Investigating Usability and Efficiency of Virtual Reality for Research, Rehabilitation, and Simulation of Visual Field Defects in the Example of Retinitis Pigmentosa

Dissertation

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“Regardless of how complex a simulation is, the reality is always more complex.”
- Marc-Uwe Kling

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Contents

Abbreviations

VR	Virtual Reality
VFD	Visual Field Defect
RP	Retinitis Pigmentosa
AMD	Age-related Macular Degeneration
3D	Three-Dimensional
AR	Augmented Reality
VF	Visual Field
DynVF	Dynamic Visual Field
LMM	Linear Mixed Model
MR	Mixed Reality

Summary

This thesis explores the potential of Virtual Reality (VR) in the field of vision science and visual rehabilitation, in particular addressing peripheral visual field defects (VFDs) in retinitis pigmentosa (RP) patients. The progressive loss of the visual field caused by RP and other VFD conditions can severely impact everyday tasks, mental health, and quality of life of those affected. Additionally, for over 99% of RP patients, no effective medical treatment to cure or halt the condition exists. This calls for innovative alternative rehabilitation methods, as well as for ways to better assess how to reduce difficulties encountered by individuals with VFDs. VR technology's advancements in accessibility, performance, and flexibility, coupled with its ability to offer controlled and immersive visual scenes, make it a promising but under-explored tool in the field of vision science and visual rehabilitation.

To provide new insights into the effectiveness of VR based rehabilitation and into the feasibility of simulating VFDs for experimental approaches, a VR based visual task framework, named 'GazeQuest', is designed and developed. This framework provided the foundation for three experimental trials that are presented and discussed in this work.

The first study involved preparatory experiments, utilizing the GazeQuest to assess the impact of different systematic gaze patterns as compensatory strategies in peripheral visual field loss. Results demonstrate positive impact on collision avoidance and gaze behavior, but also reveal adverse effects in walking speed. Findings and feedback from this study shaped subsequent development and study design. The second study evaluated the efficacy of VR-based visual exercises in a home-based environment, revealing their significant positive impact on the real-world navigation performance in RP patients. The third study investigated to which degree the VR based simulation of peripheral VFDs in visually healthy participants can reflect the effects of actual RP conditions in different virtual tasks. Findings show high agreement in performance of both groups, suggesting that simulated visual field loss could facilitate research on more accessible designs and new visual aids for VFD patients.

Overall, the insights gained in this work provide guidelines for feasibility and design of future VR based tools for research and rehabilitation of VFDs. Furthermore, prompted by the findings of the experimental trials, the continued development of the GazeQuest into an effective, adaptable rehabilitation tool beyond research settings is discussed.

Zusammenfassung

Diese Thesis befasst sich mit der vielversprechenden Anwendung von Virtueller Realität (VR) in den Bereichen der Sehforschung und visuellen Rehabilitation, insbesondere im Hinblick auf periphere Gesichtsfelddefekte (VFDs) bei Retinitis-Pigmentosa-(RP)-Patienten. Der fortschreitende Verlust des Gesichtsfelds, der durch RP und andere VFDs verursacht wird, kann alltägliche Aufgaben, geistige Gesundheit und Lebensqualität der Betroffenen stark beeinträchtigen. Darüber hinaus gibt es für über 99% der RP-Patienten keine wirksame medizinische Behandlung, um den Gesichtsfeldverlust zu verhindern. Daraus ergibt sich ein dringender Bedarf nach innovativen Rehabilitationsmethoden sowie nach neuen Ansätzen, um die alltäglichen Schwierigkeiten von Menschen mit VFD zu identifizieren und zu verringern. VR-Technologie hat in den letzten Jahren große Fortschritte im Bezug auf Zugänglichkeit, Leistung und erleichterte Nutzbarkeit erfahren. Das macht sie, in Verbindung mit ihrer Fähigkeit, kontrollierte und immersive visuelle Szenen darzustellen, zu einem vielversprechenden, jedoch im Kontext der Sehforschung und der visuellen Rehabilitation nur wenig erforschten Medium.

Die Arbeit konzentriert sich auf das Design und die Entwicklung eines VR-basierten Frameworks für visuelle Aufgaben, genannt 'GazeQuest'. Die entwickelte Anwendung bildete die Grundlage für drei experimentelle Versuche, die in dieser Arbeit vorgestellt und diskutiert werden. In der ersten Studie wurden - unter Verwendung der GazeQuest - die Auswirkungen verschiedener systematischer Blickmuster als kompensatorische Strategie bei Gesichtsfeldverlust im peripheren Bereich experimentell untersucht. Die Ergebnisse zeigen positive Auswirkungen auf die Vermeidung von Kollisionen und auf das Blickverhalten, offenbaren jedoch auch eine Verringerung der Laufgeschwindigkeit. Ergebnisse und Feedback aus der Studie haben die weitere Entwicklung der GazeQuest und das Design nachfolgender Studien beeinflusst. In der zweiten Studie wurde die Wirksamkeit von VR-basiertem, von zu Hause durchgeführtem Visualtraining evaluiert. Die Analyse der Ergebnisse zeigt signifikante positive Auswirkungen des Trainings auf die Navigationsfähigkeit von RP-Patienten in

realer Umgebung. In der dritten Studie wurde untersucht, inwieweit die VR-basierte Simulation peripherer VFDs bei visuell gesunden Teilnehmern die Auswirkungen einer tatsächlichen RP-Erkrankung auf verschiedene virtuelle Aufgaben widerspiegelt. Die Ergebnisse zeigen eine hohe Übereinstimmung in der Performance beider Gruppen. Das legt nahe, dass die VR-basierte Simulation von Gesichtsfelddefekten die Entwicklung und Erforschung von nutzerfreundlichen Designs für VFD-Patienten unterstützen kann.

Insgesamt liefern die in dieser Arbeit gewonnenen Erkenntnisse Leitlinien für die Machbarkeit und das Design zukünftiger VR-basierter Lösungen in Forschung und Rehabilitation von VFDs. Darüber hinaus wird, angeregt durch die Ergebnisse der experimentellen Studien, die fortlaufende Entwicklung der GazeQuest zu einer effektiven und adaptiven Rehabilitationsanwendung diskutiert.

Publications

Accepted publications

Publication A **Neugebauer, A.**, Stingl, K., Ivanov, I., & Wahl, S. (2021) Influence of Systematic Gaze Patterns in Navigation and Search Tasks with Simulated Retinitis Pigmentosa. *Brain Sci. 2021, 11, 223*. https://doi.org/10.3390/brainsci11020223

Publication B **Neugebauer, A.**, Sipatchin, A., Stingl, K., Ivanov, I., & Wahl, S. (2024) Influence of open-source virtual-reality based gaze training on navigation performance in Retinitis pigmentosa patients in a crossover randomized controlled trial. *PLOS ONE 19(2): e0291902. https://doi.org/10.1371/journal.pone.0291902*

Publication C **Neugebauer, A.**, Castner, N., Severitt, B., Stingl, K., Ivanov, I., & Wahl, S. (2024) Simulating Vision Impairment in Virtual Reality - A Comparison of Visual Task Performance with Real and Simulated Tunnel Vision. *arXiv:2312.02812 [cs.HC]* https://doi.org/10.48550/arXiv.2312.02812. *Accepted by Virtual Reality on March 18, 2024.*

Conference contributions, talks, and achievements

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(3) Poster Award at the Pro Retina Potsdam Meeting 2023

(4) Invited Talk at the 2023 Bardet-Biedl Syndrome Patient Seminar in Bonn

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Further peer-reviewed publications

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Contributions

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Contribution of the first author: For this work, I contributed by detailing the research question of this study, defining and developing the methodology of the project, performing experimental trials, statistically evaluating the results, and writing the main draft of the manuscript.

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Publication C – Simulating Vision Impairment in Virtual Reality - A Comparison of Visual Task Performance with Real and Simulated Tunnel Vision.

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1 Introduction

The utilization of Virtual Reality (VR) technology in the fields of vision care and vision research (ophthalmology) has emerged as a promising frontier in recent years [1]–[5]. Ongoing advancements in processing power, display quality, wearing comfort, accessibility, and affordability of VR technology, as well as the implementation of features such as eye-tracking in commercial VR headsets [6], [7], all contribute to this development [8]–[10]. It can be expected that the importance of VR will further increase in the years ahead, both in the field of ophthalmology and across the broader healthcare landscape. There are various aspects in ophthalmology in which VR has the potential to improve existing methods and to provide the foundation for new innovative approaches, as will be explored in subsequent sections of this work. A field that is especially poised to benefit from the unique features of VR technology is that of visual field defects (VFDs). VFDs describe the partial loss of the visual field (Fig. 1.1) caused by damage or dysfunction in the retina or other components of the visual pathway [11]. However, the potential of VR technology in ophthalmology and particularly in the field of VFDs is little understood and has seen limited exploration up to this point. Among approximately 12.000 VFD-related papers listed in the PubMed database as of December 2023, only 30 papers (0.25%) report the utilization or investigation of VR-based methods. Accordingly, similar low ratios are observed for specific VFD conditions such as hemianopia (0.28%), glaucoma (0.08%), retinitis pigmentosa (RP) (0.06%), and age-related macular degeneration (AMD) (0.04%).

