive capacity (81). Thus, to detect fatigue, one cannot always rely on performance. It is helpful to understand what may occur in the brain while fatigue develops, which may not necessarily coincide with a decrease in performance (60,82).

2.1.3. Neural evidence of Fatigue

A body of research has attempted to pinpoint fatigue in the brain (25,85–87). Acute forms of fatigue in healthy individuals have been shown to be associated with altered activations in different brain areas and neural systems (25). As such, increased sympathetic and reduced parasympathetic activities have been reported following a 30-min mental task (86,87).

Fatigue in mental tasks involving “executive functions” may be reflected in the prefrontal cortex (25,88,89). Executive functions may include working memory and selective attention to perform a task (90). In addition, 30-min performance of the 2-back task has been reported to suppress neural activity in the right anterior cingulate cortex (91). The prefrontal cortex and the anterior cingulate cortex may also be involved in the self-estimation of the cost of actions in a given task, which partially explains the motivational aspects of the behavior during fatigue (89).

Fatigue thus seemingly involve various brain areas and neural systems that may modulate eye movements (92–96). Indeed, this corroborates the current findings in neuroscience and neurophysiology of fatigue traces in eye movements (92–94). It also highlights the neurophysiological nature of fatigue together with its subjective exposure (82–84), as opposed to the subjective views on fatigue, such as in (49).

2.1.4. Mental load

According to the book “To Err is Human[*]” (97), medical errors, caused by increased mental load, may be more fatal than breast cancer and car accidents. Mental load, cognitive load, mental workload, and cognitive effort are different terms for the same concept used in cognitive psychology and ergonomics; it is a subject undergoing intense study in nascent fields of cognitive and neuro- ergonomics. Mental load can refer to the cognitive effort one makes to perform a task. The notion of the “load” implies that there is a “mental capacity” and that each task may require a portion of the mental capacity to be performed. A sensible example of mental capacity is working memory, which is limited to a varied number of distinct pieces of information in a short time (e.g. 10 s) (98). Mental load has a subjective dimension (e.g. related to the motivation) similar to fatigue (99,100). However, researchers have suggested the use of objective measurements of mental load rather than subjective measures (e.g. self-reports), which are subject to misjudgments and misperceptions (100). Two prominent theories pertaining to mental load are the cognitive load theory (101) and the multiple resource theory (102).

Cognitive load theory specifies three types of cognitive load (intrinsic, extraneous, and germane) in association with the limited capacities of working memory. According to this theory, each task may impose an inherent amount of cognitive load (intrinsic load, e.g. a simple vs. difficult mathematical problem), but the way a task is presented conveys its

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[*] It means “everyone makes mistakes.”

extraneous load (e.g. visual vs. auditory), and the prior experiences in relation to the problem specify the germane cognitive load. Cognitive load theory is mainly applied in the design of instructional material to optimize learning.

Multiple resource theory acknowledges the ability of the brain to allocate different mental resources for multi-tasking. This theory states that if the components of a task target the same mental resources, this contributes to an increased mental load. By contrast, if distinct mental resources are targeted, then multitasking could be possible.

Mental load and fatigue can be related to each other. Mental load and fatigue has been mathematically modeled in relation to each other to explain performance variability based on catastrophe theory (103–105). The theory briefly suggests that catastrophe (due to human error) may occur depending on personal and task-related factors affecting one's ability to perform a task (103). This may highlight the multidimensionality of mental load and its similarity with fatigue pertaining to their causal factors (Figure 2-1). Mental load may vary with the development of fatigue (103). This means that there is a bidirectional relationship between the two. In one direction, underload can lead to boredom (106) and overload can lead to disengagement (107). In the other direction, the development of fatigue may increase perceived mental load. A key factor is time-on-task (108). Thus, short time-on-task may be proper to study the effects of mental load, for instance <5 min (109). On the other hand, the time-on-task has to be long enough (e.g. >20 min) to study fatigue, but it may not warrant a steady perception of mental load (109). These are some important challenges that were taken into account in the experimental design of the current PhD project.

2.2. How to impede fatigue?

Fatigue is not a desirable feeling, and people try to avoid it by using different strategies, such as drinking coffee and taking rest pauses. Caffeine is usually helpful to counteract fatigue but it is not a recommended option for everyone (110), as excessive consumption of psychoactive drugs, including caffeine, could be harmful (110). On the other hand, taking work breaks is a common behavioral strategy that is used to reduce fatigue, and it does not raise the health concerns that caffeine consumption does.

A previous study presented technologies to detect and counteract fatigue (10). Among others, the authors suggest using the percentage of closed eyes over a period (PERCLOS) to detect the fatigue caused by sleep deprivation, and it has superior detection accuracy compared to electroencephalography, eye blinks, and head-nodding technology. The same authors also have reviewed technologies to counteract fatigue while driving, categorizing fatigue countermeasures into automation and interactive technologies (10). In the automation technology, the task demands are modified based on the performance of the driver. In the interactive technology, the driver is given a secondary task that is believed to enhance alertness, or a periodic auditory alarm that is activated when the driver begins to feel fatigued.

A vital role of fatigue is to indicate that one should stop performing a task (85). However, fatigue is susceptible to being misjudged as a result of past experiences of fatiguing situations (111), or ignored due to certain work habits (112). All this underlines the need to be aware of one's own fatigue, termed fatigue awareness (113). Based on this idea, the development of a non-pharmacological strategy to impede fatigue was considered in this PhD project. Hence, a brief introduction to biofeedback and micro-breaks is needed to understand how these non-pharmacological solutions could be used to impede fatigue.

2.2.1. Biofeedback as an augmented sensory system

As mentioned earlier, the feeling of fatigue is prone to function sub-optimally due to certain conditions (48,111,112). Assistive technologies may partially compensate for such deficiencies by extracting the physiological information pertaining to fatigue and delivering it back in the form of biofeedback as an augmented sensory system. As defined in Table 1-1, a biofeedback system receives physiological signals (e.g. ocular data) associated with a phenomenon (e.g. fatigue) from an individual (e.g. a computer user), and delivers an action (e.g. alarm message) concerning a phenomenon (e.g. fatigue) to the individual through a user interface (e.g. computer screen). The action could involve triggering a micro-break, for instance.

Previous studies have shown that biofeedback systems have a positive influence in various domains. For example, they help to counteract stress and anxiety (114–117), to elaborate mental training (118), to decrease muscular load in computer work (119,120), and to adjust mental load (121).

2.2.2. Micro-breaks

Various terms have been used in the literature to refer to a common strategy to recuperate from fatigue: namely, to take a rest (pause or break) that may involve physical exercise (active pauses) (122) or no physical activity (passive). The breaks may also be specified in terms of their duration as being long (macro) or short (micro). Micro-breaks can be as short as 5 s (123) or as long as 180 s (124). Ergonomic standards concerning fatigue and mental load favor short and frequent breaks, termed micro-breaks, over long and infrequent breaks to impede fatigue development (125). These recommendations were considered in the study design of the present PhD project.

Efficient design of micro-breaks is challenging. Micro-breaks can be specified by their duration, frequency, and activity type. Interactivity of micro-breaks and subjective preferences concerning these breaks can also be integrated into a biofeedback system. These design elements should be specified and adjusted for different tasks. The recruitment of objective metrics of fatigue to trigger micro-breaks may provide an optimal solution for micro-breaks to cope with fatigue development. This idea is based on the assumption that proper micro-breaks may help psychophysiological reorganization to continue a given task.

Micro-breaks can be viewed in connection with the attention restoration theory (126). This theory aims to explain why exposure to nature (e.g. watching the trees) may have restorative effects in relation to the depletion of attentional resources. Based on this theory, attention can be captured voluntarily (directed attention), such as by doing a mental task, or involuntarily, for instance by a distracting noise. Performing a mental task requires directed attention to cognitively inhibit potential distractions (e.g. irrelevant thoughts) (127,128). Over time, the effort to sustain attention during a task may lead to fatigue – that is, directed attention fatigue (129). A different kind of activity (activating different neural networks compared with the primary task) during micro-breaks may restore attention (130,131). Based on the attention restoration theory, this can be a characteristic of a restorative activity in micro-breaks.

2.3. Eye movements

The eyes are the outer parts of the extensive neural network of the visual system, through which important information from the surrounding world is received. The visual system comprises a large area of the brain developed to enhance cognition and perception in humans. Visual information is critical in many different aspects, such as in human movements and balance (132), in reacting quickly enough to any threat or risk, and in social interactions (133). All of this is important enough for human beings' visual system to be equipped with a unique structure and functioning, for instance to enable fast, accurate, and varied movements.

Owing to decades of research, eye movements have been found to be a rich source of information about various psychophysiological processes, including fatigue development (134–137). The information is usually accessible through the study of the movements of the eyeball and dilations and constrictions of the pupil (137). Figure 2-3 provides a frontal view of the eye.

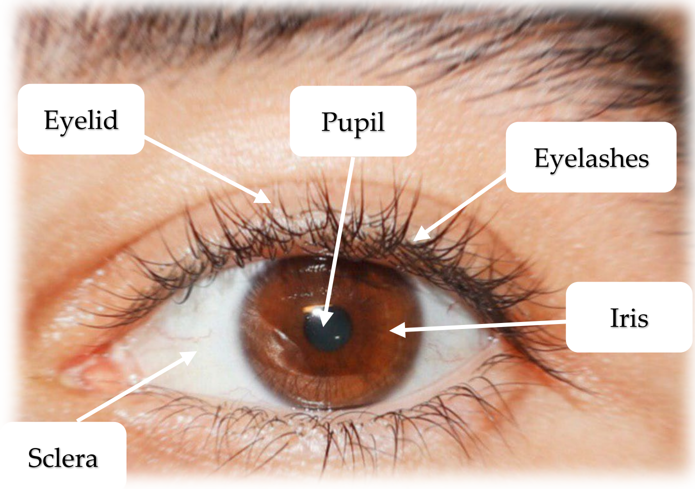

Figure 2-3 Frontal view of a human eye with the names of some of its visible parts.

Visual perception is the process in which the brain encodes the incoming light to the eyes from the surrounding world into visual information. Visual processing is required to recognize objects and their features, including shape and size. Visible light (electromagnetic waves with a wavelength of 390 to 700 nm) pass through the cornea, pupil, and lens to the retina to be transduced to electrical pulses and transmitted through visual pathways. The processing begins from the retina (e.g. to encode colors) and the axons from the ganglion cells in the retina. These form the optic nerve, which passes through the optic chiasma, creating the optic tract. The majority of the axons from the ganglion cells in the retina end in the lateral geniculate nucleus in the thalamus, from which the information is transmitted to the primary visual cortex in the occipital lobe to map the received image. The information is then distributed to other cortical areas, depending on the type of information being processed, and integrated with other sensory information (e.g. proprioception) (138). A group of axons from the ganglion cells end in the superior colliculus in the midbrain for eye movements. Other groups of axons are connected to the pretectum for light reflexes in the pupillary responses, and to the suprachiasmatic nucleus and the ventrolateral preoptic nucleus, respectively, for diurnal and sleep regulation (139).

There is a small region on the retina called fovea, with a diameter of approximately 1.5 mm, packed with special photoreceptors (cone cells) to provide high spatial frequency, enabling sharp central vision. The density of cone cells then decreases with the distance from the fovea, leading to less spatial frequency resolution in the peripheral areas (140). However, the latter provide high temporal frequency, enabling motion detection and high sensitivity to light (141,142).

An area of interest in the visual field can be scanned with the highest spatial resolution provided by central vision if the light waves are emitted on the fovea. The small size of the fovea (covering approx. 2° of visual angle) requires the eyes to move fast from one location to another to direct the point-of-gaze on salient locations in the visual field in a short time. Figure 2-4 shows a cross-sectional view of the eye with its described inner parts. The size of the region covered by vision is usually reported in degrees (°) of visual angle. It can be translated into meters with an estimated distance between the eyes and the area of interest (134).

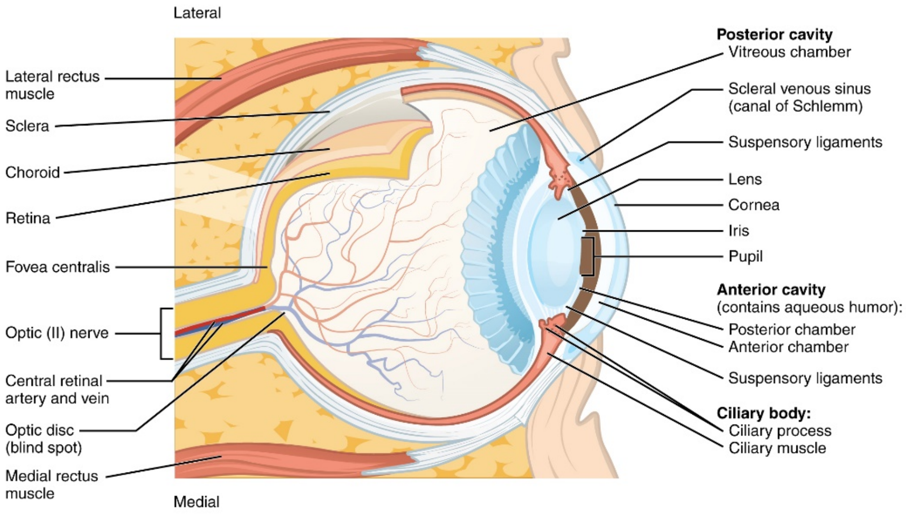

Figure 2-4 Lateral view of the eye including the inner parts. Adapted from OpenStax at http://cnx.org/content/col11496/1.6/.

The fast movements of the eyes towards different regions in the visual field are called saccades; they allow the areas of interest to be mapped onto foveal vision. A fixation is relative stillness of the eyes on a region of an area of interest. Smooth pursuit refers to the eye movements that follow a moving object in the visual field. The (eye) blink is a sequence of closing and opening of the eyelids. Further, the pupil can be enlarged or shortened in size, for instance to adjust to the incoming light intensity. This is referred to as pupillary responses. These ocular events (saccades, fixations, blinks, and pupillary responses) can be measured using an eye tracker. Pre- and post-saccadic oscillations – that is, glissades, static overshoots, and dynamic overshoots (143) – and fixational eye movements – such as micro-saccade, tremor, and drift – are other ocular events identified in the literature, but they are technically challenging to measure (144). In addition, optokinetic nystagmus and vestibulo-ocular reflexes are clinically relevant ocular events, for example, to detect abnormality in the oculomotor system (134).

In ophthalmology, eye movements are classified into version and vergence (145). Version (or conjugate) movement refers to the rotation of the eyes in the same direction, whereas vergence (or disjunctive) movement refers to the rotation of the eyes to opposite directions of each other, which can be inward (convergence) or outward (divergence). Vergence occurs if the distance of an area of interest is changed or is perceived to change, whereas version requires no change in the distance.

2.3.1. Eye tracking

Today, different technologies are available for eye tracking, falling into three categories. One category is eye-attached tracking (146), wherein a contact lens is attached to the eye. This is highly accurate, but invasive. A second category is electrooculography, which is based on the corneo-retinal standing potential (147). It provides high temporal resolution, but requires electrode attachments surrounding the eyes, which limits its applications. Video-oculography, or optical eye tracking, is a third category. In this widely used technique, eye images are recorded and processed to measure eye positions across time. A subcategory of video-oculography is based on the Purkinje reflections of emitted infrared light from the eyes, providing accurate and contactless eye tracking (148). Video-based eye trackers can be configured as remote, desktop, head-mounted, or goggles. Head movements can be compensated for by coupling the head-mounted eye trackers with a motion capture system, allowing unconstrained settings to record eye movements and accurately estimate geometrical gaze coordinates in the space. Such systems may provide technical requirements to measure quantitative features of eye movements and pupillary responses, called oculometrics.

2.3.2. Neuroanatomy of eye movements

Three pairs of muscles enable the movements of the eyeball (Figure 2-5), contributing to eye movements differently depending on where on the eyes they are attached. These three muscles are the (lateral, medial, inferior, and superior) rectus muscles, and (inferior and superior) oblique muscles, all of which are referred to as extraocular muscles (149). Furthermore, the upper eyelid is elevated using the levator palpebrae superioris muscle, while long and short ciliary nerves respectively used to control the iris sphincter and dilator muscles to change the pupil size (150).

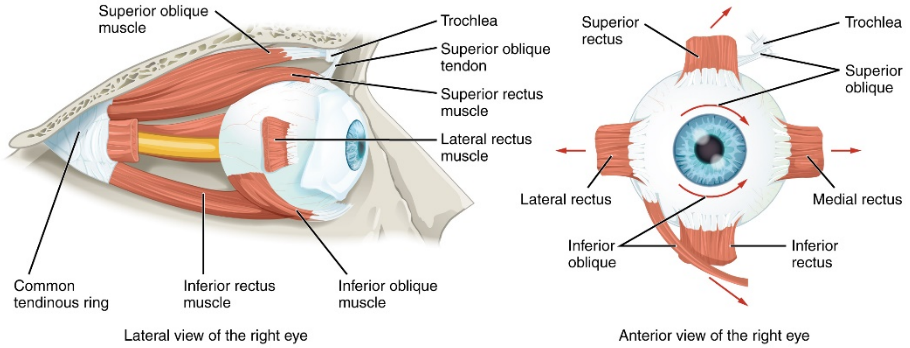

Figure 2-5 Lateral and anterior views of the right eye showing the muscles involved in eye movements. Adapted from OpenStax at http://cnx.org/content/col11496/1.6/.

Ocular muscles are innervated from the midbrain, caudal midbrain, and pons as follows (138,149): 1) the oculomotor nerve ends in the superior, medial, and inferior rectus muscles, inferior oblique muscle, and levator palpebrae superioris muscle; 2) the trochlear nerve is connected to the superior oblique muscle; and 3) the abducens nerve innervates the retractor bulbi muscle. Eye movements are mediated by cognitively driven commands from cerebral areas (151–153). This suggests that cognitive processing can be traced by eye movements.

2.3.3. Eye movements in relation to fatigue and mental load

In the study of fatigue and mental load, eye movements and pupillary responses have been of particular interest as proxies to the nervous system (13,154–158). The following summarizes the literature on these subjects.

Blinks are semi-autonomic closures of eyelids and can fall into voluntary, spontaneous, and reflex blinking categories (159). These three categories refer to the blinks occurring consciously and voluntarily, blinks occurring involuntarily with no conscious effort, and blinks in response to external stimuli (e.g. tactile, visual, and auditory), respectively. The three categories of blinks may differ in some aspects (e.g. amplitude) (159,160). Voluntary and spontaneous blinks appear to be more relevant to the nature of computer work than the reflex blink.

In a systematic review of 21 studies on the association of fatigue or mental load with blinks (156), 13 studies showed a link between fatigue and blinks, and eight have found significant associations between blinks and mental load. The authors of the review conclude that blinks are reliable indicators of fatigue and mental load in many tasks, including driving, flight, air traffic control, and surgery (156). However, blinks have been less investigated in computer work, which may reveal specific blink patterns that could be different from blinks during other activities, such as watching a video (161).

The duration and frequency of blinks have been used to characterize fatigue and mental load (Table 2-1). For instance, studies have demonstrated the inhibition of blink executions to avoid information loss in visual attention, as evidenced in the digit-sorting and Stroop tasks (162), and in the detection of a specific sequence of letters, the detection in the change in luminance of visual stimuli, and the Simon task (163). These studies indicate that blinks may be associated with cognitive processing. Furthermore, the duration and frequency of blinks have often been shown to increase with raised mental load and fatigue (156). However, other studies have not found this association (164). The authors have investigated the effects of time-on-task and mental demands of an arithmetic task (count backwards with different step sizes) on blinks. They found that blink frequency did not significantly increase with the time-on-task or the task difficulty. In another study, the duration and frequency of blinks were reported to be significantly lower before and after flight tasks compared with a landing task using a flight simulator (165). This effect may have been due to the visual demands: namely, checking several flight control options in a large visual scene. In contrast, the blink frequency has been observed to increase with 40-min time-on-task in coincidence with suppressed power of the delta band captured by electroencephalography (166).

Table 2-1 A list of studies on the association between fatigue, mental load, and blinks

Study	Participants[1]	Task	Eye tracking[2]
(164)	5 m & 6 f, 32±6 y	arithmetic task (count backward with different step sizes)	EyeLink 1000, 500 Hz, DR, HS
(165)	13 m & 1 f, 20-30 y	simulated flight task	Electrooculography, 100 Hz, NS, NS
(166)	9 f & 3 m, 21±2 y	reaction to appearing visual targets (a vigilance task)	Monocular EyeLink 1000 (remote), 500 Hz, DR, UC
(167)	13 m, 22-26 y	simulated driving in virtual reality	Electrooculography, 100 Hz

(168)	13 m (no age information)	arithmetic and verbal vigilance	Electrooculography
(169)	11 (no other information)	geometric shape detection task	Electrooculography
(93)	33 f, 21-26 y	customized Mackworth clock test (170)	Electrooculography

1) Healthy participants unless otherwise mentioned: sex/gender combination (m: male, f: female), age (mean ± standard deviation), range in years (y), other specifications.
2) Eye tracking: the model of eye tracker or method, sampling frequency, in dark room (DR) or light room (LR), with head stabilization (HS) or unconstrained (UC), or condition not specified (NS).

Blinks have been postulated to differ depending on task properties leading to phasic (stimulus-driven) or tonic (free viewing) responses (171). Watching a video and looking at a fixation point are the tasks that may require phasic and tonic blink responses, respectively. The differences in blink metrics among tasks with different task properties are thus conceivable.

Most studies have found blink duration and frequency to increase with fatigue (35). Increased blink duration and frequency have been observed in 40 min of responding to arithmetic and verbal information (168). Increased frequency of blinks has also been reported in a simulated driving task (167), 90-min detection of geometric shapes (169), and 7 min of performing the Mackworth clock test (93). Blink frequency has been reported to decrease under high temporal demands (93). Further, blink metrics have been used to detect fatigue using classification models (35,167,168). Changes in blinking behavior have been linked to the dopaminergic system (93), in which dopamine levels may positively correlate with blink frequency. Dopamine is closely linked with attention and working memory (171).

Some of the differences among the studies could be explained by the differences in the algorithms used to compute blink metrics, or their use of different tasks and experimental set-ups. For example, a criterion to identify blinks is their duration; this varies from one study to another, ranging from, for instance, 50-500 ms (172) to 71-300 ms (173), which in turn may change blink frequency. Another shortcoming is that the samples of the studies are rather small (164) and/or biased (165). Moreover, some key information that may influence the results has not been fully reported concerning the experimental set-up. For example, even the position or the refresh rate of the computer screen in the visual field may change the blink rate (161,171).

Furthermore, the light condition during the experiments may also lead to different findings in relation to blinks. For instance, blinks may occur less frequently and with shorter duration in low levels of light than in a bright room condition (174). To approach an ecologically valid condition for computer work, the experiments should be done in a standardly lit room, which is a missing point in the studies conducted in dark or dimmed light conditions (Table 2-1).

Another common behavior of the eyes with fatigue development is the appearance of partial closure of eyelids for some moments. This behavior is quantified using the percentage of closed eyes (PERCLOS) to determine the percentage of periods in which the eyes are totally or partially closed over time (175). In contrast to computer work, PERCLOS has been extensively studied in the context of driving to detect fatigue and drowsiness (10).

Saccades involve plenty of information about the oculomotor system. Saccade centers and the neural areas that are involved in the generation and execution of saccades have mostly been identified (176). This neural network consists of the superior colliculus in the brainstem as a center of saccade generation, in connection with cortical areas, the basal ganglia, and the cerebellum, which may also be affected by visual attention and fatigue (176). The brain needs to prepare the direction and the amplitude (size) of the saccades from one point of gaze to another. Saccades in horizontal and vertical directions are associated with the paramedian pontine reticular formation in the pons and the rostral interstitial nucleus in the midbrain, respectively, and simultaneous activation of both nuclei leads to oblique saccades (138). In the integration of visual and other sensory inputs, the frontal eye fields, the supplementary eye fields, the parietal eye fields, as well as the basal ganglia, may modulate saccades via the superior colliculus (177).

Various characteristics of saccades have been found informative in relation to fatigue and mental load. For example, saccade duration has been reported to decrease as mental load increases (134,178,179). Saccade frequency has been found to be reduced with increasing mental demands in mental calculation of arithmetic multiplications while following a visual target with stepwise motion on the circumference of a circle (180). The peak velocity of saccades has been found to decrease in response to increased mental load in a simulated driving task with three levels of complexities (low, medium, and high) according to different traffic densities and the presence of hazardous road barriers in the medium and high levels (181). However, researchers have found no significant effect of the task levels on the mean velocity and duration of saccades. On the other hand, a recent study has shown that some saccadic metrics (e.g. peak velocity) may be partly modulated voluntarily in association with motivation (182). Thus, different factors in addition to task properties might have contributed to the differences in the findings.

As outlined in Table 2-2, the detection of fatigue via saccades has been the topic of research in various domains and occupations, including aviation (183,184), nursing and surgery (13,185), and driving (181,186). The duration and peak velocity of saccades have been respectively increased and decreased by increasing fatigue (186). The relationship between saccade peak velocity and amplitude, knowns as main sequence, has also been reported to be influenced by fatigue and mental load (184,187). Saccade velocity and amplitude have been found to decrease with decreased vigilance (166) or increased mental demands in watching a video and memorizing items (178).

Table 2-2 A list of studies on the association between fatigue, mental load, and saccades

Study	Participants^1	Task	Eye tracking^2
(155)	10 m & 2 f, 30±4 y, 2 authors	air traffic control	binocular EyeLink 1000, 500 Hz, DR, HS
(13)	6 m & 6 f, 30±2 y, all surgery residents	peg transfer, precision cutting, and guided saccades	Binocular EyeLink II, 500 Hz, DR, UC
(184)	26 m, 29±5 y,	simulated flight and guided saccades	Binocular EyeLink II, 500 Hz, DR, UC
(186)	5 m & 5 f, 24±5 y	simulated driving and guided saccades	Monocular Eyelink 1000 remote, 500 Hz, DR, NS
(181)	9 m & 9 f, 18-33 y	simulated driving with reaction to visual and auditory stimuli (secondary task)	Monocular Eyelink II, 500 Hz, NS, NS
(187)	9 m & 9 f, 18-33 y	Firechief microworld: a decision making task (188)	Monocular Eyelink II, 500 Hz, NS, NS
(189)	11 m, 27±2 y, all navigators	guided saccades in overlap and gap paradigms	Electrooculography, 200 Hz, DR, UC
(178)	12 m, 19-36 y, all basketball players	three levels of mental demands in watching a game video clip and recalling player positions	Head-mounted ASL Eye-Trac 6, NS, UC

1) Healthy participants unless otherwise mentioned: sex/gender combination (m: male, f: female), age (mean ± standard deviation), range in years (y), other specifications.

2) Eye tracking: the model of eye tracker or method, sampling frequency, in dark room (DR) or

light room (LR), with head stabilization (HS) or unconstrained (UC), or condition not specified (NS).

Saccades can be categorized based on how they are elicited. This categorization is important to know, since the way saccades are evoked may affect the complexity of neural control of saccades and the involvement of cortical processes (190). A *visually guided saccade* occurs when a fixation target is visually cued (e.g. pro-saccade task). The saccade in this task can be a reflexive saccade with a typical latency of 200 ms (176,191). Another type of visually guided saccade is the *express saccade*, with typical latency of approx. 100 ms. Express saccades may occur when there is a short gap between the onset of a fixation target and the offset of a fixation point (192–194). *Memory-guided saccades* are elicited when the position of the target is provided by visual memory (195). *Predictive saccades* to targets that are temporally and spatially predictable (196). Finally, an a*nti-saccade* is a saccade in the opposite direction of a fixation target; it appears on the periphery of the visual field in an attempt to inhibit reflexive saccades to the target (197).

In a broad classification, a saccade that is triggered by the intention to freely explore a visual field is termed voluntary saccade to distinguish it from the reactive (or reflexive) saccades that are executed to sudden cued targets (176,198). Voluntary saccades appear more frequently in daily-life situations (198). In computer work, saccades may occur in the form of (voluntary) scanning saccades in different sizes, directions, and trajectories to explore the elements of a stable visual scene (176). Reactive and scanning saccades partly involve different neural substrates (199), but scanning saccades have generally been much less studied (176). In the present studies, this led to the examination of saccades within a cognitive task with voluntary visual explorations, where the scanning saccades could appear frequently.

Pupillary responses are the dilations and constrictions of the pupil, which involve sensory components (e.g. sensitivity responses to light exposure) and cognitive components (in response to mental demands) (200,201). The most common characteristic of pupillary responses is that the pupil diameter (size) increases with mental load (178,202–205): Pupil diameter has been shown to reach higher peak values with high mental load compared with low mental load (206). Similarly, task-evoked pupillary responses positively correlate with increasing mental load; they are measured as the peak amplitude of the pupil's first dilation and the duration to reach the peak amplitude following an event onset in a task (207,208). Task-evoked measures may be limited to in-the-lab tests and studies.

Pupillary responses have been shown to provide complementary information to blinks regarding cognitive demands in digit-sorting and Stroop tasks (162), suggesting the utilization of multiple ocular events. In addition to the Stroop task, there are a number of cognitive control tasks, including the n-back task, the digit span task, and mental multiplications, where raising task demands may lead to increased pupil dilations (158). To elaborate on the mechanisms behind pupillary responses, it is necessary to know about the neural substrates that contribute to such changes.

Different neural circuits are involved in the control of pupil size. There is a parasympathetic pathway connecting ganglion cells in the retina to the pretectal olivary nucleus, followed by the Edinger–Westphal nucleus and back to the ciliary ganglion to constrict the pupil; and a sympathetic pathway from the hypothalamus through the medulla, the spinal cord, and the superior cervical ganglion to dilate the pupil (209). In addition, pupil size is mediated by cognitive activities; this involves the locus coeruleus-norepinephrine system and the superior colliculus (209). Pupillary responses can be indirectly modulated by the frontal and parietal cortices (209). These extensive neural networks lend support to the view that pupillary responses beyond the light-reflex responses may allow inferences about cognitive processing (209).

As an attempt to extract cognitive responses from pupil dynamics, pupillary responses are sometimes split into tonic and phasic components, respectively referring to low-frequency or baseline responses and high-frequency or event-related responses, reflecting neural activities in the locus-coeruleus system (210–212). Task-evoked pupillary responses (213) and the (pupillary) index of cognitive activity (214) are commonly used as phasic responses, where the higher cognitive load may lead to higher event-related peak dilations and higher occurrences of high-frequency changes in pupil size than low cognitive load. However, computation of the (pupillary) index of cognitive load has not been fully documented (215). Pupil dilation has generally been suggested to be mediated by the effort one makes to perform a mental task, underlining the role of inter-individual differences in pupillary responses (158). This suggests that machine learning could be used to capture inter-individual differences regarding pupillary responses. Furthermore, little is known about the nonlinear dynamics of pupillary responses. To address this, nonlinear quantitative features were aimed to be extracted from pupillary responses in Study I.

Furthermore, pupillary responses with prolonged time-on-task have been less studied compared with the effects of mental tasks in short periods. A few studies have observed that pupil dilation increases with time-on-task when participants become motivated to increase their own performance in the 2-back task (216). However, finding reliable metrics from pupillary responses with time-on-task is challenging (217). This has sometimes been addressed by using digital filtering or by discarding the pupil samples attributed to saccades and the samples' neighboring blinks, and using head stabilization and performing the tasks with a fixed gaze position (217). The pre-processing of the pupil signal is necessary to remove noise and artifacts, but the fixed-gaze paradigm (217) and recording pupil dilations in dimmed light conditions (216) may not provide a precise assessment of the reliability of pupil-based metrics in natural and unconstrained situations for eye movements.

Fixations have been found to be informative concerning workload (218) and fatigue (219). Fixation duration is usually used as a measure of visual attention during active vision (220) – that is, goal-oriented gaze. Long fixations may imply visual saliency (221) or difficulty in visual perception (222). However, a fixation may not always reflect visual attention (223), for instance in the case of passive vision when looking to a corner while trying to recall something. Thus, the functionality of fixation is dependent on the task and context. Depending on the task, the duration of a fixation may be as short as 50 ms or longer than a second (224,225). Fixation duration has been reported to increase with rising mental load (178,179,203,226–228) and fatigue (229) in free viewing tasks. Furthermore, the frequency of fixations (or fixation rate) has been found to negatively correlate with mental load (180) and decline with time-on-task (230,231). In general, however, fixations in relation to fatigue and mental load have been less studied than other ocular events.

Three types of involuntary eye movements may occur during fixations. First, a micro-saccade is a saccade-like movement typically characterized by a velocity of 15-50°/s and an amplitude of 10-40′ (where $1^o = 60'$) (134). Drift and tremor are other types of fixational eye movements, respectively characterized by slow (<50 ′/s) and fast (<1.5 °/s) tiny vibrations of the eyes (232). Research has shown that micro-saccades may reflect mental load (233) and fatigue (155). For instance, the magnitude of micro-saccades has been found to be sensitive to change in mental load and time-on-task (217). Furthermore, extended time-on-task and increased mental load have been shown to increase the rate (frequency) of micro-saccades as well (164). Measuring fixational eye movements (micro-saccade, drift, and tremor) requires high precision in eye tracking (234,235). The precision of the eye tracker in the present studies (Section 3.3) was beyond the recommended precision to measure micro-saccades, i.e. <0.03° (134). This technical requirement, still not met in many eye trackers (236), may limit the use of fixational eye movements as oculometrics in workplaces. Nonetheless, saccades and micro-saccades have similar characteristics (e.g. linear peak velocity and amplitude relationship), supporting the hypothesis that these two ocular events share common neural mechanisms (177,237). Thus, studying saccades may yield insights into the behavior of micro-saccades.

As briefly reviewed here, multiple oculometrics in relation to mental load and fatigue have been proposed in the literature. However, it is unclear how divergent and variable these oculometrics are in computer work across young and elderly individuals (238). Ambient light (38,239), computer screen brightness (240), and the social presence of co-workers (241) may have significant effects on the dynamics of eye movements in relation to fatigue. Given this, a serious shortcoming of most studies on the association of oculometrics and fatigue is the lack of ecological validity, as noted in this chapter. Most studies have involved head stabilization (e.g. using chin/head rests), limited types of eye movements (e.g. more reactive saccades and less scanning saccades), and limited sample sizes – for example, ≤12 participants (155,178,189) with sex bias and limited age. This makes it difficult to generalize findings to real-world scenarios. To partially address these concerns, eye tracking can be done using unconstrained head movements, and a functional task can be developed to provide a rich distribution of eye movements during computer work. This was the aim in the present PhD project.

2.3.4. Age-related changes in oculometrics

Beyond its numerical representation, age is as a multifaceted concept and is dependent on several variables, including time (242,243). Since time plays a major role in aging, it is usually used to quantify age; this can be specified as chronological age. Chronological age has been used in this PhD project to provide comparisons across similar studies, following common practices in gerontology (244). The scope of this project is limited to normal aging, including healthy young and elderly adults (Section 3.1).

Cognitive abilities may change at different rates in the process of normal aging. Not all cognitive abilities decline with aging. For example, crystalized intelligence including general knowledge and vocabulary remains unchanged or broadens as one ages (245). In contrast, fluid intelligence, reflected in processing speed, attention, memory, and psychomotor ability, has been reported to decline mainly after the third decade of life (245,246). Aging may slightly affect auditory attention span (247) but largely impact selective and divided attention (248,249). Reductions in working memory have also been observed through aging (250). Furthermore, visual construction skills may decline with aging, whereas visuospatial abilities may remain stable (251,252).

Complex functional abilities, such as driving (253), have exhibited age-related decline. The complexity of these abilities involves diverse cognitive domains, including visual attention and processing, visual perception, executive function, and memory (253). Decision making, problem solving, planning and sequencing of executive function are subject to decline with age (247,254,255). Age-related cognitive decline may be associated with neurophysiological changes. As such, one may refer to loss of grey matter in the prefrontal cortex, steady density loss of the neocortical synapses beginning at the age of 20 (256), shrinkage in white matter (252,257), decreased volume of the hippocampus (258), neuronal death (259), and morphological changes in neurons resulting in decreased neuronal size and synaptic density (260).

Some studies have reported cognitive decline from the age of approximately 50 years. In a longitudinal study on 5,198 men and 2,192 women, cognitive decline was observed from the ages of 45-49 years (261). Cognitive and functional decline over the age of 50 years has been found to be prevalent

(262–264). Furthermore, people aged 50 years and older have been found to exhibit age-related changes in the oculomotor system, reflected in saccades (265). These findings directed the present project in exploring the age-related differences between elderly (aged 50-70 years) and young (aged 18-30 years) individuals in oculomotor responses to the manifestation of mental load and fatigue. The use of the word "elderly" is based on a common terminology in the gerontology literature (266).

The ocular system can be structurally and functionally affected by age. Structural changes with aging may affect the cornea, the lens, the vitreous humor (267), and the fovea (268), and may not be limited to these parts (269). The loss of Meibomian glands and oil glands along the edge of the eyelids occurs progressively in normal aging (270). Important structures of the visual system, including neuronal density and morphology, in the primary visual cortex may only undergo slight changes with age, but the number of axons from retinal ganglion cells in the optic nerve may decrease significantly (271).

Experimental assessments have revealed some age-related differences in visual perception. One study examined saccadic adaptation in response to dislocation of saccade landing targets (272) and found that fast adjustments revealed declined cognitive functioning in elderly individuals. Furthermore, visual perception of orientation, parallelism, collinearity (273), motion (274), and contrast (275) have been shown to exhibit age-related differences. The efficiency of visual attention towards multiple targets has been shown to decrease with aging (276). Elderly individuals have also been reported to have more difficulty storing and processing information about multiple visual targets (277).

Age-related changes may affect the oculomotor system in different ways (269,278). The supranuclear structures acting upon the cranial nerve nuclei (III, IV, and VI) have been shown to lead to age-related change, which may in turn affect the execution of rotational eye movements, such as saccades, convergence, smooth pursuit, optokinetic nystagmus, and vestibular reflexes (269). Aging may affect blinking behavior: blink rate has been shown to increase with age (269). This could be linked to the decrease in dopamine functioning with aging (171). However, age-related changes may not be evident in some specific oculometrics, such as saccade peak velocity (279). Furthermore, some studies suggest that the existence of regenerative mechanisms are involved in the oculomotor system to maintain normal oculomotor functioning intact against senescence (280,281).

Aging influences the brain areas in different ways that have been studied pertaining to eye movements. The frontal and parietal eye fields respectively contribute to the neural signaling of saccades and smooth pursuits (269). In particular, reflexive saccades are less affected by aging compared to the frontal eye field, which mediates volitional horizontal and vertical saccades (269). The changes across different age groups are well established for some oculometrics, such as saccade latency (282) and smooth-pursuit gain (283), but not well understood for others, including saccade peak velocity (284). Only a small number of eye movement studies such as (284) have utilized unconstrained conditions (free head movements) to compare oculometrics between young and elderly individuals.