This underscores the vast untapped potential for innovations using VR technology in these domains. One of the primary challenges that contribute to this under-exploration is the highly interdisciplinary nature of VR applications in vision-related fields [5]. Successful designs and implementations of such solutions do require a profound understanding of the clinical background and existing challenges, as well as adeptness in clinical study design. They also require expertise in software engineering with a focus on immersive technologies, interconnection of real and virtual motions, eye-tracking implementations, and aspects of computer vision. The scarcity of experts with such

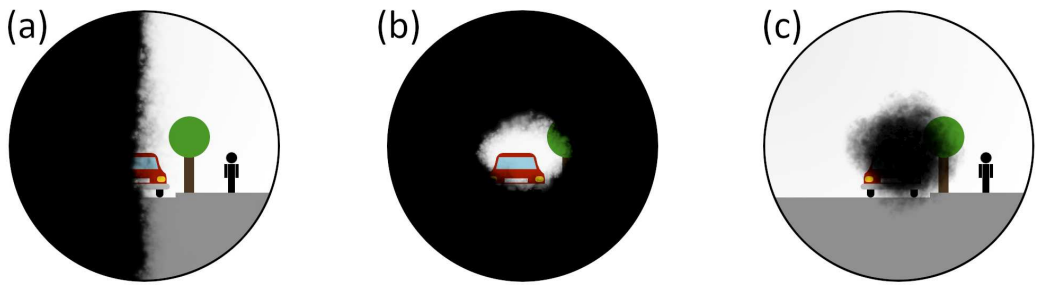

Figure 1.1: Schematic visualizations of three of the most prevalent VFDs. a) Half-sided visual field loss (hemianopia), often following stroke or brain damage; b) peripheral visual field loss as caused by glaucoma or retinitis pigmentosa; c) central visual field loss as caused by age-related macular degeneration (AMD). Size and shape of VFDs vary between patients and depend on the severeness of the condition.

multi-proficiency represents a significant barrier to the widespread adoption of VR in vision care and research. Yet, innovations in this field are urgently needed given the drastic negative impact that VFDs can have on daily activities and overall quality of life of those affected [12]–[23]. Effects of VFD conditions range from diminished navigation-, orientation-, mobility-, and driving skills [24]–[26] to decline in reading speed and visual search performance [27]–[29]. In addition, visual field loss is strongly associated with negative effects to mental health and social functioning [22], [30]–[32], including highly elevated risk of comorbid depression and anxiety [33], [34]. Yet, despite these detrimental effects, there is a severe lack of effective medical treatment options to reverse or even slow the progress of visual field loss from degeneretive retinal diseases [35]–[37]. A closer look into the challenges of medical treatment and the existing alternatives for rehabilitation will be given in later sections of this introduction. First, however, a summary of the features and advantages of VR technology will be provided, followed by a comprehensive overview over the current state of the art of VR applications in ophthalmology.

1.1 Technological features and advantages of Virtual Reality

VR headsets are head-mounted devices characterized by their ability to display immersive, three-dimensional, and interactive digital scenes [38]. Importantly, the visual

perspective of the scene presented to the user is synchronized with the device's position and orientation, ensuring that the digital perspective dynamically adjusts with the real-world movements of the user's head in six degrees of freedom. In modern VR headsets, the most common technique to realize this is inside-out motion tracking. In this method, the environment of the VR device is captured via one or multiple integrated cameras. Visual features of the environment are extracted from each frame of the captured imagery, and identical features are matched between different frames [39]. This allows computing the spatial motion of different features relative to each other as well as the spatial relation of the VR device relative to all detected features in the environment [39], effectively estimating its position and orientation in the world. VR headsets feature two separate screens – one dedicated to each eye – which provide users with a stereoscopic visual experience. Motion-tracked controllers allow for interaction with the scene through physical hand movements, with newer devices also offering tracking and pose estimation of the user's hands [40] for controller-free interactions with the virtual scene. Furthermore, some VR devices feature integrated eye trackers [6], [7], allowing to assess eye movements and estimate gaze direction within the virtual environment. These integrated eye trackers typically employ infrared cameras positioned on the inside of the VR headset, oriented toward the user's eyes. Real-time images captured by these cameras are processed using advanced computer vision algorithms [41]–[45] or machine learning [46]–[48] to detect and track dynamic pupil positions, subsequently allowing the estimation of the user's gaze direction. The implications and advantages of these technological features of VR devices are discussed in the following sections.

In ophthalmology, VR based approaches - regardless of their particular application - typically compete with two other methodologies: 1) screen based techniques that use computer screens or custom-designed setups to display visual content, and 2) setups and tasks based in the real world. While all three approaches – VR based, screen based, and real-world – have their strengths and limitations, VR uniquely combines many of the advantages of the other two categories.

1.1.1 Comparison with screen-based setups

Screen-based approaches have limited capability of providing realistic and immersive visual experiences. While computer screens can display realistic-looking imagery, this imagery is confined to a static, two-dimensional visual area in front of the user. This

not only limits the visual angles at which content can be displayed, it also eliminates many factors that contribute to real-life visual experience, such as depth perception from stereoscopic vision and shifting perspectives.

VR devices, in comparison, offer visual experiences that more closely resemble real life vision [5], [49]. Popular VR devices typically offer visual angles ranging from 90° to 110° diameter [50], exceeding standard screen-based setups ($62° \times 37°$ for a 27 inch screen in 50 cm viewing distance). In addition, the ability of VR devices to track users' head rotations enables them to expand the visual field even further. The stereoscopic view provided by the dual-screen setup of VR devices facilitates three-dimensional (3D) vision and depth perception. Furthermore, lateral head movements of the user are projected directly to the visual perspective on the displayed content, allowing for so-called parallax effects [51], [52] that further contribute to depth perception and immersion. VR setups facilitate the exclusion of external stimuli and lighting, as the device's frame represents an almost complete visual enclosure. The integrated eye-tracking capabilities offered by various VR devices [6], [7] are an essential tool in many vision-related setups, ranging from gaze- and attention analysis [24], [53] to diagnosis [54], [55], and even the utilization of gaze as method for input and interaction [56], [57]. Lastly, VR technology enables the creation of highly immersive and interactable environments, allowing users to physically navigate through the virtual space and interact with virtual objects through spatial controller- or hand tracking.

1.1.2 Comparison with real-world setups

Compared to real-world tasks and setups, the advantage of VR mostly lies in the flexibility and control it provides over the virtual environment displayed to the user. Real-world setups are limited by i) the constraints of available space and materials, ii) the time and effort it takes to set up or modify the environmental scene, iii) the measures taken to avoid accidents and risks related to activities, and iv) the laws of physics themselves. By transferring the setup into a virtual environment, those limitations are largely bypassed. Scenes can be generated, modified, or randomized in an instant and designed without physical constraints. They can simulate high-risk scenarios such as driving or street crossing tasks [24], [58]–[63] without putting the user at risk. And since developers have complete control over the content displayed in VR, it is even possible to alter the visual perception users have of the environment – for example in the form of simulated visual impairments, as will be discussed later in this work.

1.2 Current applications of virtual reality in vision research and healthcare

Having discussed the advantages and possibilities provided by VR technology, the question is now raised which specific areas of ophthalmology can benefit from it. Five different areas will be highlighted: 1. Education about visual health/impairments; 2. Diagnostics; 3. Training for medical staff; 4. Rehabilitation; 5. Vision research. While this work primarily focuses on the last two categories – rehabilitation and vision research -, a brief introduction to the first three categories will be given to provide a more comprehensive overview of the current state of VR in ophthalmology.

1.2.1 Educational content

VR has been employed to create educational content that can help raise awareness and improve understanding about VFDs and other visual impairments [64]–[68]. Friends and family, physicians and therapists, employers, and colleagues all may gain better understanding of the capabilities and struggles of a person living with VFDs, which can improve empathy and interaction [66]. These educational VR tools simulate the symptoms of specific visual conditions and display them within a virtual environment, oftentimes in a gaze-contingent manner using integrated eye tracking. This allows visually healthy individuals to perceive their virtual surroundings in a way that mimics how patients with visual impairments perceive the real world.

1.2.2 Diagnostics

In the area of diagnostics, VR technology is most commonly applied in visual field testing [54], [55], [69]–[74], a crucial method for detecting and monitoring VFDs. The results of VR based examination tools have been shown to align with those achieved using gold standard diagnostic devices like the Humphrey Visual Field Analyzer [69], [73] while offering higher portability, affordability, patient acceptance, and more customization of the displayed content. This flexibility enables new approaches that were previously difficult or impossible to realize. Such approaches include home monitoring of the visual field in glaucoma patients [71], [72], as well the gamification of testing procedures which improves motivation and acceptance especially in younger patients [74]. Kartha et al. [75] also highlight the advantage of VR in enabling the

design of visual testing paradigms that more accurately reflect activities in real life, providing a better representation of the effective visual performance of patients with low vision. Outside of VFDs, successful experimental applications of VR technology include the detection of different binocular vision disorders [76], [77], and other test exams like dark adaptation, color vision, and contrast sensitivity [78], or visual search performance [79].

1.2.3 Training of medical professionals

The utilization of VR in the training of medical professionals, such as for intraocular surgical procedures, has demonstrated a positive impact on motivation and learning outcomes when compared to non-VR training methods [80]–[84]. VR environments offer more life-like visual experiences than purely text-, verbal-, or image-based learning approaches. In addition, they allow for a more natural interaction with scene elements thanks to hand- and controller tracking technologies. Studies have further shown that performance in surgical tasks in VR environments correlates with performance in real surgical procedures [85], [86], suggesting that VR-based medical training may contribute to research and development of new surgical procedures in the future.