A study[*] has shown that elderly individuals make more repetitive fixations to already seen areas than young individuals do (285). The task involved the memorization of locations of three to five abstract visual objects. The study's authors interpret the repetitive fixations as a compensatory mechanism for the decreased capacity of working memory in elderly individuals. Another study[†] has demonstrated that the frequency of fixations decrease with age in viewing series of affective pictures. The reduced frequency of fixation was associated with self-reported low arousal. Age-related differences may also be found in pupil dilations, as has been observed in pro-saccade and anti-saccade tasks representing a lower range of dilations (blunted dilations) using a video-based eye tracker[‡] (286).

Finally, a study has found no significant difference in saccade peak velocity, saccade amplitude, and saccade frequency between elderly and young individuals in learning geographic routes followed by a test to recognize correct directions (287). This observation, involved decreased mean velocity of saccades only during the direction test. Similarly, no significant age-related difference was found in saccade peak velocity, amplitude, and the

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[*] Using a monocular head-mounted eye tracker, EyeLink II, at 500 Hz sampling rate (SR Research Ltd., Missisauga, Canada)

[†] Using a remote eye tracker, iView X, at 50 Hz sampling rate (SensoMotoric Instruments, Teltow, Germany).

[‡] EyeLink 1000 at a sampling rate of 1000 Hz (SR Research Ltd., Missisauga, Canada)

linear relationship between these two variables (288). On the other hand, age-related effects have been reported in saccade duration and reaction time in anti-saccade and pro-saccade tasks using electrooculography (283).

Chapter 3. Methodology

This chapter outlines the methodology of the three main studies. The task proposed in this PhD project, with the aim to impose mental load and develop fatigue resembling computer work, is first described. It is then followed by a brief description of the experimental protocols in using the proposed task to study the reliability of oculometrics across days and mental load levels (Study I). Following that, the use of the elongated version of the task to develop fatigue is explained (Study II). In the final section of this chapter, the implementation of a biofeedback system is outlined using the same task (Study III). In addition, the considerations in recruiting participants and applying methods and materials used for data acquisition and processing are covered.

3.1. Participants

In total, 58 healthy volunteers participated in Studies I, II, and III. The participants were familiar with computer work, used to working with a computer mouse with their right hands, and reported no history of musculoskeletal pain or mental and neurological disorders. The participants were instructed to avoid alcohol for 24 hours and caffeine, nicotine, and drugs, including cognitive enhancers (289), for 12 hours prior to experimental sessions. The properties of the participant pool including the mean (standard deviation) of age, height, and body mass for all the studies involved in the PhD project are listed in Table 3-1. In addition, the information regarding the history of chronic fatigue and eye strain, respectively using the fatigue assessment scale (290) and the visual fatigue scale (291), were obtained from the participants along with sleeping hours and the laterality index (292). The questionnaire used to obtain this information is available in Appendix A. The studies were approved by the North Denmark Region Committee on Health Research Ethics, project number N-20160023, and conducted in accordance with the Declaration of Helsinki.

Table 3-1. The properties of the participant pool in Studies I, II, and III. Abbreviations in the table are Y: young group (18–30 years old), E: elderly group (50–70 years old), f: female, and m: male. Study III involved a young group.

Studies	**Total number**		**Sex**	**Age (y)**	**Height (cm)**	**Body mass (kg)**
I & II	38	20 Y	9 f, 11 m	23 (3)	174 (8)	71 (11)
		18 E	11 f, 7 m	58 (7)	172 (7)	80 (12)
III	20		10 f, 10 m	26 (3)	174 (8)	69 (15)

Studies	**Total number**		**FAS**	**VFS**	**Normal sleep hours**	**Sleep hours before session**	**Laterality index**
I & II	38	20 Y	22 (2)	7 (5)	7.6 (0.7)	7.8 (0.8)	72 (38)
		18 E	21(2)	7 (6)	6.8 (1.1)	7.6 (1.5)	76 (44)
III	20		20 (3)	8 (5)	7.6 (0.8)	7.3 (0.8)	66 (50)

FAS: Fatigue assessment scale, VFS : visual fatigue scale

The elderly group had significantly higher body mass than the participants in Study III (p=0.041) and lower normal sleep hours than the other two groups (p<0.05) as examined by a one-way multivariate analysis of variance. Study III involved only a young group, as outlined in Table 3-1. This was because age was not found to be the main contributing factor in the prediction of fatigue development in Study II. (This is described in more detail in section 3.9)

3.2. Computer task

A novel computer task* was designed and implemented as a graphic user interface in MATLAB R2015b (Studies I, II, and III). The task was intended to impose three levels of mental load—low, medium, and high—and present an ecologically valid model of functional computer work. In the present model of computer work, the chunks of information in the form of texts and geometric shapes must be processed. It is a common approach in cognitive task analysis to break down a task into the subtasks it consists of and the possible cognitive processes it may involve (293). Cognitive processing during the task may involve working memory to momentarily remember and recall the information, visual attention to recognize the information, visual search to find the information, verbal memory to understand and interpret the information, and eye-hand coordination for computer interaction. These are the cognitive and sensory elements involved in the design of the proposed

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[*] Available online at https://osf.io/2fc7s/

task. Cognitive processes (such as memorization, attention, and decision making) have been explained as theoretical models (294,295), suggesting that these processes may have functional representation in the brain (296–298).

The task consists of a sequence of fast cyclic operations: (1) memorization, (2) washout, and (3) replication. As depicted in Figure 3-1, each cycle begins with a memorization period, meaning the memorization of a displayed pattern of connected points in different shapes with a textually cued starting point. Following the memorization period, a blank window including a fixation point (target) is displayed with the same duration as the memorization period; this is termed the washout period. Subsequently, the points of the pattern without connecting lines are displayed during the replication period. The points become connected during the replication period if they are clicked with the sequence in which they were displayed and cued in the memorization period. A distracting point is also displayed during the replication period within the distance of [0.5° 1°] to one of the pattern's points.

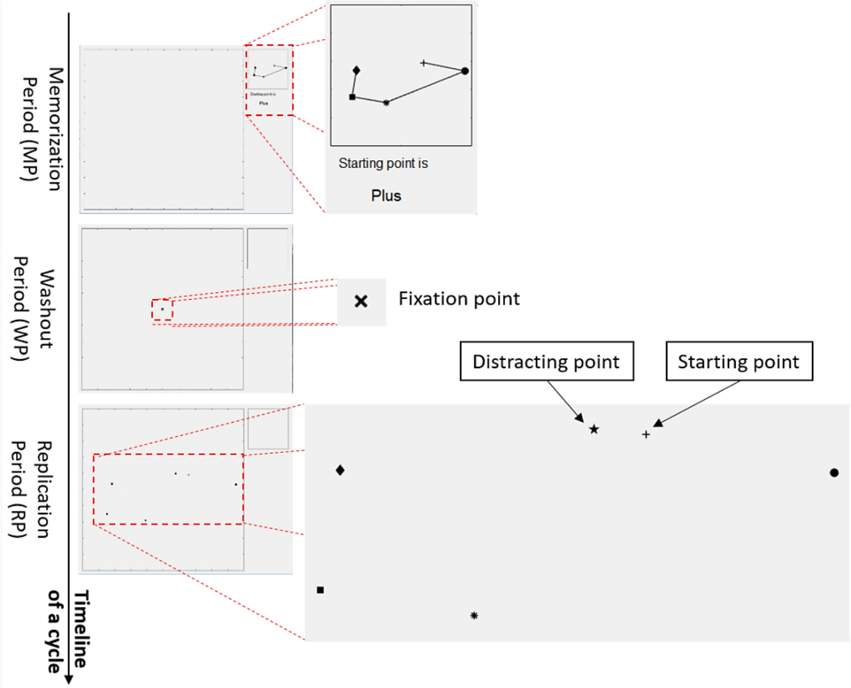


Figure 3-1. The timeline of a cycle (in the medium level), including a magnified view of the components of the three sections (memorization, washout, and replication). (Studies I, II, and III)

The graphical user interface spans approximately 27°×21° of visual angle on a 19-inch screen (864×1,152 pixels, refresh rate: 100 Hz) at a viewing distance of 55 centimeters. The mouse cursor becomes hidden during the washout period and locates on the center of the graphical user interface before the beginning of the replication period to avoid distractions and prepositioning it on the starting point. By correctly clicking the starting point, it becomes twice as large to indicate a valid start. The size change is one of the attributes to guide the deployment of attention (299).

The task also involves various cognitive processes that may be required in computer work. To accomplish the task, a sequence of memorization of the spatial and verbal information of each pattern and its textual cue during the memorization period is required. Working memory is necessary to maintain the pattern information in the mind during the washout period. In addition to working memory, decision making, motor control, and visual attention are required to click precisely and proceed with the visual feedback from the depiction of the connecting lines between the points in the replication period.

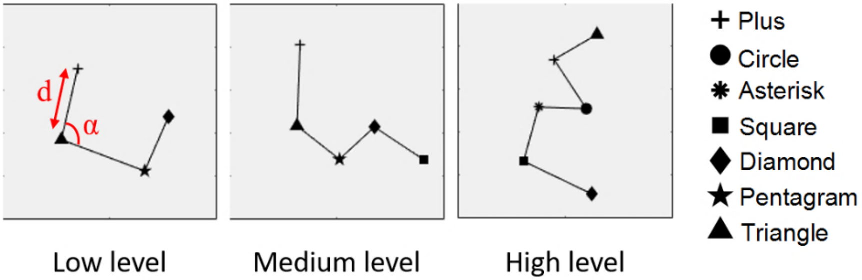
The memorization involves visual scanning within a small area and verbal comprehension to accomplish the memorization of the pattern. The memorization, thus, mainly involves sequences of short saccades and fixations. Moreover, the washout is an important element to exert temporal load on working memory to maintain the memorized picture of the pattern as spatial information may decay over time (300). The replication involves a visual search to find the position of the points, decision making to choose points to click, the action of clicking, and ignoring the distracting point with selective attention. A contributing element to the working memory (301) was to distinguish the distracting point, which required selective attention.

3.2.1. Mental load

Geometric properties of the patterns including the spatial positioning of the points are the key bottom-up elements of the task to induce mental load (302–307). There are clear limitations in memorization of items pertaining to the capacity of working memory (308–310). For instance, working memory requires holding and manipulating (translating) information in mind (e.g., the textual cue and the name of the shapes) rather than merely holding information in the short-term memory (90).

The geometric complexity of the patterns was manipulated to induce three levels of mental load (Study I), Figure 3-2. The terms used to describe the levels (low, medium, and high) may refer to the relative mental demands in each of them. The difference among the levels was experimentally supported by the different perceived mental load for each level in agreement with the performance of the participants (section 3.1). Similar terminology has been used to distinguish between the difficulty of task levels based on task characteristics (311).

Moreover, various features contribute to the geometric complexity of patterns, which may change mental demands (304,312–315). If the angles between the consecutive points of patterns approach 180°, it makes simple patterns resembling a line. Conversely, if the angles decrease, it may make the patterns visually more complex, which may require further mental effort to scan and memorize (316,317). In addition, increasing the number of connecting points may add to the complexity of the patterns (316,318,319). Furthermore, based on the grouping principles of perception (i.e., Gestalt's laws of continuity and proximity), humans may tend to group the points to make familiar patterns (320). This grouping strategy in the proposed task may help in the low level to remember incomplete square-like patterns (Figure 3-2), but the patterns become more irregular in the medium and high levels, which renders the grouping strategy less effective.



Load level	Geometric components of the patterns	
	Number of points	Angles between consecutive points (α)
Low	4	>90°
Medium	5	>60°
High	6	>30°

Figure 3-2. Examples of the patterns in the three load levels, the pool of the shapes used in the patterns and the distracting point (top right), and the constraints used in the generation of the

patterns. The Euclidean distance (d) between the displayed points was limited to approximately [2° 4°]. No overlaps/crossings of the lines were allowed in the generation of the patterns. The orientation of the shapes was also kept unchanged.

The duration of each level was according to the task demands adjusted to avoid imbalanced temporal load across levels. A technique called methods-time measurement (MTM) (321,322) was utilized to calculate the timing of each section of cycles according to MTM-100 standard (Study I). The allocated time for memorization, washout, and replication periods in the three load levels are outlined in Table 3-2. The mental load may be induced by the visual demands based on the assumption that the required information to memorize the patterns and replicate them is within the capacity of the working memory in the allocated periods. It is also required that the participants cognitively engage in the tasks.

Table 3-2. The memorization, washout, and replication periods for each load level of the task. The washout period has an equal duration as the memorization period.

Cycle section	**Mental load**		
	Low	Medium	High
Memorization Period [s]	2.06	2.34	2.62
Washout Period [s]	2.06	2.34	2.62
Replication Period [s]	4.11	5.06	6.02

3.3. Eye tracking

A monocular head-mounted eye tracker (Eye-Trac 7, Applied Science Laboratories, Bedford, MA, USA) was used in this PhD project to record gaze position and pupil diameter, with the temporal resolution of 360 Hz. The monocular recording is a common approach in eye tracking due to the symmetry of eye movements (323). Computer work intuitively involves conjugate eye movements, most of the time presuming few changes in the distance between the eyes and the computer screen. The nominal value of the precision and accuracy of the eye tracker (manufacturer's estimate) are less than 0.25° and 2°, respectively (in the periphery of the visual field). According to the datasheets of the eye tracker, it may cover a calibration plane with the size of 30–40° in vertical and 50–60° in horizontal directions. All the data from the eye tracker can be collected on a computer with built-in software (EyeTRAC7, version 1.0.6.0, MA, USA). The eye-tracking system has the capability of estimating the point of gaze (the coordinates of the point being looked at) for each timestamp, which is also called gaze tracking (324).

The (spatial) accuracy and precision were measured during the washout period of the task wherein the participants were instructed to look at the center of the replication panel (Figure 3-3). The accuracy was estimated for each cycle as the mean of the Euclidean distances (l *in centimeters*) of gaze points (detected as fixations) from the fixation target on the center of the replication panel with known coordinates (in centimeters), which were converted from centimeters to visual degrees using the tangent formula (α=2arctan(l/2d)), where d is the mean perpendicular distance (in centimeters) between the eyes and the calibration plane (the computer screen) for each of the two successive gaze points. It is worth noting that the coordinates of the fixation target during the washout period were fixed and known, and the eye-head integration allowed for capturing the coordinate of the point of gaze throughout the recording period.

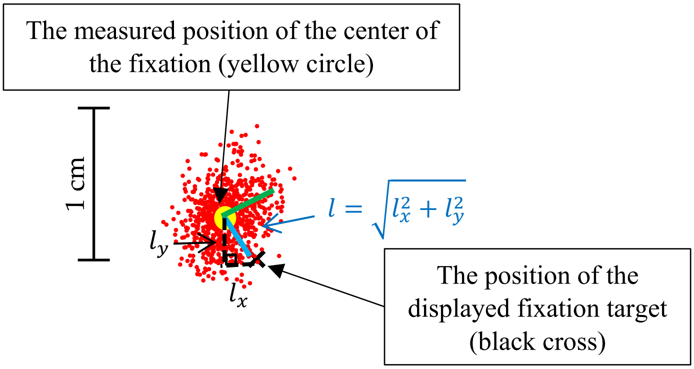


Figure 3-3. An example of the gaze points (red dots) during a fixation on the fixation point (target) from a participant during the washout period in one cycle. The position of the fixation target is displayed relative to the position of the gaze points as measured by the eye tracker. The precision and accuracy in this example are shown figuratively by the green and blue lines, respectively.

The precision of the eye tracker was computed as the standard deviation of the Euclidean distances (*in centimeters*) of the gaze points (of the samples detected as fixations) from the center of the fixations (i.e., mean of the horizontal and vertical gaze coordinates during the fixation) during washout periods. The precision was also converted from centimeters to visual degree using the abovementioned formula. According to our recordings of Studies I, II, and III, the mean (standard deviation) of the accuracy and the precision during fixations on the central fixation target during washout periods were 0.71° (0.33°) and 0.21° (0.18°), respectively, across participants. Following (134), the precision was also measured as root mean square (RMS) of the inter-sample distances during the fixations on the calibration points recorded before and after the sessions. The precision based on the RMS was, on average, 0.18° (0.18°).

Artificial models of the eye are sometimes used to measure the precision (325). This is because a source of artifacts in the estimation of the measured precision is fixational eye movements; however, the available artificial models may not fully characterize the eye and the inter-individual differences (325).

The eye tracker consists of the following parts: an eye camera, an eye illuminator, a focus friction screw, a head-mounted band, a monocular visor, and a stationary-scene camera. All these parts (except the scene camera) are attached to an adjustable head-mounted band, as shown in Figure 3-4. The monocular visor is attached to a flexible visor boom wire (Figure 3-4b). Using the eye camera and the eye illuminator of near-infrared light, the images of the eye are obtained by reflection in the visor. The stationary-scene camera was installed above the head of the participant (Figure 3-4d). The function of the stationary-scene camera is to record the participant’s field of view.

All the experiments involved in the main studies were conducted indoors with controlled noise, illumination, and temperature. A light meter (MotionWatch 8, CamNtech, UK) with a reported resolution of 0.25 lux (0–1,000 lux range) and sampling frequency of 1 Hz was further attached to the front side of the head-mounted band of the eye tracker to approximately record the light intensity to which the eyes were exposed (Figure 3-4a).

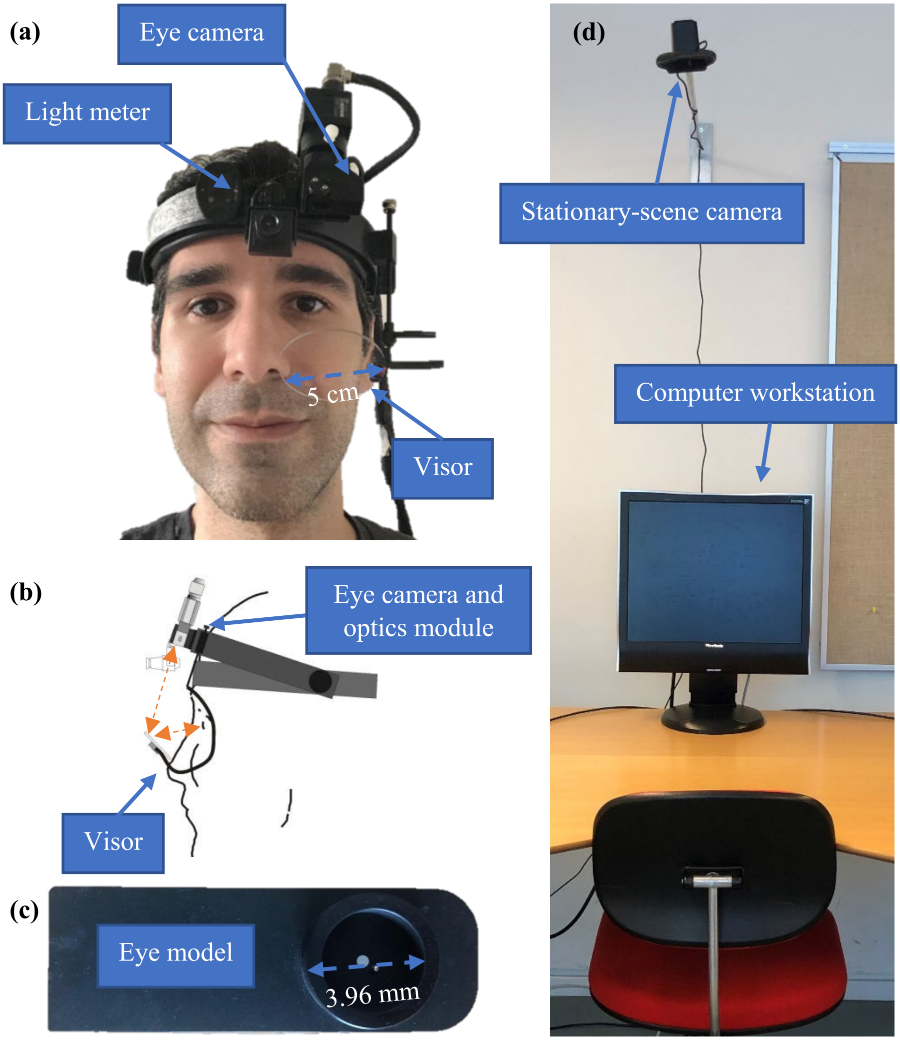


Figure 3-4. The key parts of the eye tracker: the light meter to the front view and the eye camera to the adjustable monocular visor to record the eye movements on the left eye (a), a schematic lateral view of the geometry of the emotion and reflection of invisible near-infrared light from the optics module coaxial with the eye camera to the eye through the visor (the original figure was adapted from the Eye Tracker Systems Manual ASL EYE-TRAC™ 7, version 1.5, May 2014) (b), the mechanical model of the pupil and corneal reflection, i.e., eye model (c), and the stationary-scene camera, which was installed attached to the wall above the head of the participant; it was used instead of the head-mounted eye camera as a built-in feature of the integration of head tracking with the eye tracker to avoid parallax error. The computer screen where the task was displayed during the experiments was in the field of view of the scene camera (d).