1.2.4 Rehabilitation

In the context of VR based rehabilitation protocols, an important consideration is the learning transfer from virtual context into real world application. This describes the ability of training effects and behavior adapted within a virtual environment to also manifest in real-world settings. The existence of those learning transfer effects for VR has been demonstrated for sensorimotor tasks [87] and, to limited extent, gaze behavior [88]. VR technology's unique features – such as modular and interactive training environments, wide viewing angles, and head-rotation-aware content display – make it a highly promising tool in this area. Yet, implementations of VR for the rehabilitation of VFDs and other visual impairments are scarce, and their effects are little understood as literature is limited to a small pool mostly comprised of case studies. Of these studies, several investigated the effects of training tasks in VR in patients with hemianopia or visuo-spatial neglect [89], suggesting improvements in reading speed and even visual field size [90]–[92]. For AMD, Raphanel et al. [93] proposed the potential of VR training, later developed and evaluated in a single-case study by

Sipatchin et al. [94] using a modified 'Ping Pong' game. Beyond the field of VFDs, binocular VR training has shown success in enhancing visual acuity in young individuals with amblyopia [95]–[97], a condition characterized by vision dominance in one eye and resulting deterioration of vision in the other [98]. Research also indicates that VR training during childhood may decrease myopia development [99]. So far, there are no documented studies or reports on the use of VR training on peripheral VFDs like glaucoma or RP. This gap in research is detrimental considering the severely limited availability of alternative treatment options for RP, making it a primary motivating factor for this work, in particular for the research described in Publication B.

1.2.5 Vision research and visual accessibility

As a last category, the application of VR for research on vision and particularly VFDs will be addressed. Here, the main beneficial feature of VR is its ability to simulate visual scenes as well as the user's movement and interactions within these scenes in an immersive and realistic manner. This way, it is possible to replicate real-world tasks and setups in a virtual environment. As was mentioned before, this is especially useful if these setups are complicated or even impossible to realize in the real world, or if they involve physical risks such as in street crossing tasks [61]–[63] or driving skill assessments [24], [26]. Furthermore, VR based experimental setups can be used in a pre-study design to test feasibility of a potential real-world implementation. This approach has been used, for example, to estimate the effectiveness of electronic visual aids by designing a virtual environment that simulated these visual aids [62], [100], [101]. The validity of such approaches is supported by the findings of Authié et al. [102]. Their study compared two structurally identical mobility task setups for navigation performance assessment in RP patients – one setup was realized in a virtual environment, the other in a real-world setting. They found a high agreement in patient performance between virtual and real condition, suggesting the feasibility of the use of VR-based setups in place of real-world setups.

Another promising, yet largely unexplored, research application of VR lies in the assessment of visual accessibility through simulated VFDs and visual impairments. Visual accessibility describes the identification and mitigation of elements that pose challenges to people with visual impairments, for example in architectural design [103]–[108], workplace layout [109], or device and interface design [109]. Several studies [26], [65], [67] even suggest that with the possibilities of VR, it may be feasible to

evaluate different effects of VFDs on visual performance or accessibility in a visually healthy cohort. This can be achieved through gaze-contingent simulation of the respective visual impairments in the visually healthy subjects, as was described earlier regarding the use of VR for awareness and education on VFDs. The approach would address the challenges often faced in research on rare visual conditions, where acquisition of a patient group large enough for statistical significance can be difficult [26], [110]. However, when aiming to expand or even substitute groups of actual patients with participants undergoing VFD simulation, it is crucial to first understand the degree to which simulations can replicate the impact of real conditions. This important research question has motivated the study that is described in Publication C and will be addressed again in later parts of this work.

1.3 Retinitis pigmentosa and the current state of treatment and rehabilitation methods

In the first chapters of this work, different VFD conditions were introduced. While there is a demand to investigate the potential of VR based rehabilitation and research tools for all of these conditions, this work will primarily focus on the condition of RP. At the University of Tübingen, where this work was done, RP represents a central focus of research, diagnosis, and medical care [27], [111]–[117]. Acknowledging that the investigation of VR training effects on different VFD conditions would have exceeded the planned scope for this project, a decision was made to keep design and methods of this work focused on RP, leveraging the existing local expertise and network.

1.3.1 Prevalence and existing treatment

RP describes a group of degenerative retinal diseases characterized by a progressive loss of peripheral vision as well as potential occurrence of blurriness of sight, night blindness, and glare sensitivity. It affects roughly 1:4000 people worldwide [35], [118]–[121] and is the most prevalent cause of visual field loss in people below the age of 60 [31], [122], [123]. RP is the result of gene mutations, with over 3000 unique mutations being registered to date [124]. Due to the heterogeneous nature of these diseases, individual medical approaches to cure or stop the progression of visual field loss can, at best, only target small percentages of the total population of RP patients. Consequently, widespread coverage of available and affordable medical treatments for

RP is unlikely in the foreseeable future, despite over 100 currently ongoing clinical trials [35]. To this day, only a single gene therapy has been approved by the U.S. Food and Drug Administration [35]. It targets the RPE65 mutation which affects roughly 0.3-1% of all RP patients [35] and comes at a treatment cost of USD 850,000 per individual [125]. For at least 99% of patients, no effective cure for their condition exists. This underscores the crucial need for alternative approaches to lessen the impact of VFDs and to improve patients' quality of life despite the condition.

1.3.2 Visual aids

Some of these alternative approaches are found in the form of electronic visual aids, such as Augmented Reality (AR) based solutions [126], [127]. They use AR glasses like the Microsoft Holo-lens [128] to project information of the peripheral visual field (VF) into the remaining central visual field of the RP patient. However, it was found that RP patients show a high non-acceptance rate of 81% towards this technology [129], stating reasons such as the fear of stigmatization for wearing the device in public.

1.3.3 Gaze training

Another approach for rehabilitation in patients with RP and other VFDs is gaze training, a non-invasive method aimed to support patients in adapting to their VFDs. This adaptation can occur in two ways: through conscious top-down learning [130] of compensatory gaze strategies that facilitate efficient scanning of the visual surroundings or through a more stimulus-driven, sub-conscious process of bottom-up adaptation [111]. In the context of gaze training, top-down learning mostly occurs when the training is supervised, and participants receive explicit instructions and reminders to apply the gaze strategies. Such gaze training techniques have been applied in several studies typically involving multiple days of instructed training [131]–[134]. A second method applied for gaze training is based on more inherent training effects. Here, specialized visual training tasks are designed such that the execution of desired gaze behavior directly facilitates the success rate of the task. This means that users are inherently – without external instruction – driven to follow specific gaze behavior in order to improve and progress in the visual task. This can manifest in both sub-conscious adaptation of beneficial gaze behavior, such as larger and more frequent eye movements (bottom-up), as well as in conscious application of self-developed com-

pensatory strategies (top-down). A notable advantage of this second approach is its feasibility for home-based gaze training, which has been demonstrated in two studies employing screen-based gaze training setups for a group of RP patients [111], [113]. However, results of these current gaze training solutions, especially for patients with peripheral VFDs, show limitations in their effectiveness. While significant increases in individual aspects, such as walking speed or collision avoidance, can be found, they are oftentimes small [111], limited to sub-groups of the cohort [113], [135], or accompanied by a speed-error trade-off [131]. Considering the previously discussed advantages that the application of VR could offer over screen-based setups, a VR-based gaze training could result in more significant enhancements than methods relying on traditional screens. To this date, however, no VR-based gaze training solution for RP or other peripheral VFDs exists, prompting the design, development, and evaluation of such a tool.

In summary, it has been shown that the limited pool of medical treatment options and rehabilitation methods for RP does not cover the urgent need for such solutions and does not reflect the detrimental effects that this condition can have on the lives of affected individuals. There are noticeable gaps in the understanding of various approaches that could facilitate research and design of new rehabilitation protocols through VR technology. This work strives to fill some of these gaps while also aiming for the development of a new, VR based solution. The following chapters as well as the attached publications will provide details about the objectives, processes, and results of these endeavors.

2 Objectives

The main objective of this work was the design and development of an intuitive, standalone, VR-based visual task framework called 'GazeQuest', as well as the evaluation of its potential to be used as 1) a rehabilitation tool for patients with peripheral VFD, and 2) as a tool to experimentally quantify the degree to which a simulated peripheral VFD can reflect real visual conditions.

The first major step towards this objective describes preparatory experiments assessing the impact of systematic gaze patterns as compensatory strategy in peripheral visual field loss. Ivanov et al. suggested in their work [111] that the integration of systematic gaze patterns into gaze training could improve the training's effectiveness. While this hypothesis aligns with findings for other VFDs like hemianopia [133], the effects of different gaze patterns on visual performance with peripheral VFD have not been explored before. The GazeQuest framework developed as part of this project was therefore applied to investigate the effects of two different gaze patterns in participants with simulated peripheral VFD. Methods, results, and conclusions about the investigated systematic gaze patterns are presented in Publication A.

In Publication B, a random-controlled crossover clinical trial is described. The objective of this study was to evaluate the effectiveness of VR-based gaze training – utilizing the GazeQuest framework in a four-week training period – to influence gaze behavior and improve navigation performance of RP patients in real-world settings. A positive outcome would demonstrate the potential of the GazeQuest as an effective rehabilitation tool for unsupervised, home-based visual exercise, and suggest the general feasibility of VR based gaze training methods.

Lastly, Publication C investigates the capabilities of RP patients and visually healthy participants with simulated VFD in different virtual tasks provided by the GazeQuest framework. The study compares performance as well as different aspects of gaze behavior over a four-week duration of visual exercise, analyzing how initial results and learning rates differ between groups. The aim is to provide insights into the validity of substituting or expanding RP patient groups with visually healthy participants with

peripheral VFD simulation in different experimental contexts.

3 Discussion

In this section, the software tools developed as part of this thesis and the research steps towards the application of Virtual Reality in rehabilitation and simulation of peripheral visual field defects are presented and discussed. The chapter will start with a visualization and summary of the GazeQuest framework that was utilized throughout all parts of this work, as well as a retrospection on its design and development. The lessons learned during the design and execution of the experiments will be discussed, offering a blueprint for future VR based rehabilitation protocols and for optimizing the integration of gaze-contingent VFD simulation in virtual setups. Lastly, the findings will be contextualized within the broader landscape of current and potential future research and technologies, and strategic directions for the continued development towards practical application of the GazeQuest will be outlined.

3.1 Design of the GazeQuest framework

A major part of this work was the design and development of an intuitive, immersive, and adaptable VR based framework, the GazeQuest. The GazeQuest served both as a foundation for the following experimental setups and as a benchmark for exploring the potential of VR technology in researching and rehabilitating peripheral VFDs. This chapter provides an overview of the developed application and its software architecture (Fig. 3.1 and 3.2), followed by a discussion of the rationale and specific design choices for the various aspects.

- **Hardware** Over the course of this work, the GazeQuest framework was developed for and implemented in two different devices. For the first experimental study, a FOVE 0 VR headset [136] with integrated eyetracking, connected to an external processing unit, was used. Soon, however, the GazeQuest framework was rebuilt for the newly released, stand-alone Pico Neo 2 Eye headset [137], which better suited the requirements for the following experimental setups. According to the manufacturers specifications, the Pico Neo 2 Eye features a display

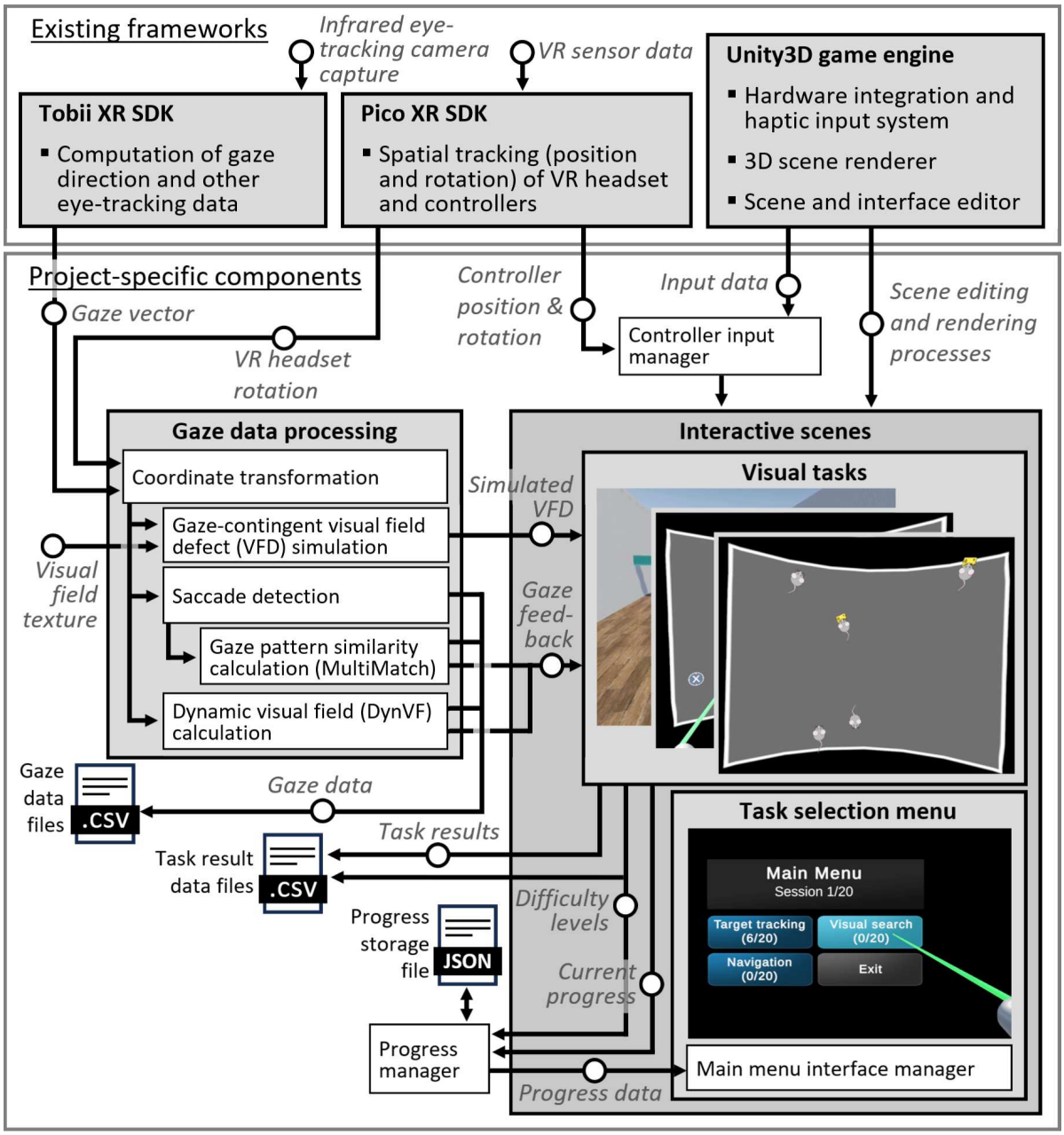

Figure 3.1: Visualization of the GazeQuest framework's software components and their interactions with each other. A structured summary and descriptions for each individual component are given in this work's supplementary information. A visualization of the software components of the three visual tasks is shown in Fig. 3.2.

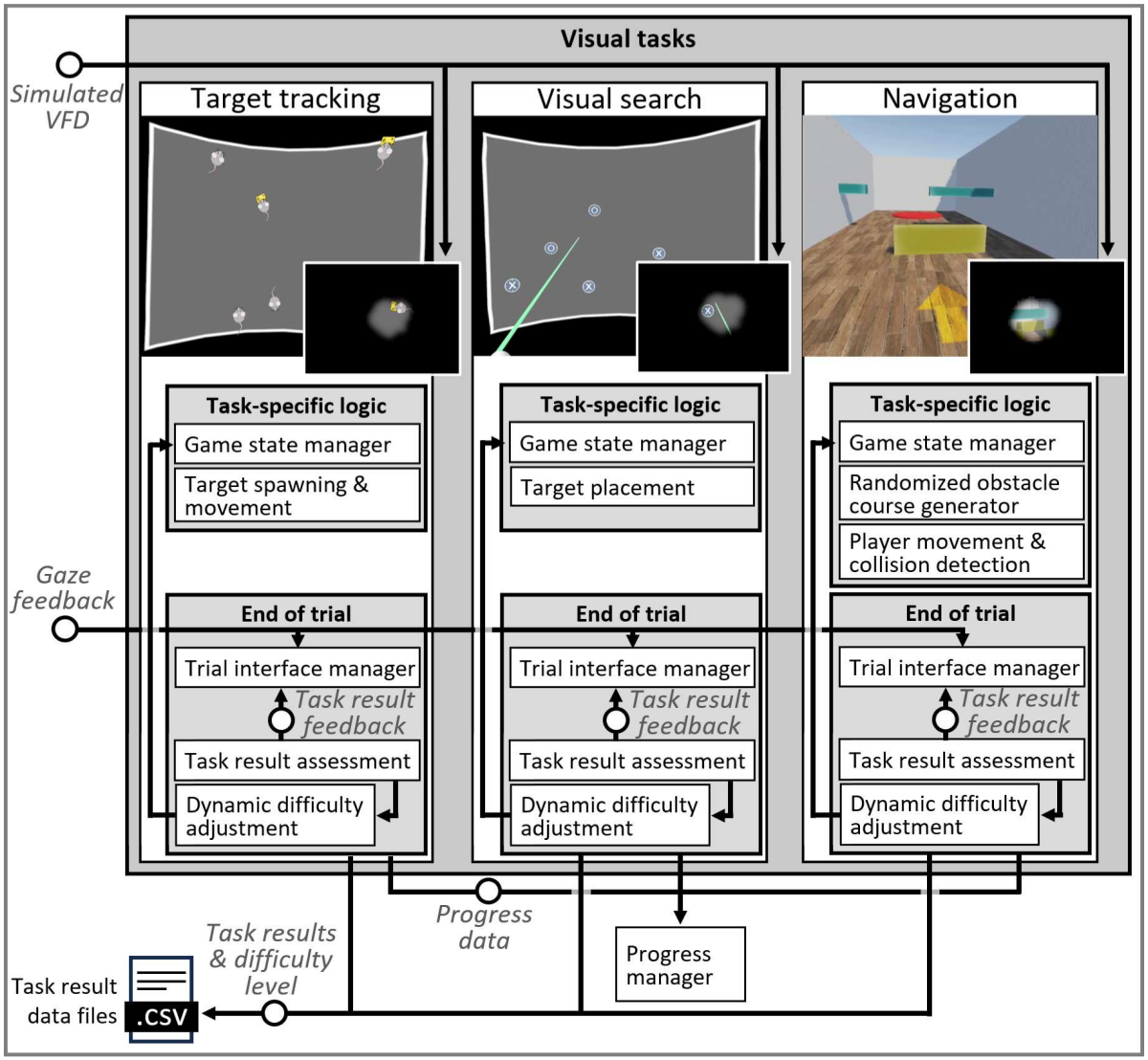

Figure 3.2: Visualization of the three visual tasks, their software components, and the interactions between those components. A description of each individual component is found in this work's supplementary information.

refresh rate of 75 Hz and display angles of 101° diameter per eye, as well as an eye-tracking device operating at 90 Hz with a spatial accuracy of 0.5°, with no information reported on latency [137]. However, independent literature suggests actual display angles of 89° [50]. Furthermore, evaluations of the HTC Vive Pro Eye, featuring comparable integrated eye-tracking [138], found an average spatial accuracy of 1.08° for eccentricities below 15° [139] and 4.16° when considering eccentricities of up to 25° [140]. The total latency of the eye tracker, based on the results by Stein et al. [141], can be estimated as 79 ms from initial stimulus to a display in the virtual scene. A potential impact of the eye tracker's latency will be discussed in the context of the findings of Publication C. Specifics about the considerations for the VR headset selection are provided in chapter 3.1.1.