The size of the head-mounted band of the eye tracker is adjustable and can be fixed on the head of the participant. The monocular visor is placed underneath the eye of the participant to find the corneal reflection (CR) in the eye image. The sharpness of the CR is adjusted by the focus friction screw. While the pupil is identified, a red circle is shown, and the CR is visualized as a small green cross at the center of the CR. The detection of both CR and pupil is required to estimate the point of gaze (Figure 3-5). The pupil size is directly measured using the built-in software of the eye tracker in the unit of pixels. It can be scaled to millimeters using a mechanical model of the eye with a known pupil diameter of 3.96 mm, provided by the manufacturer of the eye tracker (Figure 3-4c). The resolution of the eye image where the pupil is displayed is 640×120 pixels, as shown in Figure 3-5.

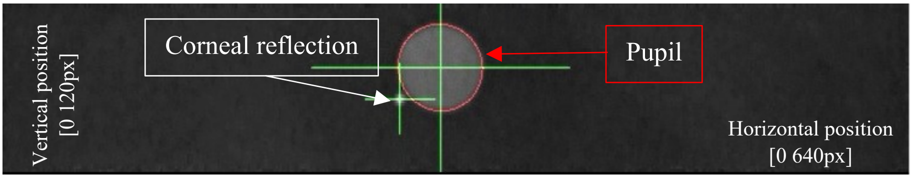


Figure 3-5. An eye image with the detected pupil (red circle) and corneal reflection (CR).

The eye tracker requires additional data to compensate for head movements via a motion-capture system (Visualeyez II system set up with two VZ4000 trackers, Phoenix Technologies Inc., Canada). The motion-capture system tracks head movements in three dimensions using two sets of three horizontally aligned cameras (Figure 3-6a). As a built-in functionality of Eye-Trac 7, the eye tracker's data is coupled with the data from the motion-capture system to precisely estimate the point of gaze.

The integration of eye and head information as a built-in functionality of the eye tracker requires two sets of calibrations: (1) scene calibration and (2) eye calibration. The scene calibration was done to determine the orientation and position of a rigid body (head-mounted plate, Figure 3-6b) to a fixed calibration surface (stimulus computer screen). The head-tracker system reports the position and orientation of an imaginary coordinate system that is attached to the rigid body with respect to the global coordinate system. The procedure to conduct the scene calibration took approximately 15 minutes for each participant as it required changing the level of the computer desk intended for the experiments to be aligned with the elbow level of the participants and the computer screen being located approximately 15° below the ear-eye line (326). The stationary-scene camera and two motion trackers were located in appropriate places where the rigid body was clearly visible to the cameras and the stationary-scene camera could capture the stimuli displayed on the computer screen (Studies I, II, and III).

The eye calibration was done using nine numbered points. The participants were instructed to only move their eyes during the calibration and to look at the numbered points in chronological order. The eye movements and pupil diameter were recorded during the execution of the computer task (Studies I, II, and III).

A technical concern regarding the head-mounted eye trackers is parallax error (327), which occurs when a head-mounted eye tracker is calibrated with respect to the image from a head-mounted scene camera that is viewing the world from a different position than the eye. However, since we used the (EyeHead) integration feature[*], the gaze computation does not make use of the head-mounted scene camera, and the parallax issue does not apply (Studies I, II, and III). The (EyeHead) integration attempts to determine the position of the eye in 3-D space (with respect to a fixed local coordinate system) and the direction of the line of gaze with respect to the same local coordinate system. It then solves for the intersection of this line with a plane whose position is also known with respect to the same local coordinate system (in this case, the plane of the display screen).

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[*] EyeHead Integration Manual for use with Eye-Trac7 head mounted optics, version 1.1, April 2014, Applied Science Laboratories.

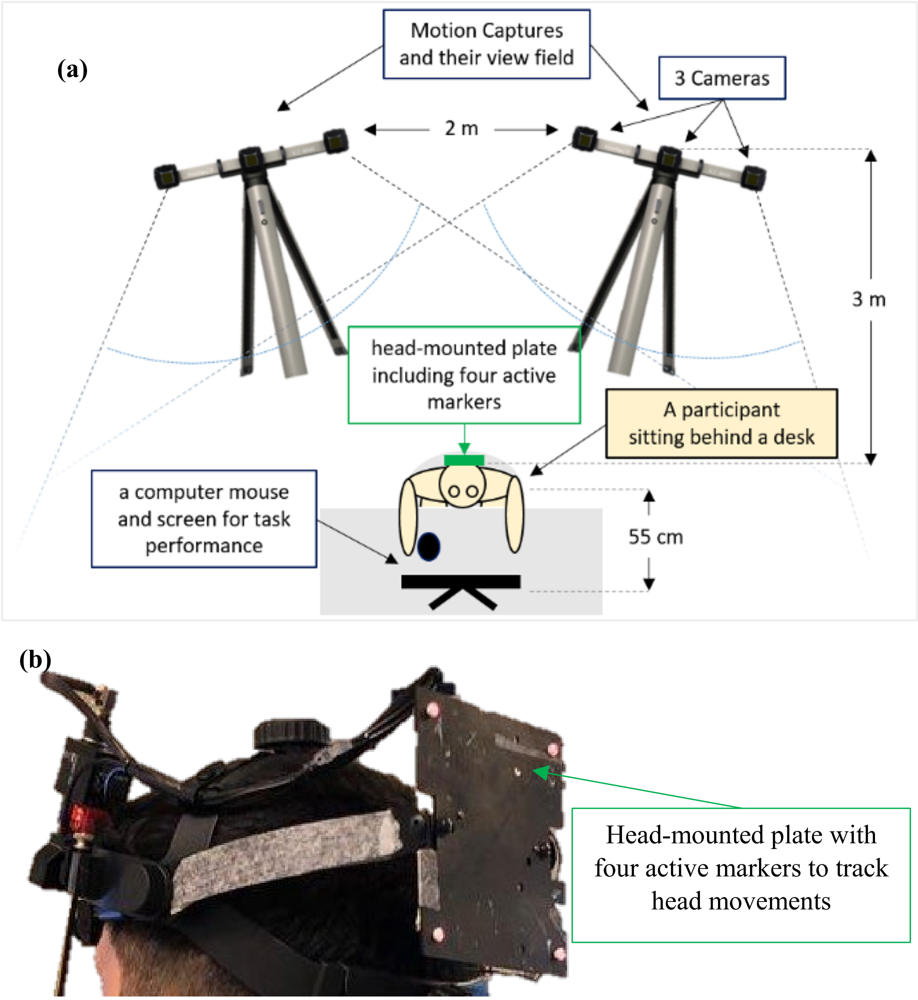

Figure 3-6. A schematic view of the experimental set-up of Studies I, II, and III with the location of motion trackers behind the participant to cover a wide area of head movements while performing the computer task (a) and a side view of the eye tracker on the head of a participant with a plate attached on the backside with four active markers (light-emitting diodes) to be detected by the cameras of the motion capture system (b). For the scene calibration, the plate is detached from the eye tracker and attached on a tripod with a laser pointer, and a standard procedure was performed according to the guideline of a built-in feature of the eye tracker[*].

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[*] EyeHead Integration Manual for use with Eye-Trac7 head mounted optics, version 1.1, April 2014, Applied Science Laboratories.

3.4. Oculometrics

A data-driven algorithm was used to extract ocular events (i.e., saccades, fixations, or blinks), from which the oculometrics (e.g., saccade peak velocity) were computed. The implemented algorithm based on (328) is outlined in Appendix B. Figure 3-7 is an example of how each ocular event may look in a sample of eye-tracking data (Studies I, II, and III).

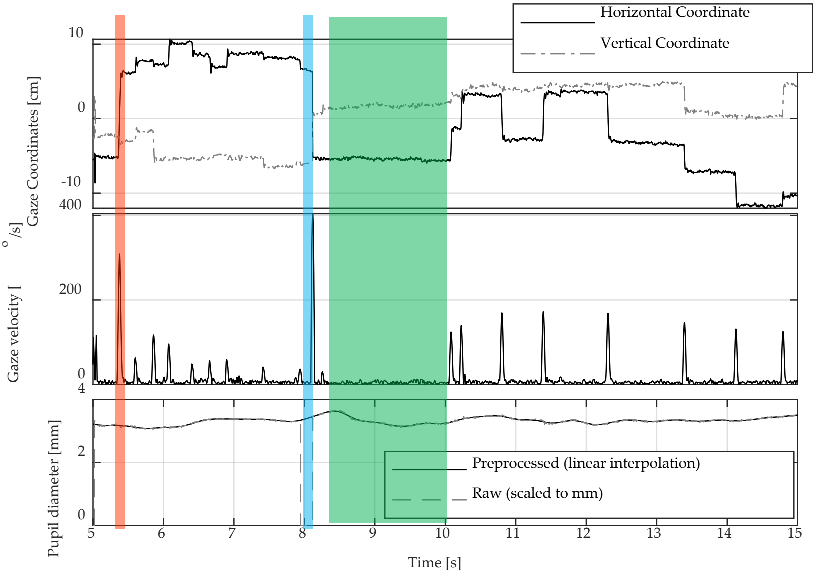


Figure 3-7. An example of a blink (blue shades), a fixation (green shades), and a saccade (red shades) during a cycle timeline of a participant while performing the computer task. Gaze length, scene number, and corneal reflection involved in the detection of the ocular events are not depicted for simplification (see Appendix B).

Table 3-3 provides the list of oculometrics investigated in Study I. The oculometrics outlined in Table 3-3 were computed due to the previous evidence in the literature linking the ocular events to mental load and fatigue (section 2.3.3). The calculations of the oculometrics are described in Study I. The oculometrics were computed for each cycle, and those values were averaged across cycles. The slope of the line regressing the saccade peak velocity to the amplitude of the saccades (SVA) was computed over the entire task timeline (approximately five minutes) as this required a bigger population of saccades than in only one cycle period (<12 s).

Table 3-3. The list of the oculometrics used in Study I, adapted from (21).

Event	Oculometrics	Definition
Saccade	SF	Saccade frequency
	SA	Saccade amplitude
	SCD	Saccade duration
	SPV	Saccade peak velocity
	SAAI	Saccade acceleration asymmetry index
	SCR	Saccade Curvature
	SVA	The slope of the line regressing the peak velocity and amplitude of saccades
Fixation	FD	Fixation duration
	FF	Fixation frequency
Blink	BF	Blink frequency
	BD	Blink duration
Pupillary responses	TPDL	Task-evoked pupillary peak dilation latency
	PSaEn	Sample entropy of pupillary response
	RRP	Recurrence rate of pupillary response
	DTP	Determinism of pupillary response
	RMEP	Recurrence map entropy of pupillary response
Gaze trajectory	MSaEn	Multivariate sample entropy of gaze trajectory
	RRG	Recurrence rate of gaze trajectory
	DTG	Determinism of gaze trajectory

Study II involved saccade peak velocity (SPV), saccade duration (SCD), and fixation duration (FD), which were shown to be sensitive to mental load and reliable in Study I. In addition, blink duration (BD) and blink frequency (BF) were also included in Study II as they were expected to reflect fatigue with time-on-task (35,156,329). Pupillary responses were quantified in Study II using the mean of pupil dilation range (PDR) across cycles as it was shown to consistently increase by increasing mental load (330).

Study III involved the oculometrics reflecting fatigue development in Study II. In addition, new oculometrics presumed to exhibit fatigue-related changes with time-on-task according to the evidence from the literature (10,166,186,216,231,331) were computed to investigate whether they improve fatigue detection using machine learning. To obtain a stable estimate of oculometrics, the whole timeline of a segment, consisting of 20 consecutive cycles, was considered for the calculation of the oculometrics (Study III).

3.5. Performance Metrics

The performance of the task was measured in terms of the speed and accuracy of the replication of the patterns. The performance was quantified as a metric called overall performance (OP), which included information regarding selective attention and reaction time (21). Selective attention refers to how successfully the participant distinguished the correct points from incorrect points and the distraction point. Reaction time refers to the time it took to click on the correct points. The gain of the computer mouse that specifies its speed was kept the same (1:12 denoting mouse movement relative to screen cursor movement) for all the experiments involved in the project. The graphical user interface reacted to correct clicks during the replication period if the Euclidean distance of the clicking point was less than 0.2 cm away from the correct point (Studies I, II, and III).

3.6. Subjective Metrics

Two subjective questionnaires were administered to assess fatigue perception (Studies II and III) and the workload of the tasks (Studies I, II, and III). A computerized version of the National Aeronautics and Space Administration Task Load Index (NASA-TLX) (332), a validated questionnaire to assess the workload of a task, was used to subjectively measure five subscales of workload: mental load, physical load, performance, frustration, and temporal load (333,334). The subscales were scored from 0 to 100 and were then compared one by one in terms of their contribution to the workload to obtain weighted NASA-TLX scores for each subscale and a total NASA-TLX score as the mean value of the weighted NASA-TLX scores.

Furthermore, the Karolinska sleepiness scale (KSS) (335), a validated scale to subjectively measure fatigue (336), was used to acquire subjective ratings of perceived fatigue on a Likert scale ranging from 1 to 9, corresponding to "very alert" and "very sleepy, fighting sleep," respectively. The perceived level of fatigue was further assessed, right before and after performing the task, on a visual analogue scale in response to the question "How much mental fatigue do you feel right now?" This score ranged from 0 to 10, for "feeling no fatigue" to "extremely fatigued," respectively.

Additionally, as mentioned in section 3.1 and Appendix A, a questionnaire was administered for screening the participants in relation to the history of mental and neurological disorders and symptoms of chronic fatigue and eye strain, as well as the consumption of any medication, drug, alcohol, and caffeine. The questionnaire was used to ensure whether the participants followed the experimental protocol and were accustomed to using their right hands to work with the computer mouse.

3.7. Study I: Mental load and the reliability of oculometrics

As mentioned, Study I was conceptualized to determine whether some oculometrics can reflect mental load and stay reliable over several days. As described in (21), two experimental sessions were conducted using the computer task, with three counterbalanced levels of mental load, with the procedure depicted in Figure 3-8. The experimental sessions were conducted either from 9:00 to 12:00 or 13:00 to 15:00 to minimize the potential influence of circadian variation (Studies I, II, and III). Circadian variations refer to the daily patterns of physiological changes leading to varied levels of sleepiness and alertness, among others, at each time of the day (337). The sequence of patterns was kept identical for all participants to avoid inter-individual variations due to different orders of patterns (Studies I, II, and III). The tasks were performed over two days at the same time of day separated by a week to assess the reliability of oculometrics (Study I).

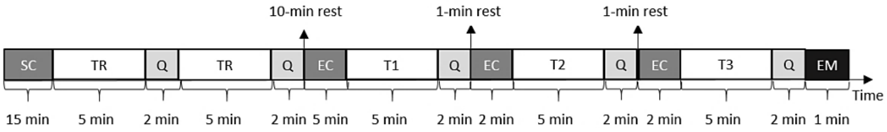


Figure 3-8. Experiment timeline in Study I. TR: training task in low and high load levels, Q: NASA-TLX questionnaire, EC: eye calibration of the point of gaze, T1–T3: three tasks with different load levels (low, medium, high) counterbalanced across participants, and EM: eye model measurement for pupil size conversion.

As seen in Figure 3-8, in the beginning of each session, the desk level and computer screen were adjusted for each participant followed by the scene calibration procedure. The tasks were performed beginning with low-load and high-load levels for training, each followed by NASA-TLX questionnaires to become familiar with the tasks and the types of questionnaires used. Three five-minute tasks with the three load levels were performed after a 10-minute rest break following the training tasks. The tasks were preceded by the eye calibration procedure and followed by the NASA-TLX questionnaires. At the end of the sessions, a short recording of the pupil size of the mechanical model of the eye was done to convert pupil diameter recordings of the participants from the unit of pixels to millimeters.

3.8. Study II: Fatigue detection via oculometrics

Study II was conducted to investigate the association between oculometrics and the development of fatigue in a long period of computer work requiring sustained attention. To this end, the computer task was conducted for approximately 40 minutes, consisting of 240 cycles and 12 KSS, as depicted in Figure 3-9. Every segment, consisting of 20 cycles, was followed by responding to the KSS. The computer task was executed in the medium level for the study of fatigue. The calibration procedure was also performed at the beginning of the experiment.

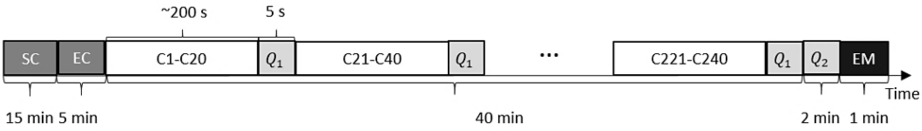
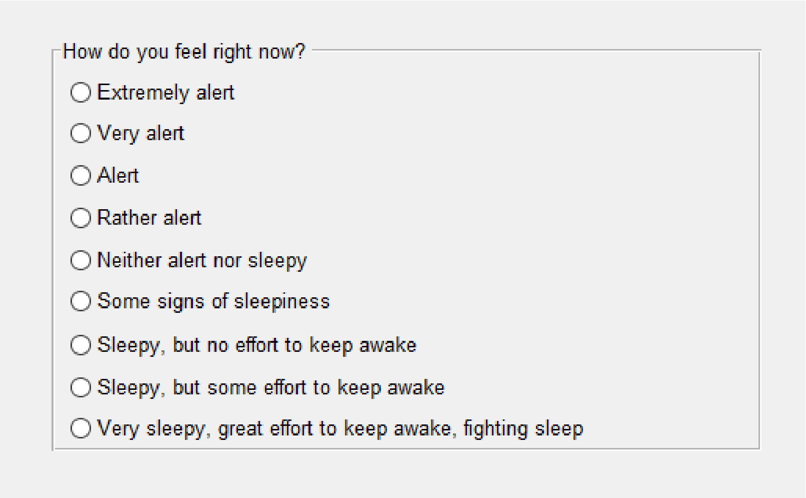


Figure 3-9. The timeline of the experiment to develop fatigue in Study II. C#: cycle number, SC: scene calibration, EC: eye calibration, Q_1: KSS – Karolinska sleepiness scale, Q_2: NASA-TLX questionnaire, and EM: eye model measurement.

Participants responded to the KSS on the graphical user interface by clicking on the item that best described their fatigue state at the end of each segment (Figure 3-10). The participants were instructed to answer the KSS in five-second periods and be ready to continue with the succeeding cycle with no rest pause. Volunteers in the second study were already familiar with the computer task since they participated in Study I as well.



How do you feel right now?