- **Existing frameworks** The software itself was built with the Unity 3D Engine (Version 2021.3 LTS), using the Unity integration of the Tobii XR SDK (Version 3.0.1) and Pico XR SDK (Version 1.2.4) (Fig. 3.1).

- **Visual tasks** The GazeQuest framework embeds three interactive visual tasks, shown in Fig. 3.2. In the target tracking task (Fig. 3.2 - Target tracking), users are challenged to track multiple moving targets simultaneously, motivating fast switches of the gaze's focus between the different targets. The visual search task (Fig. 3.2 - Visual search) consists of static targets distributed across a specified area. Users are challenged to find and select as many targets as possible in a limited amount of time, prompting them to use deliberate exploratory gaze movements to quickly scan large visual areas for the targets. Lastly, the navigation task (Fig. 3.2 - Navigation) requires users to navigate through a randomized obstacle course within the virtual environment, avoiding collisions and minimizing the time required to reach a specified goal location. Importantly, all three tasks are carried out in a seated or stationary standing position, with controls being limited to body rotation and controller input. The tasks are designed to be carried out in short trials of 20-60 seconds each.

- **Menu interfaces** A main menu (Fig. 3.1 - Task selection menu) allows to select between the three tasks and provides information on the current progress, such as completed trials and training sessions. In-between individual trials, a trial menu with result scores is displayed, providing users with different metrics about their task performance and displayed gaze behavior. The interface of this trial

menu also incorporates selections to continue with the next trial or return to the Task selection menu.

- **Gaze data processing** In addition to the content displayed to the user, the application also incorporates a set of custom functions to process the data provided by the built-in eye tracker of the VR device. At run-time performance, these functions compute various gaze-related parameters used to evaluate the gaze behavior of participants, described in chapter 3.2.1.

- **Visual field defect simulation** The gaze data is further utilized to enable gaze-contingent simulation of visual field defects. In this simulation, a masking layer is superimposed on the visual content presented during visual tasks. The mask layer occludes specified areas of the user's visual field and is dynamically adjusted to align with the user's gaze direction, mimicking the behavior of real visual field defects that shift with eye movement. Example of a visual scenes viewed through this simulated VFD are found in the small images under each visual task in Fig. 3.2 or in Fig. 2 D-F of Publication B.

- **Measurement data storage** The GazeQuest framework automatically captures and stores the results from each visual task trial, along with eye-tracking data and derived gaze-related parameters, in CSV file format. This enables easy access to the data for evaluation and analysis once the experimental phase is concluded.

Further details on the visual tasks and the analyses of individual measurement parameters are found in the methods sections of Publications A-C. Furthermore, structured descriptions of all components and component interactions shown in Fig. 3.1 and 3.2 can be found in the supplementary information of this thesis. Having provided an overview over the GazeQuest framework, the following chapter will discuss the specific design considerations made during the development of the GazeQuest. Those comprise four key aspects: Technological considerations, usability and interface design, interactive visual task design, and integration of automated data capture.

3.1.1 Technological considerations

The choice for the specific VR headset used as platform for the GazeQuest framework was important, as the headset's functionality directly shaped the range of features and methods that were available in the upcoming experimental trials. Priorities as

well as potential areas for compromise in the technical aspects of the device were identified. Given that the GazeQuest was intended for use in an unsupervised, at-home setting, it was crucial to prioritize a device that offered straight-forward setup and user-friendly operation. Simultaneously, for the experimental trials planned with the GazeQuest, the integration of an eye tracker into the VR system was essential to allow assessment of users' visual behavior. Thus, the two factors of usability and eye-tracking capability were identified as key priorities. The significance of other aspects of the selected hardware, such as processing power or field of view, was discovered to be relatively low. While it is known that low framerates in virtual simulations can induce nausea and motion sickness [142], [143], the GazeQuest was not intended to involve complex or visually realistic scenes or other processing-heavy calculations that would mitigate the devices capabilities to display content at full framerates. Regarding the field of view angles of the applied VR headset, it is noteworthy that, in visually healthy subjects, the borders of the display are typically noticeable only in the peripheral VF. A study conducted by Franchak et al. [144] finds that head-centric gaze fixations rarely exceed eccentricities above 25° in visual search and walking tasks. Considering that the GazeQuest is designed for use in people with severe loss of the peripheral VF, the edges of the users' restricted VF are not expected to exceed the borders of the display when using VR headsets with display angles of 45°-55° radius. These display sizes are standard across all popular VR devices [50], making them an insignificant factor in the selection of a suitable device for the GazeQuest framework.

Choice of VR headset

The first experimental study, described in Publication A, applied a FOVE 0 headset, which requires wired connection to an external processing unit as well as an external camera for position and rotation tracking. This severely limited the flexibility of the device and its suitability for setup and use in a home-based setting. At the time, the FOVE 0 was one of the only VR devices that provided eye-tracking capabilities. However, its limited capabilities conflicted with experimental requirements of subsequent studies. Thus, the FOVE 0 was replaced as platform for the GazeQuest as soon as the opportunity arose with newly emerging technology. The Pico Neo 2 Eye, released in 2020, was the first commercially available stand-alone VR headset that provided integrated eye-tracking capabilities. The freedom to use the headset in any place without the need for external hardware made it an ideal platform to support the aim for unsupervised at-home use of the GazeQuest.

Eye-tracking considerations

The relatively low spatial accuracy of integrated eye-tracking devices, especially in consumer-level VR headsets [7], is a reality that must be acknowledged and considered in the design of VR eye-tracking studies [140].

In addition to factors inherent to the eye-tracking system, spatial accuracy is influenced by human factors as well. In particular, calibration [145], [146] and slippage [45], [147] play a major role. Eye-tracking calibration can prove to be an especially challenging process for individuals with visual impairments [148], as it is based on visual cues that can be difficult to detect and track. Additionally, slippage of the eye tracker, resulting from head movements, is known to negatively impact its accuracy [45], [147]. This had important consequences for the planned experimental trials for the GazeQuest: even if the eye tracker could be perfectly calibrated at the start of a study – in supervised condition and with instructions –, it is unlikely that the level of accuracy could be maintained throughout an unsupervised, at-home experimental phase. Acknowledging these limitations of the experimental methods and available technology, it was mandatory to ensure that the parameters derived from the eye-tracking data within the GazeQuest would be robust against the influence of low accuracy.

Metrics involving discrete spatial classifications such as areas of interest or fixations on specific objects are known to be vulnerable to low eye-tracking accuracy [146], [149]. Especially in dynamic 3D scenes involving movement and shifting distances to objects, such as in mobility and navigation tasks, high spatial accuracy is crucial to ensure viable results [146], [149]. Consequently, such metrics were avoided in the design of the GazeQuest and in the experimental trials of this work. Instead, focus was put on gaze parameters of a more continuous nature where small errors in the eye-tracking data elicit an equally small effect in the outcome. Chapter 3.2.1 will summarize the different gaze parameters considered in this work, as well as the algorithms behind their detection and calculation.

3.1.2 Challenges in accessible, self-sufficient, and flexible design

The development of a VR framework tailored for individuals with VFD presented a set of interface and usability design challenges, heightened by the aim to enable its use in unsupervised experimental settings. Addressing these challenges was crucial to ensure the GazeQuest's successful utilization in a home environment where exter-

nal assistance, reminders, or instructions from experimenters are unavailable. Aiming for accessible design, the GazeQuest framework adopts a minimalist and unobtrusive interface. The design was adapted and modified based on feedback and suggestions from members of the Pro Retina Advice Center Tübingen [150], a consultation service catering to patients grappling with degenerative retinal diseases like RP. Large surfaces are kept in dark colors to minimize glare effects which RP patients are often sensitive to [114], and text is presented in sizable fonts with strong contrast. Interface elements become visually highlighted when the VR controller's selection ray hovers over them, clearly telegraphing button presses and mitigating the risk of unintended menu selections.

To ensure the feasibility of at-home usage, the GazeQuest framework must additionally be fully self-sufficient. This entails a simple and intuitive design that allows independent operation by users who otherwise may struggle with the use of VR technology in consequence of their visual condition. Thus, the interface was deliberately kept simple, with menu screens including only a few large, color-contrasted buttons at the center of the field of view (Fig. 3.1 - Task selection menu). Another consideration for the integration of the VR based setups in a home environment is that of spatial independence and risk mitigation. VR devices apply position tracking to detect physical locomotion of the user, projecting that real-world movement into the virtual scene. However, as the interior layout of each user's home varies, it cannot be guaranteed that there is sufficient space to move around effectively and safely. Thus, the VR framework was designed for use solely in stationary standing or sitting position, minimizing risks for accidents or collisions during use. Lastly, patients were provided with direct automated feedback regarding different aspects, including their task performance and information on different gaze-related aspects, as will be mentioned in later parts of this work. Performance feedback has been shown to positively impact training effectiveness [151], as it allows patients to better self-assess the impact that their different actions and approaches within the training have.

3.1.3 Rationale for visual task design

One of the central goals for the GazeQuest is its use as a gaze training tool, evaluating its effectiveness to influence real-world navigation performance and gaze behavior of RP patients. This aim guided the design and implementation of visual tasks. Again, the design process came with a unique set of considerations and challenges, aggravated by

the lack of established principles in VR based gaze training – especially for peripheral VFDs. It was previously mentioned in chapter 1.3.3 that in the context of unsupervised training settings, gaze training tasks must inherently facilitate specific gaze-related behavior and strategies that can improve the performance in daily visual tasks. The metrics defining 'positive' gaze behavior, described in chapter 3.2.1, generally involve larger and more frequent eye movements, along with efficient eye movement patterns that result in a larger observed visual area. Consequently, the visual training tasks for the GazeQuest were specifically selected and modified to incentivize such desirable gaze behaviors.

A second key factor guiding the design process was a profound understanding of the daily challenges faced by individuals living with peripheral VFD. This was done to ensure that the results acquired within the VR framework are representative of – and relevant to – the real-life experience of patients. Three prominent challenges consistently associated with peripheral VFD were identified and addressed.

The first challenge involves the difficulty of **motion perception and tracking of moving targets**. Peripheral vision plays a crucial role in motion perception [152]–[154], as even the most de-centric regions of a healthy VF are still sensitive to moving stimuli, despite their low spatial resolution. The loss of peripheral vision – as caused by conditions such as RP – thus majorly impairs the ability to detect motion and to predict motion paths. Acknowledging this challenge, the first visual task of the VR framework was built around moving target tracking. The design was inspired by previous implementations in the field of attention allocation [155]–[157].

The second challenge addressed through the visual task design is related to **visual search** [158]–[161]. Individuals with a reduced VF are severely limited in the area they can observe at any one time, and there are no peripheral visual cues to assist in the search process. This limitation can significantly prolong the time required for everyday visual search situations, such as locating keys or products in a supermarket [160]–[162]. To partially offset the impact of a decreased VF, patients must utilize gaze movements to scan their visual surroundings. The second task implemented in the VR framework provides a basic visual search task that encourages patients to develop strategies that increase their ability to scan large areas in a short amount of time. The task is based on previous gaze training solutions by Ivanov et al. [111] and Nguyen et al. [113].

Lastly, the third challenge connected to peripheral VF loss is that of **navigation and obstacle awareness** [162]–[166]. Two factors play a role: For one, the decrease of

the VF increases the risk of entirely missing an obstacle and colliding with it due to unawareness of its existence. At the same time, the peripheral VF is known to be related to visuo-spatial perception [167], [168], describing the ability to estimate spatial dimensions and relations. Thus, a lack of the peripheral VF makes it more difficult to navigate around obstacles even if the existence of the obstacle is known. Furthermore, the lack of a complete picture of the spatial surroundings makes optimal path planning more difficult. To address these challenges, a third task was integrated into the VR framework, focusing on obstacle awareness and navigation. The task follows the concept of mobility courses as they are used in various experimental settings [102], [169], [170].

A notable innovation in the design of the GazeQuest lies in the implementation of adaptive difficulty levels. This approach of adaptive training involves the integration of variable parameters into visual tasks [171], such as the speed or quantity of targets to be observed, or the dimensions of the search fields in which targets may appear. These parameters dynamically adjust to the user's current performance utilizing a step-wise performance threshold. Once a user consistently performs above a specified performance threshold, set individually for each task based on the respective success criteria, the system incrementally shifts the variable parameters towards higher difficulty. Similarly, consistent performance below the defined threshold gradually decreases the difficulty of the task. This adaptive feature ensures that tasks consistently challenge users, irrespective of their inherent capabilities or training experience. It thereby optimizes the user experience and motivation and maximizes the potential for skill development [171], [172]. The advancements in task performance are conveyed to participants through a visual progress indicator, expanding upon the performance feedback scores discussed in the previous chapter.

3.1.4 Considerations in automated data capture

The use of the GazeQuest outside of the controlled confines of an experimental environment required considerations towards the method and quality of data capture. During home-based experiment phases, all measurements of task performance and gaze behavior were saved in CSV file format directly on the VR device. This facilitated the extraction and evaluation of data once the experimental phase was completed and the device was returned. However, the approach still raised a challenge: In controlled experimental environments, interference from external factors is rare and if it occurs,

the experimenter can exclude affected trial data from the data set. In uncontrolled environments, interference from external factors is more prominent and can potentially falsify the results. Sudden distractions, such as a ringing doorbell, or unexpected hardware issues, such as signal loss of a controller, might force the user to interrupt the training mid-trial. To avoid such events impacting the results captured with the GazeQuest framework, the menu screen in-between each trial featured the option to mark a trial as invalid and to re-set all progress from the trial. While this feature could potentially be abused by patients to exclude valid trials in which they performed below average, users were instructed to use this feature only in cases where the results were clearly influenced by external and unforeseen factors. A retrospective analysis of the trials marked as invalid did not reveal any signs of misuse.

3.2 Experimental implementation

The GazeQuest has been applied in three distinct experimental studies, described in detail in Publications A-C. These studies served two purposes: Firstly, they evaluated the adequacy of the GazeQuest's design, determining its feasibility and effectiveness as a home-integrated tool for gaze training and RP research. Secondly, the study outcomes offer valuable insights, uncovering innovative approaches for rehabilitating VFDs in RP patients and for facilitating visual accessibility tests through VFD simulation. The following chapters will summarize the purpose, methods, and results of each study and discuss their roles in the broader context of the project. First, however, a brief overview of the different gaze-related concepts and parameters used in these studies will be provided.

3.2.1 Relevant gaze parameters, definitions, and methods of detection

In eye-tracking and gaze behavior research, the temporal change of the gaze is usually described through **fixations** and **saccades** [173], [174]. Fixations describe moments, typically only lasting for a fraction of a second, in which the gaze has a steady focus on a single fixed point in the world. Meanwhile, saccades describe the rapid eye movements between fixations. However, raw eye-tracking data samples typically only consist of a time stamp and a gaze direction vector, from which the angular gaze speed can be calculated. To determine whether a data sample is part of a saccade or fixation,

different algorithms have been suggested over time [174]–[178]. In this work, a well-established algorithm by Nyström et al. [174] is applied. Specifics on the method are described in the methods sections of Publications B and C, and a visualization of the saccade detection results is found in Fig. 14 in Appendix C of Publication B.

- The **dynamic visual field (DynVF)**, also called dynamic field of view in Publication A, is a parameter that describes visual area observed over time. In other words, it describes how effectively an individual with VFD scans their surroundings. In this work, DynVF is measured over three-second intervals and is reported as percentage of a healthy visual field. DynVF is largely unaffected by low eye-tracking accuracy, as it relies on the relative motion of the gaze across the visual field, rather than exact gaze positions. A comprehensive explanation on the calculation of DynVF is found in Appendix S1 C of Publication B, and a visualization of it is found in Publication C, chapter 2.6.2.

- **Exploratory saccade ratio** is a metric used in the context of VFDs [111], [179]. It describes the ratio of saccades that target a fixation point outside of the visual field.

- Other parameters used in the evaluation include i) the **saccade frequency** as the number of detected saccades per second, ii) the **ratio of vertical to horizontal gaze movements**, and iii) the **ratio of head- to eye-related gaze movements** describing how much head motion contributed to the total average saccade amplitude.

- Lastly, the **gaze pattern similarity** describes how closely specific saccade sequences displayed by a user match a pre-determined 'ideal systematic gaze pattern', which will be defined in Publication A and chapter 3.2.2. A theoretical similarity value of 100% indicates that the user perfectly followed the suggested gaze pattern. Similarity values of 50% or lower typically indicate that no effort is made to follow the suggested gaze pattern. The gaze pattern similarity is calculated using an implementation based on the MultiMatch algorithm [180], described in the Appendix S1 A of Publication B. Applying a binary search tree [181], real-time performance of the implementation was achieved, allowing to provide users with direct feedback within the GazeQuest training. Unlike many other 'Scanpath' analysis methods that are often used in gaze analysis and describe a sequence of fixations on different areas of interest [182], [183],

this MultiMatch-based analysis is independent from predefined areas of interest [184]. As was explained in chapter 3.1.1, this independence facilitated the method's usability for dynamically changing scenes and reduced the impact of low eye-tracking accuracy.

3.2.2 Summary and discussion of Publication A: Evaluation of systematic gaze patterns

Systematic gaze patterns describe sequences of deliberate eye movements that aim to efficiently 'scan' the visual surroundings for a given task. The potential benefit of such systematic gaze patterns on VFDs has been suggested in several studies [133], [163], [185] primarily related to hemianopia, and Ivanov et al. hypothesized their positive effect on gaze training for RP patients [111]. This motivated the investigation of the influence of different systematic gaze patterns in individuals with peripheral VFDs, evaluating their potential effectiveness for gaze training.

Two gaze patterns were considered (visualized in Publication A, Fig. 1). The first describes a horizontal pattern of alternating horizontal left-right and right-left gaze movements (Publication A, Fig. 1a), as applied by Nelles et al. [133] and commonly suggested in Orientation & Mobility guides for individuals with visual impairments [186], [187]. The second pattern describes alternating saccades between the center of the VF and the periphery at varying angles, creating a radial pattern that systematically scans the periphery (Publication A, Fig. 1b). A similar pattern has been described by Kübler et al. [24] to correlate with higher driving performance in glaucoma patients.

Methods

To test the influence and effectiveness of the gaze patterns on visual tasks, as well as to test the application of the early GazeQuest prototype under experimental conditions, a minimum viable proof-of-concept study was conducted. A group of nine visually healthy participants was recruited and a peripheral VFD was simulated and applied to the virtual content displayed to the participants within the GazeQuest framework, aiming to replicate the effects of an RP condition. As was mentioned in chapter 1.2.5, this simulation approach was suggested in preliminary studies [65], [67], [85] based on qualitative findings. The choice for this approach was driven by the fact that individuals who participated in this preliminary proof-of-concept study would not be eligible to participate as naïve subjects in the subsequent gaze training experimental

trial. Recognizing the inherent challenges in recruiting even smaller sample sizes of patients with rare visual conditions such as RP [110], any measures that would further diminish the pool of potential participants for the gaze training trials were avoided.