○ Extremely alert
○ Very alert
○ Alert
○ Rather alert
○ Neither alert nor sleepy
○ Some signs of sleepiness
○ Sleepy, but no effort to keep awake
○ Sleepy, but some effort to keep awake
○ Very sleepy, great effort to keep awake, fighting sleep

Figure 3-10. The KSS (Karolinska sleepiness scale) items as they appeared on the graphical user interface (Studies I and II).

A monetary reward of 100 Danish kroner was announced for the best performance to strengthen participants' motivation to continue to actively perform the task in Studies II and III. Furthermore, to provide social incentives, the participants were informed that their performance would be compared with those of other participants, and their performance was under observation of the experimenter. These motivators were based on the previous studies showing the effectiveness of monetary and social incentives in task engagement (70,71).

3.9. Study III: Intervention in the process of fatigue development

The findings from Studies I and II provided the steppingstone for Study III. The oculometrics that reflected the mental load and perceived fatigue were found in Studies I and II, respectively. In addition, the trend of fatigue development with time-on-task while performing computer tasks was elucidated in Study II. To accurately predict fatigue, further features were investigated in Study III in addition to the found oculometrics, including the age and sex of the participants.

The prediction of fatigue based on oculometrics can be treated as a statistical classification problem with the aim to identify whether a participant is fatigued according to the KSS scores. Thus, an intervention in the process of fatigue development was planned based on a statistical classification model to predict fatigue levels (classes) for the participants given relevant oculometrics (as quantitative features) in response to fatigue development in Study II. A predictive model of fatigue was developed based on the dataset collected in Study II. The model was a deployed classifier, which was trained with a set of selected oculometrics as inputs and the fatigue classes as outputs. The KSS scores were divided into fatigued and alert classes, with the fatigued class corresponding to the KSS scores of [5 10] (338,339). The model may, thus, indicate the current fatigue level and whether a participant was becoming fatigued assuming that fatigue develops with time-on-task. Fatigue prediction in this context implies the growing nature of fatigue with time-on-task (340,341). The parameters outlined in Table 3-4 were used to assess the classification of the fatigue.

Table 3-4. The parameters used to describe the classification performance of the predictive model of fatigue for each participant (Study III).

Classification Assessment Parameters		Description
Abbreviation	Description	
TP	True Positive	The detected class was fatigued where KSS≥5
TN	True Negative	The detected class was alert where KSS<5
P	Positive	Total number of segments where the detected class was fatigued
N	Negative	Total number of segments where detected class was alert
$TPR=\frac{TP}{P}$	True Positive Rate - Sensitivity	Total number of correctly detecting fatigue to the total number of times that the detected class was fatigued
$TNR=\frac{TN}{N}$	True Negative Rate - Specificity	Total number of correctly detecting alertness to the total number of times that the detected class was alert
$ACC=\frac{TP+TN}{P+N}$	Accuracy (Classification Performance)	Total number of correct classifications compared to the total number of classifications

As described in (22), a set of oculometrics including the saccade frequency (SF), the slope of the regression line of saccade peak velocity and amplitude (SVA), the blink frequency (BF), the pupil diameter interquartile range (PDIR), and the percentage of closed eyes (PERCLOS) were selected in a sequential floating forward feature selection (342). The age and sex were not selected using the feature selection scheme, indicating no substantial improvement in the classification performance using these two features. The predictive model of fatigue was developed using leave-one-person-out cross validation. Furthermore, an ensemble of decision trees (DT ensemble) was chosen to be deployed in the real-time detection of fatigue in Study III, based on its higher classification performance compared to the other candidate classification models (Figure 3-11). An overall view of the processes to develop the DT ensemble model and deploy it in an oculometrics-based biofeedback system is depicted in Figure 3-11.

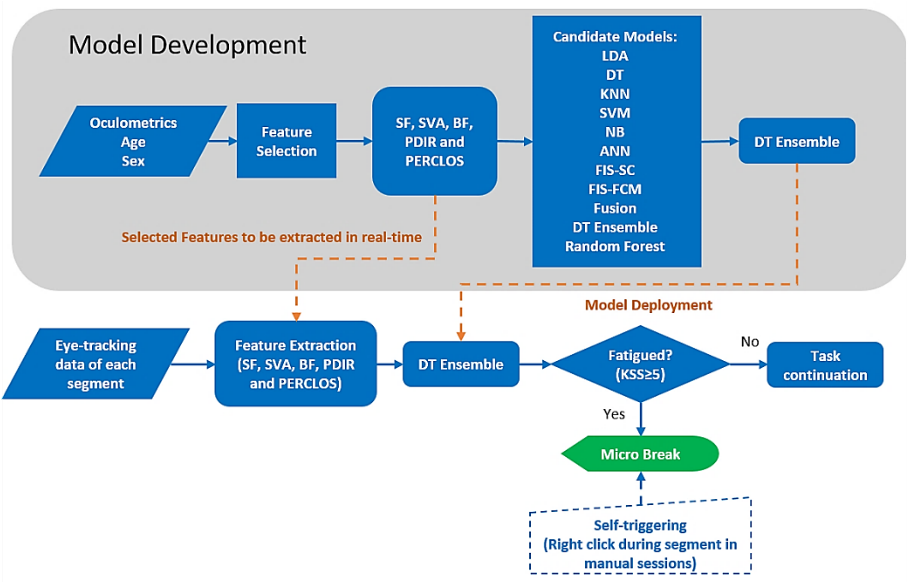


Figure 3-11. The flowchart of the development and deployment of the predictive model of fatigue in the oculometrics-based biofeedback system (Study III). SF: saccade frequency, SVA: The slope of the line regressing saccade peak velocity on saccade amplitude, BF: blink frequency, PDIR: pupil diameter interquartile range, PERCLOS: percentage of closed eyes, LDA: linear discriminant analysis, DT: decision tree, kNN: k nearest neighbors, ANN: artificial neural networks, FIS-SC: fuzzy inference system (subtractive clustering), FIS-FCM: fuzzy inference system (fuzzy C-means clustering), and KSS: Karolinska sleepiness scale (adapted from (22)).

Study III involved two counterbalanced experimental sessions (a manual and an automatic session) with similar task configuration to Study II, as illustrated in Figure 3-12. As demonstrated in Figure 3-11, in automatic sessions, the biofeedback system was enabled to alert the participants about their fatigue state. The fatigue state was determined at the end of each segment using the selected oculometrics computed over a segment. The oculometrics were fed into the DT ensemble. This triggered a micro-break for

25 seconds if the output of the model was the fatigued class; otherwise, the task was continued. In the manual session (as a control task), the micro-break was triggered at the participant's discretion by a right click using the computer mouse (Figure 3-11).

During the micro-breaks, the participants were instructed to rotate their shoulders with an elastic band while the elbows were bent approximately 90° in the seated condition, in which the shoulders were abducted horizontally up to 45°. This exercise was chosen due to potential benefits of active pauses (343) and considering the limited mobility and movability of the participant due to the experimental setting. Moreover, the seated exercise was accompanied by mindful breathing (344,345). The breathing rate was at the participant's discretion as it may vary between individuals (346). The graphical user interface displayed a message, "A short break, the task continues in [RemT] seconds," where the RemT was of the 25-second micro-break updated every second on a green background, as the color green has been shown to have restorative effects on attention and cognition (347,348). In addition, active pauses (349) and mindful breathing may improve oxygenation and counteract fatigue and stress (350,351), especially during computer work (352).

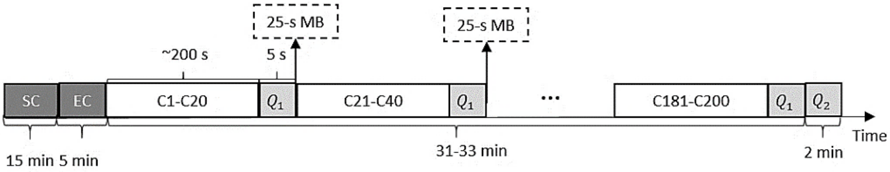


Figure 3-12. The timeline of the experiment in Study III. C#: cycle number, SC: scene calibration, EC: eye calibration, Q_1: KSS—Karolinska sleepiness scale, Q_2: NASA-TLX questionnaire, and MB: micro-break.

3.10. Statistical analysis

All three studies involved common statistical analysis. Each outcome measure, including oculometrics, subjective ratings, and performance metrics, was assessed for normality using Kolmogorov–Smirnov and Shapiro–Wilk tests. A repeated-measures analysis of variance (RM-ANOVA) was used to examine the effects of the three levels of mental load as the within-subject factor and the age groups (young and elderly) as the between-subject factor in Study I. A Greenhouse–Geisser correction was applied if the assumption of sphericity was not met. In addition, a Bonferroni adjustment was performed in multiple comparisons. The relative and absolute reliability of the oculometrics were assessed using two-way mixed single measures intraclass correlation coefficient ICC (3,1), absolute agreement (353), and the limits of agreement (LoA) accompanied by Bland-Altman plots. The values of $LoA\% = 100 \times (1.96 \times SD(diff)/grandmean)$ for 95% of the confidence interval (CI) as defined in (354), being limited to [-30 30], were interpreted as acceptable reliability (355). Finally, the values of the ICC, being above 0.75 and 0.40, were interpreted as excellent and good reliability, respectively (356).

Study II involved utilizing the RM-ANOVA followed by the pairwise comparisons, in which the within-subject factor was time-on-task (segments). In addition, the mediating effect of the performance on fatigue development was tested by adding the performance as the covariate to the statistical model.

In Study III, statistical classification was used to develop the predictive model of fatigue. The RM-ANOVA was also used to investigate the association of the oculometrics, performance, and KSS scores in the presence of micro-breaks and to see whether there was a difference or interaction in the outcome measures between the automatic and manual sessions. The perceived workload was also compared between the manual and automatic sessions using paired t-test with the effect size reported in terms of Cohen's d_z (357). The interaction effects of the time of day between the sessions held in the morning (9:00–12:00) and afternoon (13:00–15:00) were also evaluated on the classification performance (ACC) to assess the robustness of the predictive model against the circadian variations.

Chapter 4. Results

This chapter presents a summary of the main results found in the studies. Detailed descriptions are provided in Study I (21), Study II (8), and Study III (22).

4.1. Study I: Mental load and the reliability of oculometrics

Table 4-1 provides an overview of the oculometrics that were sensitive to mental load, including their direction of change for the young and elderly groups. For example, the sample entropy of the pupillary response time series (PSaEn) decreased in the elderly group but did not change significantly in the young group. Among the oculometrics that were sensitive to different levels of mental load, saccade peak velocity (SPV), slope of the line regressing the peak velocity and amplitude of saccades (SVA), fixation duration (FD), and saccade duration (SCD) were reliable in that the intraclass correlation was >0.40 and the LoA% was limited to [-30 30] in both the young and elderly participants and in the three load levels.

Table 4-1. The sensitivity of the oculometrics in response to increasing mental load levels indicated by an upward arrow as increase and a downward arrow as decrease and the reliability of the sensitive oculometrics to mental load in terms of ICC, adapted from (21). ICC>0.75, ICC>0.40, and ICC≤0.40 (or LoA% exceeding [-30 30]) indicate excellent, good, and poor reliability, respectively.

Event	Oculometrics	Sensitivity	Reliability	Sensitivity	Reliability
		Young group		Elderly group	
Saccades	SF (Hz)	↓	Poor	↓	Poor
	SA (°)	↓	NA	-	NA
	SCD (ms)	↓	Good	-	Excellent
	SPV (°s^{-1})	↓	Good	↓	Good
	SAAI (a.u.)	-	Poor	↓	Poor
	SCR (°)	-	NA	-	NA
	SVA (s^{-1})	↓	Good	↓	Good
Fixations	FD (s)	↑	Good	↑	Good
	FF (Hz)	↓	Poor	↓	Poor
Blinks	BF (Hz)	-	NA	-	NA
	BD (s)	-	NA	-	NA
Pupillary Responses	TPDL (s)	↑	Poor	↑	Poor
	PSaEn (a.u.)	↓	Poor	↓	Poor

	RRP (%)	-	NA	-	NA
	DTP (%)	-	NA	-	NA
	RMEP (bit)	↑	Poor	-	Good
Gaze Trajectory	MSaEn (a.u.)	-	NA	↓	NA
	RRG (%)	↑	Poor	↑	Poor
	DTG (%)	-	NA	-	NA

SF: saccade frequency, SA: saccade amplitude, SCD: saccade duration, SPV: saccade peak velocity, SAAI: saccade acceleration asymmetry index, SCR: saccade curvature, SVA: The slope of the line regressing the peak velocity and amplitude of saccades (main sequence), FD: fixation duration, FF: fixation frequency, BF: blink frequency, BD: blink duration, TPDL: task-evoked pupillary peak dilation latency, PSaEn: sample entropy of pupillary responses, RRP: recurrence rate of pupillary response, DTP: determinism of pupillary response, RMEP: recurrence map entropy of pupillary response, MSaEn: multivariate sample entropy of gaze trajectory, RRG: recurrence rate of gaze trajectory, and DTG: determinism of gaze trajectory, LoA: limits of agreement, ICC: intraclass correlation coefficient.

The manipulation in the task demands from the low to high level was in accordance with the significant increase in the NASA-TLX scores. The increased perceived mental load was also accompanied by a decrease in the overall performance (OP) in the young and elderly groups (Appendix A).

Study I also provides an insight to the reliability of the oculometrics that changed significantly with the task levels. Among the nonlinear metrics, recurrence rate of gaze trajectory and sample entropy of pupillary responses reflected perceived mental load in both the young and elderly groups in Study I. The reliability of these nonlinear metrics was, however, poor in some of the load levels or groups, leading to the exclusion of these oculometrics from Study II.

Study I was conducted to examine the sensitivity of oculometrics to mental load and to assess their reliability. However, this does not reveal the temporal changes of oculometrics in a prolonged session and whether these temporal changes are associated with fatigue. Study II was conducted based on the results from Study I, in which saccade peak velocity and duration, fixation duration, and slope of the line regressing saccade peak velocity and amplitude were found reliable. Previous studies also supported the reliability of the blink frequency, blink duration, and pupil dilation range (35,156,329,330). Thus, these oculometrics were used in Study II to investigate whether they reflect fatigue in 40-minute time-on-task.

4.2. Study II: Fatigue detection via oculometrics

The development of fatigue was reflected in decreased saccade duration and peak velocity, as well as increased pupil dilation range, blink duration and frequency, and fixation duration with time-on-task in both young and elderly groups (8). However, no significant interaction was found between the age and the time-on-task in any of the oculometrics. The development of fatigue was validated in the KSS scores, which increased significantly with time-on-task in both groups. The OP was shown to have no monotonous trend with time-on-task in the young group but exhibited an increasing trend in the elderly group. In addition, no mediation effect of the OP on the KSS scores was found (Study II).

Study II showed that fatigue can be reflected in saccade duration and peak velocity, fixation duration, peak dilation range and, blink duration and frequency. The slope of the line regressing saccade peak velocity and amplitude did not exhibit a monotonic relationship with time-on-task and thus was excluded from Study II which was based on a general linear model. It was also not clear whether these oculometrics could explain individual differences in the patterns of fatigue in the KSS scores. To do this, as described in section 3.9, classification models were needed in Study III to further investigate the possible complex relationships between the oculometrics and the subjective scores for fatigue on the KSS. After finding the best features to explain fatigue development, the possibility of counteracting fatigue via biofeedback and micro breaks was examined in Study III.

4.3. Study III: Intervention in the process of fatigue development

As described in (22), the ensemble of decision trees predicted fatigue development with the approximate (classification) accuracy of 70%, the sensitivity of 60%, and the specificity of 74% on average in the automatic sessions, and the accuracy was not significantly affected by the time of day. The overall performance (OP) and KSS scores significantly increased with time-on-task, but the increase in KSS occurred in the later segments in the automatic sessions compared with the manual sessions. The development of fatigue was also reflected in the oculometrics, where the saccade frequency decreased, the percentage of closed eyes (PERCLOS) increased, and the blink frequency tended to increase with time-on-task in both the manual and automatic sessions. The perceived workload as indicated by the NASA-TLX scores was significantly lower in the automatic sessions compared to the manual sessions, while the number of applied micro-breaks was not significantly different between the manual and automatic sessions.

As reported in (22), a set of oculometrics, including slope of the line regressing peak velocity and amplitude of saccades (SVA), saccade frequency, blink frequency, PERCLOS, and the pupil dilation interquartile range (PDIR) were used in the classification of fatigue. As explained in section C.3, the oculometrics were reliable in response to fatigue-related changes. The repeated-measures analysis of variance revealed that saccade frequency, blink frequency, and PERCLOS followed increasing trends with time-on-task, while SVA and PDIR did not change monotonically with time-on-task. No significant difference between the sessions was found in any of the oculometrics. In addition, no significant interaction between the sessions and time-on-task was found in any of the oculometrics (Study III).

Inter-individual differences in the OP along with the presence and absence of the micro-breaks following each segment for the manual and automatic sessions are depicted in Figure 4-1 (a) and (b), respectively. According to Figure 4-1, there were six participants who decided not to have any micro-break during the task in the manual sessions, whereas in the automatic sessions, three participants received no micro-breaks. On the individual level, the participants in general exhibited a non-monotonic pattern of performance with time-on-task.

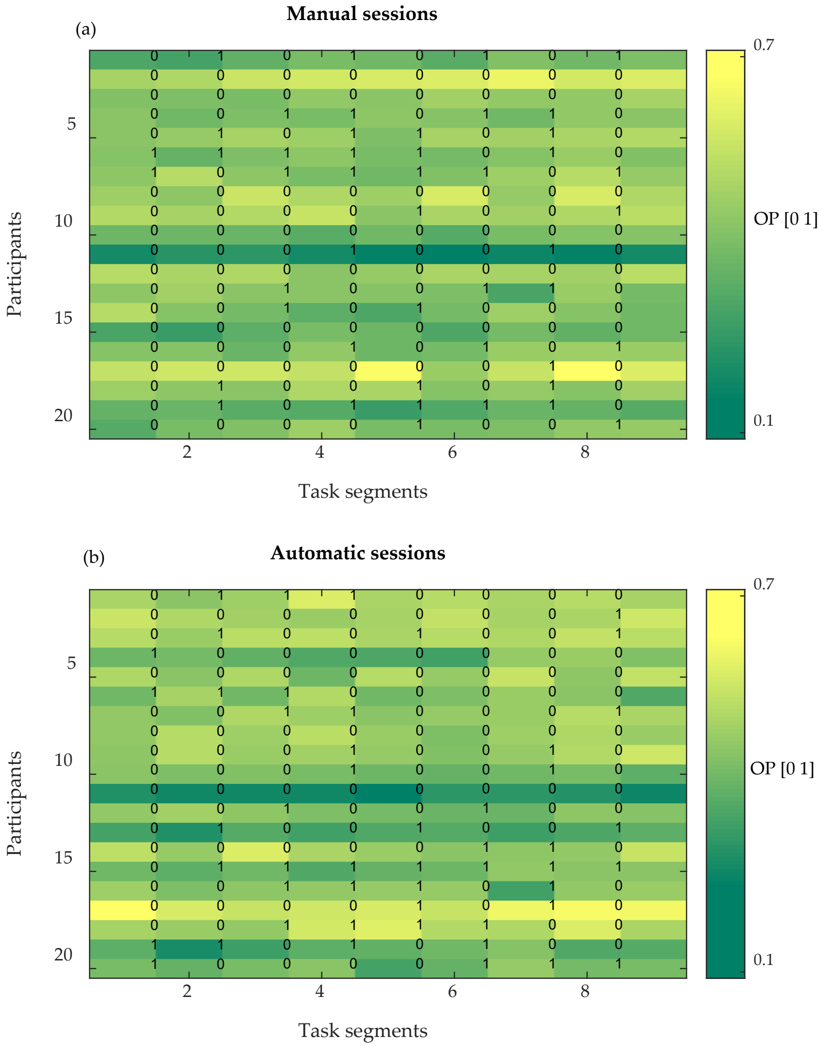


Figure 4-1 The overall performance (OP) of the participants (not sorted by sex) in the manual (a) and automatic (b) sessions through segments and the presence (1) and absence (0) of micro-breaks between the segments. The OP ranges from 0 to 1, indicating low to high performance, respectively. (adapted from (22))

4.4. Summary of the main results

The three presented studies are interconnected and informative in relation to one another (Figure 4-2). In brief, Study I showed the potential of oculometrics to reliably exhibit changes related to mental load. The reliable oculometrics were assumed to exhibit fatigue-related changes because fatigue could develop with prolonged exposure to mental load. In Study II, a number of potentially reliable oculometrics were assessed using a general linear model to see whether they have a monotonic relationship with time-on-task and to what extent this aligns with the perceived fatigue and task performance. Study II was conducted to better understand the relationship among oculometrics, perceived fatigue, and performance along with time-on-task. In addition, it was of interest to identify the oculometrics that were more robust to age-related changes because this could facilitate the development of a statistical model based on oculometrics to detect fatigue. It could also help to identify behavioral indicators of fatigue from performance and whether the subjective ratings could be associated with such metrics. Study III was conducted, firstly, to find the set of oculometrics that could, in combination with each other, partly explain the fatigue-related changes using statistical classification and, secondly, to implement a classification model based on relevant oculometrics.

Study I

- A novel task was developed to resemble computer work that was found mentally and temporally demanding with significantly different performance between three levels of task loads.
- SF, SPV, SVA, FD, FF, and TPDL reflected different load levels in both young and elderly participants.
- The significant change in the load level (in SCD and SA and SAAI and PSaEn) was found in the young and elderly groups, respectively.

Study II

- Among the oculometrics reflecting the load levels, SPV, FD, and SCD satisfying the reliability criteria that the ICC>0.40 and **LoA% being limited to [-30 30]** for all task levels in both groups investigated in Study II.
- BD, BF, and PDR were also included due to their reliable responses associated with fatigue and mental load from previous studies.
- Performing the task for 40 minutes was alinged with significant increase in perceived fatigue.
- Performance did not decrease with the time-on-task.
- The oculometrics significantly changed with time-on-task in both groups, implying that the oculometrics may be useful to detect fatigue in Study III.
- Age-related changes were found in the FD, SCD, and performance.

Study III

- Studies I and II gave insights into the oculometrics that could reflect fatigue or mental load, or both, in young or elderly individuals, or both.
- A group of oculometrics was investigated to find a set of oculometrics to best explain fatigue on the individual level using machine learning.
- BF, PERCLOS, SVA, SF, and PDIR were seleccted using a feature selection scheme (sequential forward feature selection).
- The selected oculometrics were beneficial to detect fatigue using a classification model (ensemble of decision trees) both on the dataset collected from Study II and the real-time application in Study III.

Figure 4-2 An overview of the results and the connections among the three studies. SF: saccade frequency, SPV: saccade peak velocity, SVA: the slope of the line regressing saccade peak velocity and amplitude, FD: fixation duration, FF: fixation frequency, TPDL: task-evoked pupil dilation latency, SCD: saccade duration, SA: saccade amplitude, SAAI: saccade acceleration asymmetry index, PSaEn: sample entropy of pupillary responses, BD: blink duration, BF: blink frequency, PDR: pupil dilation range, PERCLOS: percentage of closed eyes, PDIR: pupil dilation interquartile range, and ICC: intraclass correlation.

Chapter 5. Discussion

The aim of this PhD project was to investigate the quantification of mental load and fatigue in computer work via oculometrics considering potential age-related changes. Study I was directed toward finding the oculometrics reflecting mental load during a standardized model of computer work in young and elderly individuals. Furthermore, the relative and absolute reliabilities of the oculometrics were examined using the intraclass correlation (ICC), the limits of agreement (LoA), and Bland-Altman plots. Study II focused on the effect of fatigue development on oculometrics using a prolonged version of the computer task. Based on the findings from the first two studies, Study III was conducted to develop a biofeedback system based on the oculometrics to reinstate alertness using mindful active pauses. The results are discussed thoroughly in the articles in connection with the three studies overviewed here (Studies I, II, and III).

5.1. Study I: Mental load and the reliability of oculometrics

In Study I, the mental load induced by the manipulations in the task properties was in concordance with the performance and subjective metrics of the workload. As hypothesized, the mental load was further reflected in saccades, fixations, pupillary responses, and nonlinear dynamics of the gaze trajectory. Among the oculometrics, saccade peak velocity (SPV), slope of the saccadic main sequence (SVA), and fixation duration (FD) were sensitive to mental load, induced by the task demands in each level, in both the young and elderly groups, and the effect remained consistent across days. The SPV and SVA decreased, while FD increased as the level of mental load increased in the computer task, in agreement with previous findings (180). With the increased number of points, more visual attention might be required to perform the task, and since visual information can be obtained during fixations (358), longer duration of fixation could be expected. With the increased geometric complexity of the patterns, it is likely that the participants might prefer to scan the key points and overall path of the patterns rather than performing a detailed scanning of all points. This change is partially supported by the decreased number of saccades and fixations, as well as the decreased performance with the task levels. The decreased SPV and SVA are somewhat explainable by different levels of uncertainty in initiation of motor commands originating from the involved geometric complexities of the task, supporting the effect of parameter uncertainty (359).

Furthermore, no substantial difference was found in the reliability of the oculometrics based on the qualitative (Bland-Altman plots) and quantitative (ICC and LoA) measures between the young and elderly groups and among the three levels of mental load (21). This implies that the oculometrics exhibited similar reliability across the two age groups and the load levels. The definition used to interpret the reliability as poor, good, and excellent has also been previously used in the reliability assessment of oculometrics in clinical studies (360–362). More conservative interpretations are also used in the literature, for example, fair reliability for the ICC of [0.40 0.60) (363). Intraclass correlation is a proper statistical method to assess the test-retest reliability compared with correlations (e.g., Pearson), which considers between-subject variance and fails to measure within-subject variance. This means if there is a systematic difference between the sessions in a metric, the ICC may reveal the difference but not the correlation analysis (360).

Previous studies have assessed the reliability of oculometrics in rather strict and conservative experimental settings (360,364,365). For example, most of these studies used head stabilization (e.g., head and chin rest) while recording eye movement, which may provide a higher level of reliability than when head movements are allowed as they may add more computational and physiological complexities in the execution of the eye movements (e.g., the presence of torsional eye movements). It was addressed in Study I by the reliability assessment of various oculometrics in a task with unconstrained head movements and the execution of a wide range of eye movements (e.g., scanning saccades in different sizes and directions). By contrast, the tasks in the previous studies usually allow specific eye movements (such as anti-saccade: saccade executions in opposite directions of fixation targets). On the one hand, it is beneficial to use such standardized tasks for clinical assessments to diagnose abnormalities such as Parkinson’s disease, but on the other hand, it may limit the generalizability of the results of these studies to occupational applications. Such studies were also designed to minimize possible effects of alterations in the motivation, alertness, and similar state fluctuations on the reliability of oculometrics (364). According to the observations in Study I, different levels of the perceived mental load did not appear to have systematic influence on the reliability of oculometrics.

Previous studies have also highlighted the impact of age on the reliability of oculometrics (364–368). For instance, in two sessions, with a week apart on average, 20 heathy adults and 14 participants with Parkinson's disease (both groups aged >50 years) made horizontal and vertical saccades with the sizes of 5°, 10°, and 15° in three conditions: sitting with a chin rest, standing with self-restricted head movements, and walking on a treadmill (367). The saccades were reported to be highly consistent across sessions except for horizontal saccades in 15° of amplitude during walking. In comparison, test-retest reliability of saccade latency has been found acceptable in 65 participants with Parkinson's disease (aged 66±8 years) using the sampling resolution of 250 Hz[*] (366). Long saccades, as appeared in (365), and the use of a mobile eye tracker[†] with the low sampling frequency of 50 Hz (compared to 360 Hz in Studies I, II, and III) might have contributed to their observation of poor reliability. However, saccades longer than 15° were not present in Study I, and such long saccades may not occur frequently, especially during computer work, based on normal gaze patterns (369,370).

Furthermore, oculometrics in pro-saccade, anti-saccade, and smooth pursuit tasks were mostly reliable[‡] in 105 participants (aged 16–39 years) with approximately 19-day intersession interval (368). Similarly, saccade latency and main sequence have been found highly reliable (368), as well as latency, gain, and frequency of saccades (360)[§] in a pro-saccade task. Similar results have been evidenced in 327 participants aged 9–88 years with good to excellent scores in most of the saccadic metrics, including the saccade reaction time (ICC>0.40) in pro-saccade and anti-saccade tasks with a binocular eye tracker[**](364), which was further supported by similar findings (371,372). In a reading task with head stabilization[††] on 298 participants (aged 18–46 years),

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[*] Video-based eye tracker EyeLink-II (SR Research, Ottawa, Canada)

[†] Dikablis (Ergoneers GmbH, Germany)

[‡] using a head-mounted eye tracker: JAZZ-novo (Ober Consulting, Poznan, Poland) – sampling frequency: 1000 Hz

[§] IRIS model 6500; Skalar Medical BV, Delft, The Netherlands – sampling frequency: 500 Hz

[**] IRIS, Skalar; Delft, Netherlands

[††] The eye tracker used in the study: EyeLink 1000 with a sampling rate of 1000 Hz in monocular mode (left eye)

the test-retest reliability of 101 oculometrics was analyzed between two sessions (30 minutes apart) (363). Many oculometrics have been found highly reliable, including the frequency and duration of fixations and saccades, as well as saccade peak velocity and main sequence (363). In agreement with the results obtained in Study I, these findings support the reliability of the oculometrics concerning age-related changes.

Other factors, including the time of day (373) and participants' sex (365) (374) have not reported to make significant difference in the reliability of oculometrics including saccade peak velocity. Visual aids (glasses and contact lenses) may reduce the test-retest reliability (367), likely related to the artifacts caused by incorrect reflections from the lens or glasses. A similar issue is valid for eye makeup that may impair the video-based eye tracking, which was controlled in Studies I, II, and III. Thus, it appears that most of these studies have confirmatory results to support the reliability of the oculometrics in standardized tasks.

Study I is among the few studies to report the reliability of oculometrics for applying them as valid indicators of fatigue or mental load. The task used in Study I may have practical implications for computer-aided design, where the designer may use a computer mouse (or similar devices) to make repetitive movements (315). Furthermore, the oculometrics were shown to be useful to quantify mental load in Study I, as opposed to using electromyography of upper trapezius in a similar task of connecting points using a computer mouse to reflect task demands (315). To proceed with Study II, it was assumed that the reliability of the oculometrics might not reduce with time-on-task. This was partially supported by the reliability of the oculometrics in different load levels and previous findings on sustained visual tasks (375).

5.2. Study II: Fatigue detection via oculometrics

According to the results from Study II, saccades, fixations, blinks, and pupillary responses changed significantly with time-on-task in the young and elderly groups. The saccade peak velocity (SPV) and saccade duration (SCD) monotonously decreased, while blink frequency (BF), blink duration (BD), and pupil dilation range (PDR) increased with time-on-task. The fixation duration (FD) increased with time-on-task as well, however, with a fluctuating trend. The duration of fixations and saccades were higher and lower, respectively, in the elderly group than the young group. Since the efficacy of visual search has been reported to decrease with age (376), longer fixations in the elderly group was conceivable. In addition, head movements during gaze shifts have been reported to significantly increase with age (377), which may explain the difference in saccade duration between the different age groups. The nonsignificant interaction effect between the age and the time-on-task indicates that the results did not provide any evidence that age significantly contributes to the changes of the oculometrics with time-on-task. Neither was the effect of age modified by time-on-task, as the extent and direction of change in oculometrics with time-on-task were similar in both groups. Elderly individuals may have decreased capacity in bottom-up processing compared with young adults, and this difference could appear with nonsignificant age-related interaction with time-on-task (378). Finally, the results supported the hypothesis that the oculometrics reflected fatigue development (Study II).

Fatigue development was verified by the significant rise in the KSS scores with time-on-task. The performance fluctuated in the young and increased in the elderly group with time-on-task. This likely occurred due to a combination of motivation and learning effects. Learning the task might have taken longer for the elderly group. Such a pattern in performance was seen in the two-back task as opposed to decreasing performance in the zero-back task (379). Thus, it has been suggested that motivation may mediate performance in cognitively challenging tasks but not very much in mundane tasks (380).

Another explanation is that a compensatory mechanism might be involved to maintain cognitive capacity (88,381). This mechanism may be exhibited in the difference between young and elderly individuals in the loss of motivation and the depletion or reallocation of cognitive resources with time-on-task (382,383). For example, error rate has been found to increase with time-on-task in young individuals, whereas it followed a decreasing trend with time-on-task in the elderly individuals in a Stroop task (383). A compensatory mechanism was reported in elderly individuals whereby increased performance is sometimes associated with a shift in neural activity from the occipital lobe to the frontal lobe, leading to increased activation in frontal areas and decreased activation in occipital areas (384). Similar results have been reported in a typing task wherein a young group (aged 18–30 years) exhibited decreasing performance with time-on-task, while the elderly group (aged 50–70 years) exhibited a rather stable performance with time-on-task. This was partly related to an error-aversive strategy in the elderly individuals compared to the young individuals, who may tend to put more effort into speeding up the task performance and less on the typing accuracy (385). These findings may also partly explain the differences in the patterns of fatigue development, especially between young and elderly individuals.

The significant difference between the age groups in Studies I and II may support the concept of declined cognitive functioning (386) and motor control efficacy with age (283,387), especially in computer work (388). The performance did not change linearly with time-on-task, which further supports the existence of a complex relationship between performance and fatigue that may involve compensatory neural activities (88). This is in accordance with the studies wherein fatigue was reflected in the subjective ratings but not in the performance of the participants (13).

The findings from Studies I and II are in agreement with a great body of research concerning how different oculometrics reflect fatigue or mental load. Many factors may, however, contribute to different observations in the literature observed in the literature review, as discussed in (8,21). Discrepancies between findings may be associated with different task demands and cognitive processes leading to varied modulation of oculometrics. Furthermore, different measurement techniques or the computational algorithms in eye tracking can influence the results (389,390). These issues are briefly discussed below.

Current findings in relation to blinks underline both visual demands (i.e., the amount of visual information to perceive, attributable to the extraneous cognitive load) and fatigue. In agreement with (164), there is a nonsignificant change of blinks with the task levels in Study I. However, in contrast to the significant increase in blink duration and frequency with time-on-task reported in Study II, the aforementioned study did not report a significant increase with time (164). The absence of visual exploration to perform the task in (164), as opposed to the task presented in this project, may provide an explanation for this difference as visual demands seem to be a key component in influencing blinks. For example, a visually demanding flight task in (165) was displayed on a large screen spanning 60°×45° (> 2 × the display size in our studies), which makes it even more demanding to explore. Moreover, a review by (35) suggests that the mental load imposed by a high level of attention decreases both blink duration and blink frequency. Taken together, if a task requires high levels of visual demands, the participants may tend to have short and infrequent blinks; this behavior, however, may not last for a long period when fatigue develops (93).

Concerning the results in Study II, there might be an initial decrease in the blink duration and frequency due to the visual demands of the task (e.g., to distinguish points of the patterns); as the time-on-task extended, these blink metrics increased due to participants' gradual adaptations to the task and the development of fatigue. This behavior can also be explained by gradual loss of blink inhibition due to fatigue development, leading to an increased number of blinks (391). Increased blink frequency has further been documented in relation to decreased arousal (392) and vigilance (166). In line with the observations in Study II, age has not been shown to significantly affect the frequency of blinks (393,394).

Fatigue in association with attentional effort may have possible impact on the neural excitations in connections between the frontal cortex and the reticular formation in the brainstem, which may modify the relationship between saccade amplitude and peak velocity (13). Performing the task requires fast, successive decisions to execute saccades to relevant areas to identify and locate the points. This process may involve cognitive processing to choose between competing visual targets (395). Over time, this cognitive ability may decline, leading to more conservative saccades with decreased peak velocity, as observed in Studies I and II are in line with (155,184,396). Such reduction in peak velocity may also decrease saccade duration following the saccade main sequence (397). In addition, the peak velocity of saccades sometimes may not follow the linear relationship between saccade duration and peak velocity, for example, performing a task with varying difficulty over time (155).

As opposed to blinks and saccades, the findings on fixations and pupillary responses are still limited concerning fatigue and mental load. The increase of pupil dilation with mental demands has been reported in (398–400), likely due to the limitations of the working memory. For instance, a heuristic classifier based on pupil dilations has been found viable to classify the mental load imposed by three levels of the n-back task (400). The fluctuations of pupil dilations with time-on-task in Study II could also highlight the role of the dopaminergic system in ongoing cost and reward processing in connection with the locus coeruleus norepinephrine system (216,401). Parts of the change in pupil dilations could be related to varied uncertainty where the number of competitive choices differs from one task level to another (402).

Similarly, increased fixation duration on viewing medical images has been reported to reflect fatigue as a result of nightshifts (403). Fixation duration has been shown to increase in response to fatigue due to the circadian rhythms but not with time-on-task in free visual exploration of nature pictures (229). Conversely, saccade velocity has been reported to decrease with time-on-task but not with the circadian rhythms (229). It has been suggested that the fatigue induced by time-on-task may affect omnipause neurons and thereby the velocity of saccades (392), while the anterior cingulate cortex and dorsolateral prefrontal cortex might have been responsible for the changes in (404). The increase in fixation duration with time-on-task for both young and elderly groups was evident in the fixations with the duration of 150-900 ms which has been suggested to capture the fixations relevant to cognitive processing (391).

A collective and convergent view on Studies I and II indicates that the oculometrics exhibited similar behavior in response to fatigue development and increased mental load, which implies that the two phenomena may share similar neural mechanisms. This parallels the simultaneous changes in the oculometrics with fatigue, which followed similar patterns in the young and elderly groups. These co-occurrences could be traced back to the shared neural systems involved in the modulation of eye movements (176,405). One such system is the corollary discharge (efferent copy), a theory claiming that the copies of initial motor commands to muscle fibers, including ocular muscles, are also delivered to different cortical areas to integrate sensory and motor information. This theory has been demonstrated to be involved in the control of consecutive saccades (406,407). Based on previous findings linking oculometrics and cognitive processing (209,408,409), the cortical areas dealing with fatigue and mental load could possibly have similar modulation effects on eye movements. Furthermore, the cerebellum, which regulates eye movements (410), may also be influenced by fatigue and mental load

(411,412). In addition to these possibilities, future research may need to elaborate on the role of neurotransmitters, e.g. dopaminergic system (93,413), to reveal the similarities between mental load and fatigue.

5.3. Study III: Intervention in the process of fatigue development

The results from Study III support the hypothesis that favored the effectiveness of the biofeedback framework over self-triggering of micro-breaks to counteract fatigue. Indeed, it has been shown that the oculometrics-based biofeedback resulted in delayed fatigue and reduced perceived workload. This improvement implies that the oculometrics-based biofeedback may enhance the timing plan of micro-breaks.

The classification accuracy (ACC) of the deployed model used to predict fatigue remained stable across different times for experimental sessions (9:00 – 12:00 or 13:00 – 15:00), which supports the robustness of the fatigue detection against circadian variations. Although the model did not detect fatigue perception with 100% accuracy, the biofeedback system might have been preferred according to the decreased workload expressed subjectively. The nonsignificant interaction between the sessions and time-on-task reflected by the oculometrics should also be noted; it is possible that the effect of micro-breaks on the oculometrics might require longer time-on-task to induce a measurable effect.