Participants carried out three supervised 90-minute sessions using the GazeQuest. Each session was dedicated to one of the three gaze conditions: Two sessions focused on the two systematic gaze patterns; the third session included a 'free' gaze condition in which patients were not instructed to follow any specific gaze pattern. A VR based interactive visualization of the respective systematic gaze pattern was presented to participants at the beginning of a session. Following that, the participants were tasked to carry out multiple sets of visual task trials provided by the GazeQuest, while simultaneously following the instructed systematic gaze pattern. Notably, only the visual search task and navigation task of the GazeQuest framework were included in the experimental setup for this study. The moving target tracking task was determined unsuitable for the test of systematic gaze patterns, as a more effective strategy in this task is a dynamic, fast, and frequent switch of fixations between the randomly moving targets, which would interfere with the execution of systematic gaze patterns.

Results and discussion

Data on visual task performance as well as gaze direction was collected during all three sessions. The results (Publication A, Fig. 4) show that adopting the horizontal gaze pattern led to higher performance and more efficient visual scanning than the radial pattern in the navigation task. Visual scanning efficiency was measured in the form of the DynVF displayed by patients. Compared to the reference condition of 'free' gaze movement, the adoption of the horizontal gaze pattern significantly improved DynVF ($p=0.034$) and collision avoidance ($p<0.001$) in the navigation task. However, the average walking speed within the navigation task was significantly decreased ($p=0.0011$). No significant differences were found in DynVF ($p=0.099$) and task performance ($p=0.804$) in the visual search task. Patient questionnaires that were conducted after each session found that the horizontal systematic gaze pattern was favored over the radial pattern, being described as more intuitive and less physically and mentally straining. In conclusion, the findings of this study came with a nuanced perspective. While the horizontal gaze pattern showcased enhanced performance in visual scanning and collision avoidance, it concurrently led to a significant reduction in average walking speed during the navigation task. This observation is consistent with prior research by Gunn et al. [131] which reported a trade-off between enhanced

obstacle avoidance and reduction in walking speed following instructed gaze training. Consequently, this study's findings suggest further research into the effectiveness of the horizontal systematic gaze pattern, including its impact after a longer adaptation phase. However, based solely on the existing findings, the integration of a systematic gaze pattern as mandatory and actively enforced component of the GazeQuest's training paradigm was not justifiable. Still, the positive effects regarding collision avoidance and DynVF have to be recognized. Thus, the execution of the horizontal gaze pattern was included as a voluntary objective in the gaze training, as will be described in the next chapter.

3.2.3 Summary and discussion of Publication B: Evaluation of VR based gaze training for retinitis pigmentosa patients

Earlier in this work, the crucial need that exists for rehabilitation methods tailored to people coping with VFDs was introduced. Challenges encountered in everyday visual activities [160]–[162], [165], increased risk of accidents [159], [166], and a notably heightened risk of anxiety and depression [33], [34] collectively underscore the detrimental impact of VFDs on the quality of life for those affected. This need is further strengthened by the severe lack of medical treatment options that exists especially in the field of inherited retinal diseases such as RP [35], [124]. Gaze training was introduced as a non-invasive and engaging rehabilitation tool. It can facilitate the effective use of the remaining field of view of patients and the development of compensatory strategies through specialized visual tasks [111], [113], [131]. However, its effectiveness, especially in peripheral VFDs, is little understood.

It was also discussed that VR technology provides a multitude of features that make it a promising tool for visual training and research paradigms. Despite this, no study has so far investigated the feasibility and effectiveness of VR based gaze training for patients with peripheral VFD. Even for other VFDs, existing literature on VR gaze training is scarce and its effect on real-world performance and behavior is little understood. Thus, this study represents an important first step in the field of VR based gaze training for RP patients, and it can provide a blueprint for future studies investigating the effect on other VFDs.

Methods

In this study, ten individuals diagnosed with RP, featuring VF sizes ranging from 8°-25° diameter, participated in a four-week gaze training period. Two of the patients discontinued their participation early on, stating issues related to the use of VR technology, as will be discussed later in this chapter. The training, conducted at home, involved daily 30-minute sessions using the GazeQuest. All three visual tasks – moving target tracking, visual search, and navigation – were incorporated into the training. The study design included a second four-week phase void of any gaze training activities, serving as reference and control for the training phase. Both phases were completed by the same group of patients in randomized order. As mentioned in the previous chapter, patients were visually introduced to the horizontal systematic gaze pattern prior to training and were informed about its potential benefits and limitations. To assess the effectiveness of gaze training on performance and gaze behavior in real-world settings, an obstacle course was set up (Publication B, Fig. 6). Before and after each phase – training and control - patients were tasked to navigate the obstacle course, prioritizing collision avoidance while also emphasizing high walking speed. Each session consisted of 20 trials per participant, with the obstacle layout randomized between trials. Results were statistically analyzed applying Linear Mixed Models (LMMs) for walking speed and gaze parameters, and a negative-binomial Generalized Linear Mixed Model that addresses an issue of high zero-inflation found in the collision parameter.

Results

After training, navigation performance in the real-world obstacle course – described by collision avoidance and walking speed – improved significantly compared to the control phase (Publication B, Fig. 8). Patients, on average, displayed 50.0% fewer collisions and 17.0% higher walking speed following the training period. This significantly surpasses the 10.4% reduction in collisions ($p=0.0165$) and the 5.9% increase in walking speed ($p<0.001$) that were detected after the control phase. Individual patients displayed notable positive changes in DynVF and other gaze-related parameters (Publication B, Fig. 9). The average increase in DynVF after training was 4.4%, which represents a significant increase compared to the results pre-training ($p<0.001$) but was not significantly higher than the 2.1% increase detected after the control phase ($p=0.394$).

Gaze training influence on spatial navigation

Patients who exhibited noticeable positive changes in their gaze behavior also demonstrated substantial improvements in navigation performance, indicating a positive correlation. However, there were instances where patients showed enhanced navigation performance without a substantial increase in DynVF. This suggests that the benefits of gaze training on real-world navigation performance may extend beyond improved visual scanning ability. One potential contributing factor could be that of visuo-spatial perception. VFDs are oftentimes associated with distortions in visuo-spatial perception [167], [168], which make it challenging to accurately estimate distances and spatial relations. A study conducted by Kang et al. [188] demonstrated that training in an immersive virtual environment significantly enhanced visuo-spatial perception in individuals with cognitive impairments. This enhancement is attributed to so-called neuroplasticity: A process of neural restructuring in the brain – in case of visuo-spatial perception in the visual cortex [167] – that improves cognitive abilities related to specific tasks [189] and can occur even in older adults [190]. This suggests that the VR based gaze training might induce neuroplasticity processes in the visual cortex, enhancing visuo-spatial perception. Importantly, due to the neurological nature of this effect, it would not necessarily manifest in observable changes to the gaze behavior. Consequently, this neurological effect provides a possible explanation for the observed increase in navigation performance even in the absence of gaze behavior changes.

Effectiveness of visual task design

Measurements of task performance and gaze data were also taken during training within the VR framework. Here, significant improvements over the course of the four-week training phase are found across all patients and parameters. Task performance increased in all three visual tasks ($p<0.01$ for all tasks) (Publication B, Fig. 11). DynVF during tasks increased by 43.4% in the moving target tracking task ($p<0.001$), 29.9% in the visual search task ($p<0.001$), and 19.8% in the navigation task ($p<0.001$). Notably, the DynVF increase within the virtual training setting is drastically higher than the increase of 4.4% found in the real-world setting after training. These findings have two important implications. Firstly, they highlight that the design of the visual training tasks of the GazeQuest is successful in achieving its intended objective, which is to prompt larger and more efficient gaze movements in patients, without a need for external reminders or instructions. However, this adopted gaze

behavior only seems to minimally transfer from virtual to real-world settings, specifically in real-world mobility tasks. It remains to be evaluated whether these results on translation of gaze behavior differ in other tasks, but it aligns with results reported by Harris et al. for transfer of gaze behavior in visually healthy people [88]. Furthermore, the results suggest investigations on adjustments to the gaze training paradigm to increase the transfer rate of adopted gaze behavior. Such adjustments could include more life-like and realistic scenarios, as suggested by Levac et al. in the context of motoric skills [191]. Another alternative will be discussed in a later chapter in the context of emerging technologies, in particular that of Mixed Reality.

Systematic gaze pattern

There was no indication of patients adopting the horizontal systematic gaze pattern that was introduced to them as voluntary objective (Publication B, Fig. 10). Similarity between the systematic gaze pattern and the gaze patterns displayed by patients did not change significantly after training ($p=0.168$). However, two patients stated to have successfully adopted a different systematic gaze pattern over the course of training. One of the two patients described their gaze pattern as a sequence of circular motions, starting with a small circle around the central field of view, gradually extending outward to encompass larger circles covering the periphery. Notably, of all the participants, this patient demonstrated the highest enhancements in real-world measurement parameters of collision avoidance, walking speed, and DynVF after the training sessions. They also reported to have adopted this pattern in daily activities, with a positive impact on their quality of life. Overall, the observations suggest that the horizontal gaze pattern does not seem to be well adoptable among the patients, as even patients who showed interest in following systematic gaze patterns preferred to develop their own pattern. While this does not prove the ineffectiveness of the horizontal gaze pattern, it does highlight the importance of considering alternative, possibly individualized, patterns in future gaze training designs, and it expands the original hypothesis of Ivanov et al. [111].

Comparison to literature

A comparison of the GazeQuest to screen-based gaze training approaches with similar experimental setups suggests that VR based gaze training provides more consistent and distinct improvements in navigation performance. Reported effects on real-world

navigation performance in previous experimental setups were mostly limited to one of the two investigated parameters of collision avoidance or walking speed. Ivanov et al. [111] found a small increase in walking speed, but no change in obstacle avoidance after training. Meanwhile, Kuyk et al. [135] and Gunn et al. [131] report enhanced obstacle avoidance, but no significant change or even reduction in walking speed. A direct comparison between the different approaches under standardized experimental conditions is required to validate their statistical relation.