At a group level, the proposed model of fatigue has provided a mean accuracy of approximately 70%, significantly higher than the chance level, to prove the feasibility of fatigue detection using the oculometrics. On an individual level, fatigue was detected for 75% of the participants (better than the chance level of 52%) in both of their sessions (22), highlighting that the subjective expression of fatigue was temporally aligned with their objective reflection of fatigue on the oculometrics. The current model (ensemble of decision trees) was found to be potentially appropriate for the current setting. In real-world settings with long records of streaming ocular data during computer work, alternative models for fatigue detection may also be useful. For example, deep learning has been shown to be powerful in machine learning, which should also be investigated, e.g., dynamical models for sequential data (414,415). However, deep learning is usually used for end-to-end problems (i.e., from raw data to class labels - no feature extraction) and has the limitations of low interpretability, high computational costs, and the need for large datasets (416). Considering the potentials and limitations of the deep learning, it is an interesting subject for future studies.

Furthermore, while previous studies have provided comparable accuracies for fatigue detection (331,417), a common shortcoming is the lack of information on the classification performance on the individual level. In addition, in such studies, the classification models have not been compared with other alternative models, as opposed to Study III. More importantly, the classification models have been examined using k-fold cross validation, as opposed to Study III, wherein leave-one-person-out cross validation was used. To avoid selection bias and have a robust estimate of classification accuracy (418), leave-one-person-out cross validation has been favored to k-fold and hold-out cross validation. In (331), the mean accuracy of 77.1% in fatigue detection has been reported using a support vector machine in 10-fold cross validation based on 31 features from saccades, fixations, blinks, and pupillary responses. The study was conducted using a remote eye tracker[*] with participants watching five-minute video clips in three successive blocks, with two 17-minute cognitive tasks[†] in between. In addition, the first and third task blocks were considered as non-fatigued and fatigued classes despite the fact that the subjective ratings of fatigue exhibited large inter-individual differences not in complete agreement with the group labeling.

In another test using eye tracking[‡] with head stabilizer in a two-hour driving task, a mean classification accuracy of 67.6% was reported using a logistic regression model with oculometrics from saccades, fixations, pupillary responses, and smooth pursuit as features and the KSS of ≥8 as the fatigue class (417). The classification accuracy was assessed using 6-fold cross validation with the cut-off value of KSS=8 corresponded to high levels of fatigue, i.e., resist sleeping (417), which may be too high to be practically useful since this level of fatigue may rarely occur (419–421). Moreover, it is not clear whether micro-breaks could be effective at such a high level of fatigue.

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[*] EMR ACTUS nac Image Technology Inc, (Japan). - sampling frequency of 60 Hz

[†] Modified paced auditory serial attention test (467)

[‡] Hi-Speed 240 system from SensoMotoric Instruments (Berlin, Germany) - sampling frequency of 240 Hz

The design of the micro-breaks was an important challenge in Study III. According to the results, directing the attention away from the task to the slow breathing and the moderate physical activity appears to be a good strategy to impede fatigue. This may support the view that the activity type during a micro-break should involve cognitive elements different from the primary task (422).

Study III was limited to a young group of participants, yet the model must be assessed on an elderly group of participants as well. However, age and sex were not recognized through the feature selection scheme as contributing factors to detect fatigue in the model. Nonetheless, age-related changes were reflected in some characteristics of saccades and fixations (Studies I and II). Thus, even though age and sex did not contribute directly to the model, some traces of age- and sex-dependent information might have been conveyed to the model via the selected oculometrics.

The oculometrics were computed according to the established definitions in the computation of oculometrics (134). Task-dependent oculometrics (e.g., TPDL) were not used for Study III since their generalizability to real-life applications was of interest. It is, however, acknowledged that real-life situations may pose important limitations, e.g. various lighting conditions on sensitive pupillary oculometrics (423,424), and, hence, limit the use of the oculometrics.

Another related issue is finding proper signal lengths to provide reliable yet sensitive oculometrics to fatigue development (189), which is intuitively more challenging if different activities are involved in computer work. For instance, some activities during computer work may involve limited eye movements even during a long period (e.g. reading), whereas other activities (such as web browsing) may include a rich distribution of oculometrics (e.g. frequent saccades in various lengths and directions) during a short period.

5.4. Perspectives

The presented computer task was shown to be useful in inducing mental load (Study I) and developing fatigue (Studies II and III). To better understand the influence of low-level stimulus features on the oculometrics, the geometric complexities as bottom-up features can be further manipulated (e.g., making curves instead of lines) (425). Using three-dimensional patterns or the effect of rotation and reflection on visual perception of the patterns are other examples to be explored in this context (426). Such changes may also be applicable in gamification and cognitive engineering, where different cognitive and perceptual elements would be of interest in the task. Future strategies can be considered to decrease the temporal demands in the task (e.g. self-paced performance of cycles rather than time-limited performance), to provide numerical or semantic feedback on performance (motivational effects), and to use the keyboard to navigate instead of the computer mouse (to explore extra degrees of freedom using separate fingers or hands in the task performance).

Another issue for the current biofeedback system as a personalized solution for fatigue detection is to consider the contextual and preferential information. For instance, the task has no varying emotional element and has been found to be emotionally neutral, using neutral colors and shapes (427). However, it is important to infer about changes in arousal levels in a long run of the task (392). This can be done by measuring emotional states via self-assessment manikin (428) along with the KSS or via supplementary biosignals, e.g. skin conductance or galvanic skin response (429).

The preferences of the participants can be used in future studies to improve micro-breaks in terms of their frequency, duration, and activity type. An excessive number of micro-breaks, due to false alarms, may naturally induce the feeling of fatigue without the actual development of fatigue. It is, hence, suggested to integrate the biofeedback system with self-triggering micro-breaks to investigate the effect on impeding fatigue. Concerning workplaces, unpredicted interruptions in the middle of a critical and uncompleted task may cause stress and fatigue, according to Cohen's model of cognitive fatigue (430,431). In this scenario, a computer user may decide whether to take micro-breaks triggered by the biofeedback system. The user's preference may also be applied to change the length of micro-breaks. Furthermore, a generalizable behavioral indicator of fatigue in computer work could be beneficial since it is not feasible to frequently interrupt people in workplaces to ask about their perceived level of fatigue. Nonetheless, the frequency of micro-breaks triggered by a biofeedback system based on oculometrics in workplaces is expected to be less than in Study III, assuming that the tasks in workplaces are less demanding.

In addition, the performance of the activity during the micro-breaks may be monitored (432) to enhance the quality of the micro-breaks. For example, the quality of mindfulness can be assessed using respiratory measurements (433). Alternative modalities to visual feedback (e.g., tactile and auditory) in micro-breaks should be considered, especially for occupations involving long exposure to computer screens, to avoid eyestrain. Alternative activities during micro-breaks can also be examined in less-constrained settings to include resistance and stretching exercises (434) in the upper and lower limbs (435).

Since different activities can be performed during computer work (e.g. programming, browsing, typing, graphic design, and monitoring tasks), adding contextual information to a predictive model of fatigue to develop it for workplaces may also be beneficial. In practice, such supplementary data are available from the embedded sensors of cellphones, smartwatches, and online platforms (436,437). However, contextual information can also be obtained from different patterns of eye movements for various activities (such as reading or browsing) (438,439).

Moreover, studying the behavior of the oculometrics and the performance for longer periods could be quite informative. However, longer recording periods might be subjected to confounding factors. For instance, the weight of the eye tracker could cause pain or discomfort in longer recordings. This limitation was considered in the experimental design of Studies I and III, wherein the length of the tasks was short enough to avoid any discomfort and pain due to the weight of the eye tracker. In addition, the participants were instructed to withdraw from the task if they felt discomfort or pain. The perceived low physical demands according to the NASA-TLX also support the comfort of the set-up (Appendix C). Furthermore, longer exposure to visual tasks could also cause visual fatigue (440). In addition, sitting too long could result in other sources of pain and discomfort (441), especially among the elderly group of participants.

In addition to eye tracking, brain-imaging techniques have previously been shown to be useful to study fatigue and mental load in laboratory settings. As such, electroencephalography and near-infrared spectroscopy can provide neural information from cortical areas about working memory and mental load (442–444), as well as fatigue development (445,446). However, these techniques for real-life situations are often limited, compared with (video-based) eye tracking, due to work obstructions and dealing with environmental noise and movement artifacts (447).

Head-mounted eye trackers have often been considered the most versatile (robust) solutions for eye tracking concerning eyeglasses, contact lenses, drooping eyelids, eye makeup, and steep viewing angles (134). Remote or lightweight mobile eye trackers may, however, be required for fatigue detection in workplaces for comfort. However, each eye-tracking technique may have some important limitations; for example, remote eye trackers may allow eye tracking with free head movements only in a limited space and distance with respect to the eye tracker, and the vibrations of the computer desk due to the mouse clicks may reduce the recording quality in the remote systems (448). Therefore, future studies are required to assess the feasibility of using remote (449), lightweight (450,451), and affordable eye-tracking solutions (452) together with other psychophysiological signals to detect fatigue. Owing to recent advances (453), such psychophysiological signals can be recorded unobtrusively (including heart rate variability (454,455), posture (456,457), sitting patterns (458), respiratory responses (459), and facial expressions (11,460). Thus, the integration of eye tracking with these other modalities may facilitate fatigue detection in real-life settings.

Finally, the current findings can contribute to the understanding of eye movements and pupillary responses in association with mental load and fatigue during computer work. In addition, the findings may support theories that favor psychophysiological views of fatigue (27–31,83,461), as it was objectively detected using oculometrics. This subject is an active research area within ergonomics in connection with human computer interactions (432,462–466). Healthy computer work involves multiple dimensions (cognitive, emotional, and physical), and fatigue also seems to exhibit this multidimensionality, which should be further investigated.

5.5. Conclusion

In summary, the findings of this research support the idea that the quantification of mental load and fatigue through oculometrics is warranted in healthy young and elderly individuals.

Perhaps the most insightful result of this PhD project pertains to the contribution of oculometrics to the timing plan of micro-breaks: the oculometrics-based biofeedback system outperformed self-triggered micro-breaks in impeding fatigue. This implies that the biofeedback commands based on fatigue prediction might enhance the effectiveness of micro-breaks during computer work.

Altogether, this project may broaden the understanding of the complex relationships among oculometrics, mental load, and fatigue in young and elderly individuals and provide practical implications of using eye tracking for the prevention of associated health risks in computer work.

Chapter 6. Literature list

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Appendix A. Subject questionnaire

Subject ID:

Thank you for your interest to participate in this experiment. We would like to kindly have some information about you. Please specify the following information and if you have questions about any item please feel free to ask.

NB: Please detach your watch and turn off your mobile phone you can leave them on the counter in the lab. Please feel free to ask to go to the toilet if it is needed now.

Age:		
Sex:	○ Female	○ Male
Handedness:	○ Right	○ Left
Vision:	○Normal	○ Corrected to normal (with ○ Glasses or ○ Contact lenses)
Alcohol consumption:	○ Never	○ Sometimes (○ including yesterday or today)
Coffee consumption:	○ Never	○ Sometimes (○ including today)
Black/Green tea consumption:	○ Never	○ Sometimes (○ including today)
Tobacco consumption:	○ Never	○ Sometimes (○ including today)
Other drug/medication consumption:		
Any Neurological /Mental disorder:		
Hours of sleep last night:		

Normal hours of sleep:

Please specify how regular you have the below mentioned feelings by checking one of the regularities (Never, Sometimes, Regularly, Often and Always).

Table A-1 The Fatigue Assessment Scale (FAS) (290). Each statement was answered on a 5-point scale (1, never to 5, always), thus the overall FAS score varies between 10 and 50. This caption was not written in the actual form of the subject questionnaire.

	Never	Sometimes	Regularly	Often	Always
I am bothered by fatigue					
I get tired very quickly					
I don't do much during the day					
I have enough energy for everyday life					
Physically, I feel exhausted					
I have problems starting things					
I have problems thinking clearly					
I feel no desire to do anything					
Mentally, I feel exhausted					
When I am doing something, I can concentrate quite well					

Please fill out the table below about your **eyes**: If you have any of the symptoms of the first column specify it by marking the yes column in front of each and then its frequency under the occurrence part and its intensity on the difficulty part.

Table A-2 The questionnaire concerning the symptoms of eye fatigue and discomfort (291). The VFS scores ranged from zero to 60, respectively indicating none to all of the symptoms associated with the eyestrain. This caption was not written in the actual form of the subject questionnaire.

	Yes	No	Occurrence			Difficulty		
			Few times	Every weekday	Everyday	Negligible	Slight	Pronounced
Smarting (feel a sharp stinging pain)								
Itching								
Gritty feeling (feeling of having sand in your eye)								
Aching								
Sensitivity to light								
Redness								
Teariness (Excessive tearing or watery eyes)								
Dryness								
Eye fatigue								
Headache								

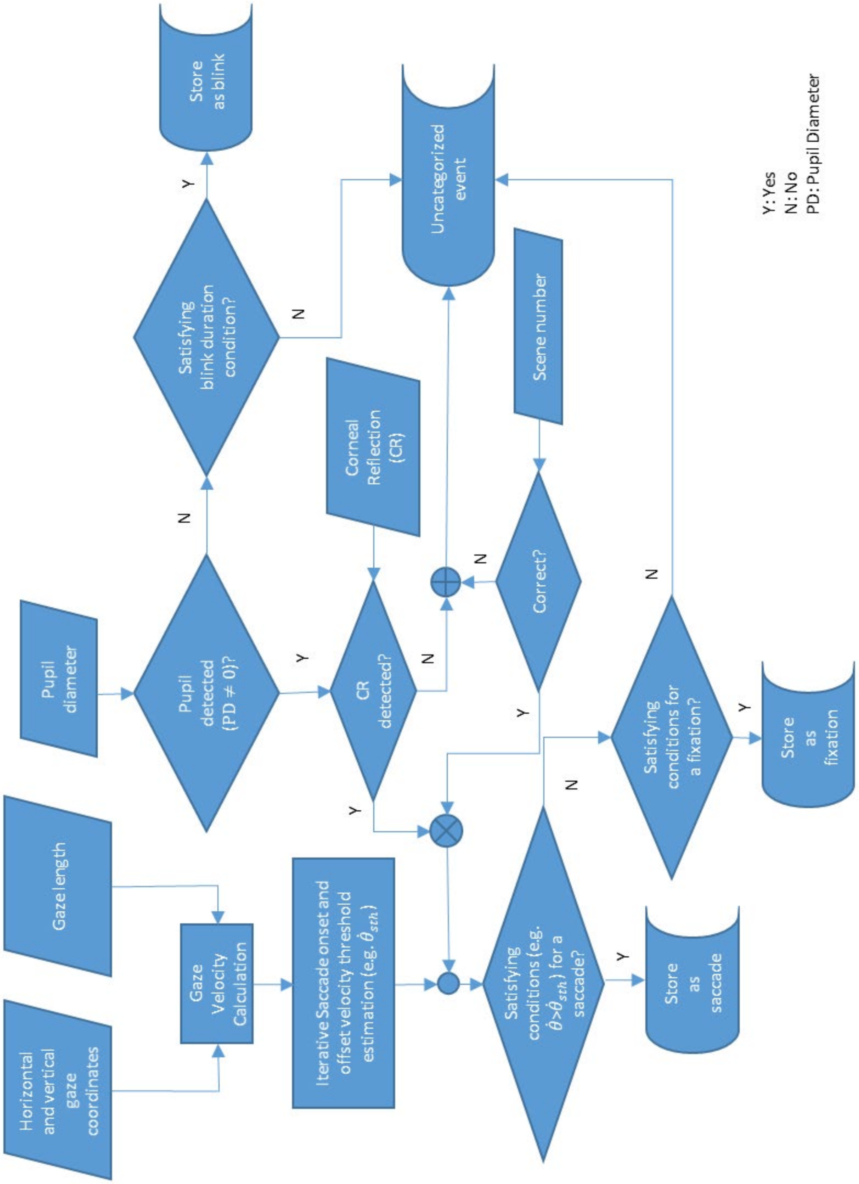
For each of the activities below, please indicate:

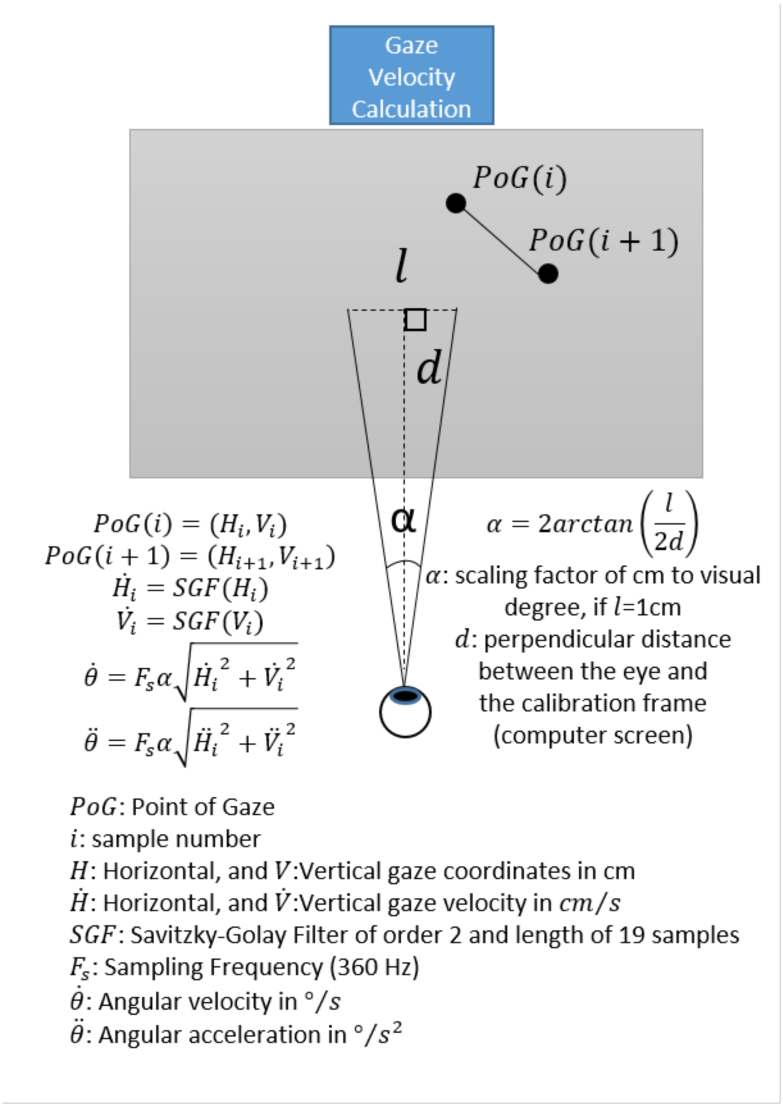
Which hand you prefer for that activity? Do you ever use the other hand for the activity?

Table A-3 The questionnaire for the assessment of handedness (Laterality Index), the Edinburg inventory (292). This caption was not written in the actual form of the subject questionnaire.

	Left	No preference	Right	Do you ever use the other hand?
Writing				○ Yes ○ No
Drawing				○ Yes ○ No
Throwing				○ Yes ○ No
Using Scissors				○ Yes ○ No
Using a Toothbrush				○ Yes ○ No
Using a Knife (without a fork)				○ Yes ○ No
Using a Spoon				○ Yes ○ No
Using a broom (upper hand)				○ Yes ○ No
Striking a Match				○ Yes ○ No
Opening a Box (holding the lid)				○ Yes ○ No
Holding a Computer Mouse				○ Yes ○ No
Using a Key to Unlock a Door				○ Yes ○ No
Holding a Hammer				○ Yes ○ No
Holding a Brush or Comb				○ Yes ○ No
Holding a Cup while Drinking				○ Yes ○ No

Appendix B. The algorithm to detect ocular events





$$PoG(i) = (H_i, V_i)$$
$$PoG(i+1) = (H_{i+1}, V_{i+1})$$
$$\dot{H}_i = SGF(H_i)$$
$$\dot{V}_i = SGF(V_i)$$
$$\dot{\theta} = F_s \alpha \sqrt{\dot{H}_i^{\,2} + \dot{V}_i^{\,2}}$$
$$\ddot{\theta} = F_s \alpha \sqrt{\ddot{H}_i^{\,2} + \ddot{V}_i^{\,2}}$$

$$\alpha = 2arctan\left(\frac{l}{2d}\right)$$

α: scaling factor of cm to visual degree, if l=1cm
d: perpendicular distance between the eye and the calibration frame (computer screen)

PoG: Point of Gaze
i: sample number
H: Horizontal, and V:Vertical gaze coordinates in cm
$\dot{H}$: Horizontal, and $\dot{V}$:Vertical gaze velocity in cm/s
SGF: Savitzky-Golay Filter of order 2 and length of 19 samples
F_s: Sampling Frequency (360 Hz)
$\dot{\theta}$: Angular velocity in $°/s$
$\ddot{\theta}$: Angular acceleration in $°/s^2$

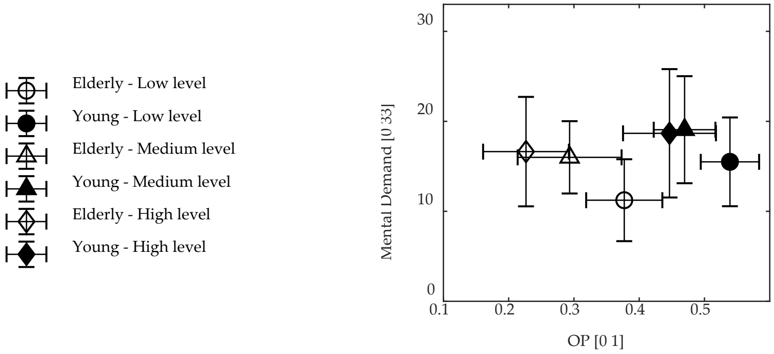
The algorithm is partly adapted from (328).

Appendix C. Supplementary materials

This section provides further information regarding the difference between the young and elderly participants in Studies I and II in terms of performance, subjective assessments, and their relationships. Furthermore, the reliability assessment of the oculometrics used in the fatigue prediction model in Study III is included here.

C.1. Study I

In Figure C-1, the scores (median ± interquartile range) obtained from the participants for the six subscales of NASA-TLX are plotted against the OP for the three levels of the task (low, medium, and high) in the young and elderly groups. The difference between the task levels is more evident in the mental demand and effort than in the other workload subscales, but the temporal and mental loads contributed the most in the overall perceived workload. The temporal load was conceivable since the task was fast-paced. However, the geometric manipulations and visual elements of the task might have contributed to the perception of mental load, which was also in line with the performance of the participants in Study I.



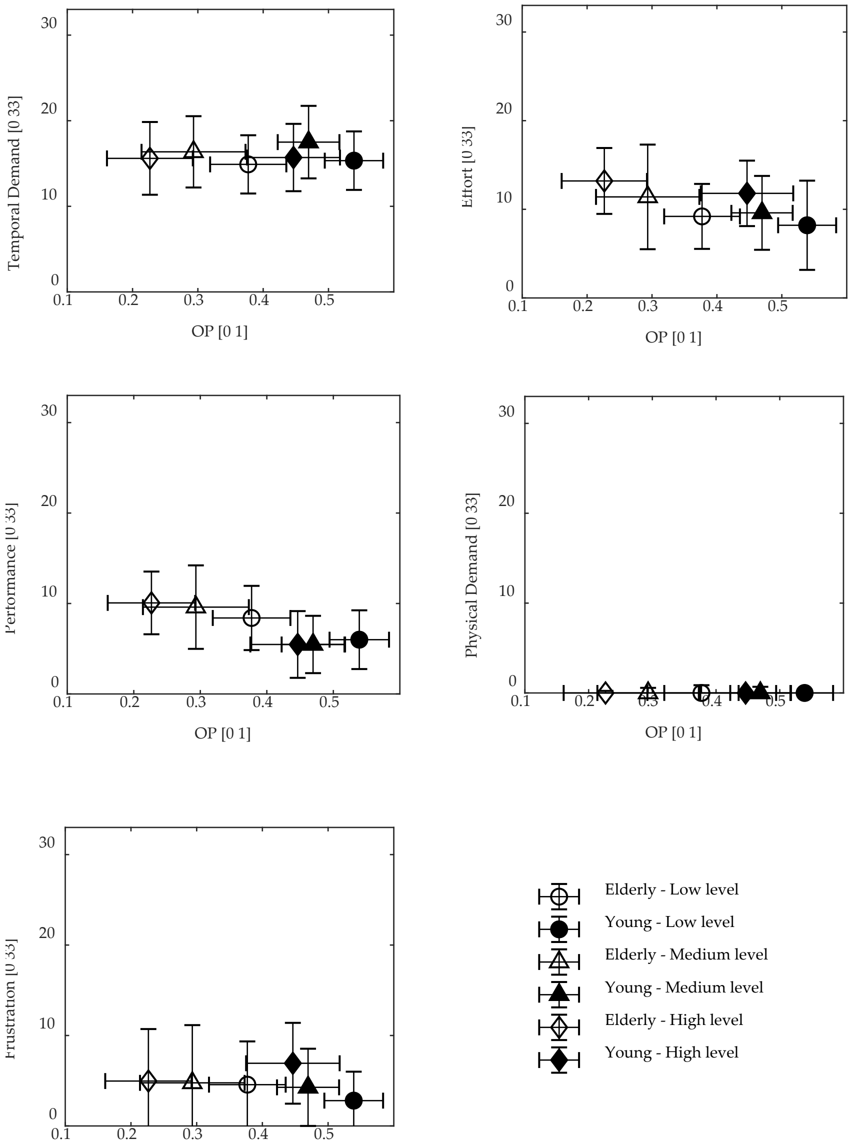


Figure C-1 .The median and interquartile range of the NASA-TLX subscales against the overall performance (OP) in each of the task levels across the young and elderly groups, adapted from (21).

C.2. Study II

In Figure C-2, the weighted scores of the NASA-TLX subscales are depicted against the total scores of NASA-TLX for the elderly and young participants. It appears that the young group, on average, perceived higher mental load than the elderly group.

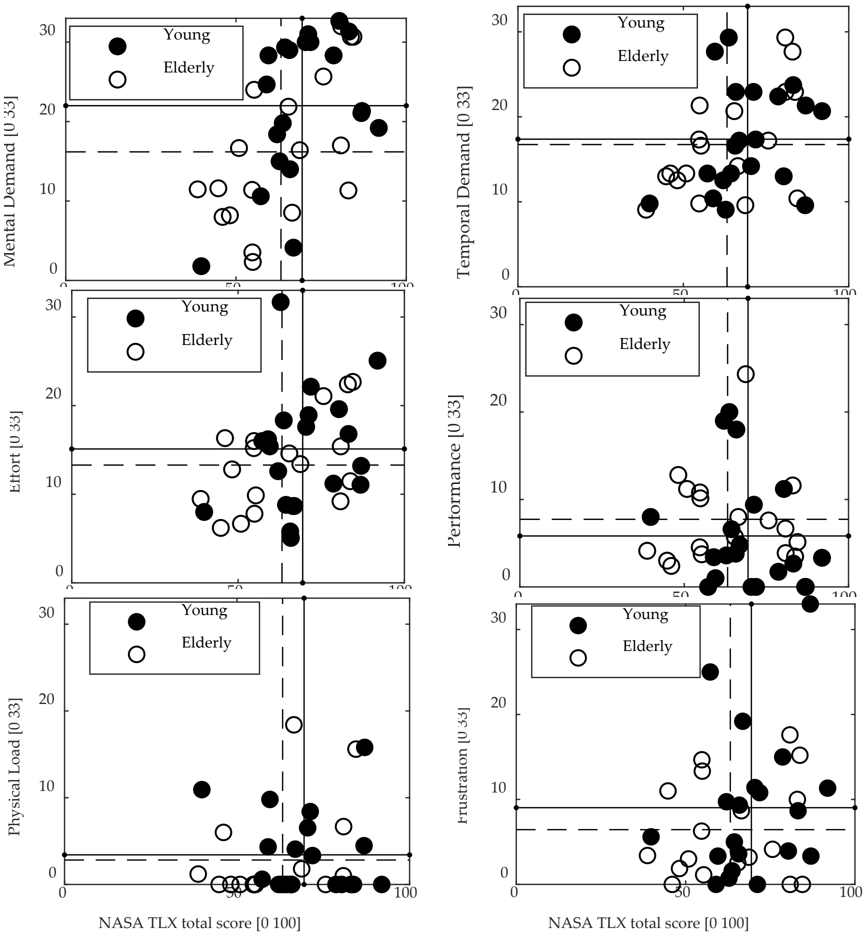


Figure C-2 An overview of the NASA-TLX subscales against the total scores of NASA-TLX in the elderly and young participants (Study II). The mean values of each item for the young and elderly groups are indicated by solid and dashed lines, adapted from (8).

Furthermore, according to Figure C-3, the participants felt more mentally fatigued after the task (post-task) compared with prior to the task (Pre-Task).

The elderly group reported significantly lower fatigue than the young group based on this scale $F(1,36) = 102.7, p < 0.001, \eta_p^2 = 0.7$.

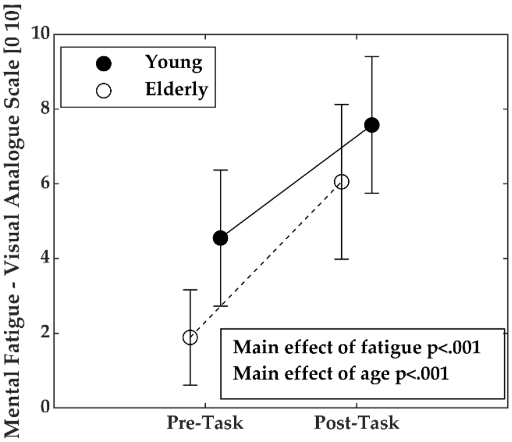


Figure C-3 The subjective ratings for mental fatigue as obtained using a visual analogue scale. The young and elderly groups are indicated by solid and dashed lines, respectively.

Figures C-4 and C-5 illustrate further inspection on the parameters involved in the calculation of the overall performance (OP). The mean number of correct clicks, incorrect clicks, and clicks on the distracting point is plotted against the OP for each cycle in Figure C-4. The main difference between the young and elderly groups was mostly related to the number of correct clicks, whereas the number of incorrect clicks and the clicks on the distracting point are in a similar range according to Figure C-5.

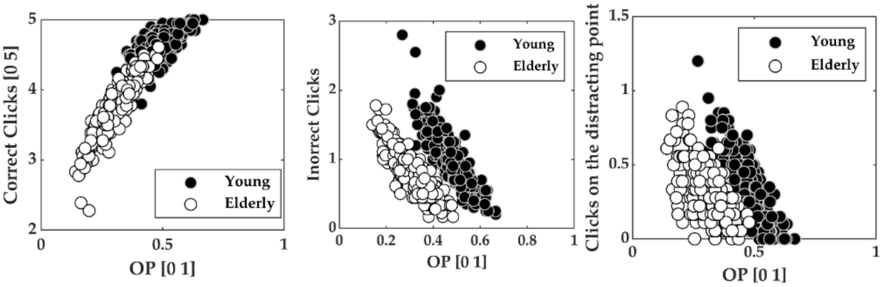


Figure C-4. The mean of the number of correct clicks, incorrect clicks, and clicks on the distracting point against the overall performance (OP) for each of the 240 cycles across the young and elderly participants. Correct clicks can range from 0 to 5, and OP can range from 0 (lowest performance) to 1 (highest performance).

The correct clicks, incorrect clicks, and clicks on the distracting point used to calculate the OP are illustrated in relation to each other (Figure C-5). The difference between the young and elderly groups, indicated by circles and triangles, respectively, is evident in Figure C-5. Both groups can be better clustered based on the correct clicks than the incorrect clicks and the clicks on the distracting point. This difference may imply that the elderly group needed more time to complete the patterns than the young group. To visualize the temporal changes in the performance based on these parameters, the 240 cycles are divided into cycles of 1–80 as a beginning phase, 81–160 as the intermediate phase, and 161–240 as the advanced phase of the task. In contrast to the evident differences between groups, these three phases cannot be distinguished based on these parameters to reflect the progression of time-on-task.

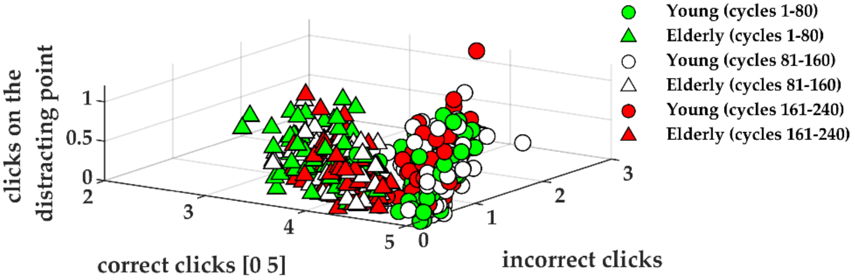


Figure C-5. The mean of the number of correct clicks, incorrect clicks, and clicks on the distracting point across the young and elderly groups for each of the 240 cycles. Correct clicks can range from 0 to 5 (Study II).

C.3. Study III

As mentioned in section 3.9, five oculometrics (i.e. the slope of the line regressing peak velocity and amplitude of saccades (SVA), saccade frequency (SF), blink frequency (BF), percentage of closed eyes (PERCLOS), and pupil dilation interquartile rage (PDIR), were selected in Study III to be used to develop the predictive model of fatigue. The Bland-Altman plots for these five oculometrics are depicted in Figure C-6, wherein the difference of the values of the oculometrics across the days is plotted against the average of the days for all participants and load levels. The points are scattered uniformly around the midline. No consistent bias was observed nor a significant proportional bias or trend as assessed using linear regression of the difference values in relation to the mean values (Table C-1). However, there are a few points outside the limits of agreement, suggesting that an estimated level of uncertainty should be considered in the use of the oculometrics in a predictive model of fatigue.

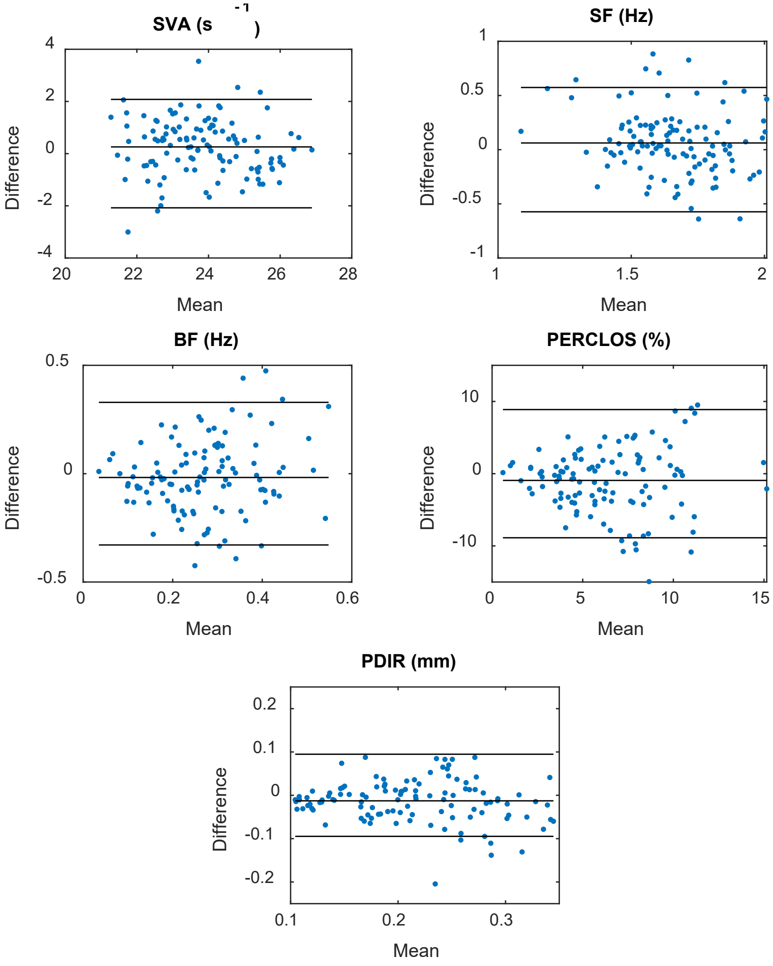


Figure C-6 Bland-Altman plots for the five oculometrics computed over the whole five-minute task timelines. The horizontal lines indicate upper and lower Limit of Agreement (LoA) and the grand mean as the midline. The Y-axis and X-axis are the difference between days and mean of the two days, respectively. SVA: the slope of the line regressing peak velocity and amplitude of saccades (main sequence), SF: Saccade Frequency, BF: Blink Frequency, PERCLOS: Percentage of closed eyes, PDIR: pupil diameter interquartile range.

Table C-1. Linear regression of the difference between days and mean of the two days for oculometrics. SVA: the slope of the line regressing peak velocity and amplitude of saccades (main sequence), SF: Saccade Frequency, BF: Blink Frequency, PERCLOS: Percentage of closed eyes, PDIR: pupil diameter interquartile range. The linear regression formula is $y = \beta_0 + \beta_1 x$, where y is the difference between days and x is the mean of the two days.

Oculometrics	β_0	β_1	**F(1,113)**	R^2	***p*-value**
SVA (s^{-1})	1.784	-0.064	0.711	0.006	0.401
SF (Hz)	0.582	-0.315	4.296	0.037	0.083
BF (Hz)	-0.078	0.225	2.436	0.021	0.121
PERCLOS (%)	-0.013	0.054	0.134	0.001	0.715
PDIR (mm)	0.008	-0.098	1.927	0.017	0.168

SUMMARY

Mental load and fatigue are important multidimensional phenomena concerning aging and computer work. Fatigue may be associated with reduced cognitive resources and increased errors. Micro-breaks are strategic solutions to impede fatigue subject to design constraints, such as a timing plan. The present work aimed to use eye tracking as a promising technology to measure mental load and fatigue in young and elderly adults (Studies I and II), and to apply micro-breaks based on fatigue-related changes in eye movements to decelerate fatigue development (Study III). A novel task resembling computer work was developed to induce mental load in young and elderly individuals (Study I). Eye movements were recorded during the task execution. The task was performed with three load levels across two days. In addition to the load effects on performance, perceived workload, and the oculometrics, the test-retest reliability of 19 oculometrics was assessed. In Study II, the effect of 40-min time-on-task was explored on oculometrics. Then, a predictive model of fatigue was developed (Study III). Oculometrics-based biofeedback was implemented to detect fatigue using the developed model, which triggered micro-breaks upon fatigue detection to impede it. Perceived fatigue and workload were compared between a session with the biofeedback and a control session with self-triggering micro-breaks. A set of oculometrics were found to reflect mental load (Study I) and fatigue (Study II) in both age groups. Similar trends in oculometrics with increased mental load and fatigue, implying shared neural systems for both conditions (Studies I and II). Age-related differences were exhibited in a few of the oculometrics (Study II), but age as a feature did not significantly contribute to fatigue detection (Study III). The biofeedback reduced workload and fatigue development, suggesting an improved strategy to design the timing plan of micro-breaks (Study III). Overall, the findings may support the viability of detecting the effects of fatigue and mental load on oculometrics to apply oculometrics-based biofeedback in computer work.

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