Usability

The successful completion of the VR training in eight patients of varying ages, from 20 to 60 years, supports the general feasibility of the GazeQuest for unsupervised, home-based training. However, two instances in which participation was discontinued highlight the fact that there are limitations in the application of VR gaze training that need further addressing. These include difficulties in independent operation and orientation within the virtual environment, which has led to inability to complete the training. Furthermore, a possible correlation between the use of VR and an increase in migraine attacks has been reported. Such limitations must be considered and addressed in future implementations of VR based gaze training solutions.

3.2.4 Summary and discussion of Publication C: Evaluation of simulated peripheral visual field defects

As previously discussed, the relatively low prevalence of visual conditions such as RP poses a notable challenge in visual research and accessibility assessments for these specific groups [110]. The small pool of individuals with these conditions complicates the process of recruiting large study populations. This can result in prolonged acquisition phases, insufficient data samples for establishing statistical significance, and a lack of prototype testing with actual patients.

One potential approach to address the issue involves the simulation of specific visual conditions in visually healthy individuals. This method allows the individuals to experience visual scenarios akin to the way actual patients do, enabling them to participate in experimental trials focused on visual impairments. This method has been successfully employed in studies related to low-vision conditions, examining the impact of visual acuity on perception of ramps and stairs [192] or the influence of lighting conditions for different visual impairments [193]. In the field of VFDs, this

approach has been proposed following the emergence of VR technology integrated with eye-tracking capabilities [65], [67] that enable gaze-contingent simulations. As mentioned, this also motivated the simulation approach described in Publication A. However, it must be acknowledged that the full extent of living with VFDs cannot be perfectly replicated with current technology [5]. Even if the visual experience of the simulation could be exactly matched to real conditions – an ongoing challenge in itself [5], [194]–[196] – other critical factors must be considered as well. Patients develop coping mechanisms and adapt to their visual conditions over years, whereas individuals using a simulation lack this type of adaptation [197]. Furthermore, the brain tends to automatically compensate for missing visual information in areas affected by VFD, often leaving patients unaware of the full extent of their condition [198], [199]. In contrast, visually healthy participants actively perceive the areas of missing visual information. Recognizing these inherent limitations in VFD simulation, it becomes imperative to understand and directly compare the impacts of real and simulated VFDs on various skills and behaviors. Such a comparison relies on three crucial components: A data set from a group of patients with VFD, a data set from a group of visually healthy participants with simulated VFD, and a standardized experimental setup in which both data sets are acquired under the same experimental conditions. However, previous studies [66]–[68] have so far only investigated effects of VR based VFD simulations on visually healthy individuals, lacking a reference group of actual patients and thus insights on the quantitative relationship between real and simulated VFD conditions.

The GazeQuest framework, combined with the data set from the previous gaze training study, provided an ideal groundwork for a study addressing this gap. The GazeQuest framework offers a standardized experimental environment. Meanwhile, the data that was captured within the VR setting in the previous study represents task performance and gaze behavior of a patient group with VFDs, particularly RP. This covers two of the three mentioned components and offers the possibility to acquire the third component – a data set from visually healthy participants with simulated VFD – within the GazeQuest framework.

Methods

A group of eight visually healthy participants was recruited. The group was age-matched to the eight RP patients from the previous study. Utilizing data of the VFs of the RP patients, a set of eight custom simulated VFDs were created to match the

dimensions of VFs of the patients. The eight visually healthy participants then underwent the exact same four-week at-home gaze training that was described in the previous chapter. Notably, however, participants were subjected to gaze-contingent simulated VFDs that were displayed within the virtual environment of the gaze training. The simulated VFDs were assigned such that each participant experienced a VF loss mirroring that of the corresponding age-matched RP patient. Different parameters on visual task performance and gaze behavior were measured during training in the virtual environment and were statistically compared to the results of RP patients. Notably, two separate statistical models were applied for each parameter: A 'two one-sided test for equivalence' method [200] was used to test for significant similarity between both groups. Meanwhile, LMMs or generalized LMMs were applied to test for differences between groups. Cases in which neither of the two tests show significance indicate that the sample size for the measurement parameter is insufficient to make clear statements.

Results and discussion

Both groups – RP patients and individuals with simulated VFD – demonstrate similar performance in most visual tasks ($p<0.001$ for visual search, collision avoidance, and walking speed; $p=0.98$ for moving target tracking) (Publication C, Fig. 5). These results are surprising, as they suggest that the patients' years of experience in adopting to their condition have little influence on visual task performance. It must be noted, though, that all findings of these experimental trials only relate to performance and behavior within a virtual setting. In both groups, six out of eight patients reported to be completely unfamiliar with the use of VR technology. It is possible that, especially in the early stages of the trials, the impact of this unfamiliarity – which is similarly present in both groups – outweighs the impact of the different experience levels with VFD. Given that the applied method of gaze-contingent VFD simulation is inherently limited to virtual settings, a comparison between groups in a real-world environment is not possible with the current setup. However, chapter 3.3 will address a potential solution to this limitation that utilizes the emerging technology of Mixed Reality.

Regarding the gaze behavior of the two groups within the virtual setting (Publication C, Fig. 6), fewer similarities are found. Most noticeable are differences in the ratio between head movements and eye movements ($p<0.01$ in all three visual tasks). Participants with simulated VFD display a higher number of head movements compared to the RP patient group. This observation must not indicate an inherent difference

between RP patients and visually healthy individuals but can rather be explained by the technical limitations of the setup. It was mentioned in chapter 3.1.1 that the latency of the applied eye tracker is assumed to be around 79 ms. According to Albert et al. [201], latency in eye-tracking starts becoming noticeable in the range of 50-70 ms. This suggests that patients, consciously or subconsciously, perceived the latency as delay in the simulated VFD. This could decrease their reliance on eye movements for scanning. Notably, only one participant with simulated VFD reported to have noticed a slight delay of the simulated VFD, though it was described as unobtrusive.

Another important finding of the analysis of gaze behavior in both groups is the existence of significant effects which indicate a convergence of gaze behavior over the course of the four-week training phase. In other words, while both groups display different gaze behavior at the beginning of the training, these differences decrease significantly over time. This is a crucial insight, as it suggests that participants with simulated VFD may adapt similar gaze behavior to that of real patients already over a relatively short period of time.

3.2.5 Summary of experimental achievements

The works detailed in the previous chapters represent a substantial advance for understanding VR's potential in the rehabilitation and simulation of VFDs. They also provide new insights and raise considerations that will influence future iterations and new implementations of VR based solutions for VFDs.

Experimental results revealed substantial training-related improvements in collision avoidance and walking speed in RP patients after VR based gaze training, with more consistent results than reported for non-VR training solutions [111], [113], [131], [179]. Observations from this work further suggest another advantage of VR based setups: The enhancement of visuo-spatial perception in patients with VFD, attributed to the realistic visual experience offered by VR devices. The findings of the gaze training highlight the importance to consider an individualized approach on systematic gaze pattern training, as patients may benefit more from developing personal systematic gaze patterns than applying pre-defined patterns. A quantitative and controlled evaluation of the validity of VR based simulated peripheral VFDs reveals a surprising similarity between visual task performance under real and simulated conditions. It also shows convergences of gaze-related parameters between real and simulated VFD conditions that suggest that individuals with simulated VFD may relatively quickly

adopt gaze behavior mirroring that of real patients. Lastly, the experimental trials demonstrate both the feasibility, but also the remaining challenges related to the use of VR in home-based solutions for training and research on VFDs.

3.3 Current and future opportunities in research and technology

The findings of this work revealed prospective advancements in the application of VR technology in the field of VFDs. However, it also raises challenges and questions that prompt further research, as well as exploration of new and emerging technology to approach these challenges. Looking beyond the scope of the thesis, this chapter delves into some of these prospective research topics and technological advancements, providing a brief overview and discussion.

3.3.1 Cross-condition applicability

To ensure homogeneity in the clinical pictures of participant groups, the experimental trials of this work focused solely on the condition of RP. The positive outcomes observed in the presented studies, however, prompt investigation into the applicability of VR solutions for a broader range of VFDs. It can be expected that the demonstrated approaches for both gaze training and VFD simulation translate well to other conditions with peripheral visual field loss, such as glaucoma (Fig. 1.1b), without the need for major adjustments to the setup. While only explicitly tested for RP, the GazeQuest's design – including that of the visual tasks – is based on visual challenges associated with all causes for loss of peripheral vision [152], [158], [164]. Thus, there is strong reason to believe that glaucoma patients would benefit from the GazeQuest framework to a similar degree as the recruited RP patient group. Furthermore, glaucoma is the most prevalent cause of visual field loss in elderly individuals [202], affecting an estimated 3.5% of people between the age of 40 and 80 [203]. Therefore, statistical evaluation of the effectiveness of VR based gaze training in glaucoma patients will be a main priority of subsequent research on the GazeQuest. For hemianopia (Fig. 1.1a), visual task design would likely have to be adjusted, as the half-sided visual field loss found in this condition requires different adaptive strategies [132], [133]. Lastly, AMD (Fig. 1.1c) is associated with an entirely separate set of visual challenges compared to those faced by individuals with peripheral VFD [204], [205]. While VR based training

for AMD patients has previously been implemented [94], significant effectiveness of the approach has not yet been shown.

3.3.2 VR as a multi-purpose tool for visual field defects

In the introduction of this work, a large number of studies investigating the use of VR technology for perimetry – measurement of the visual field – was highlighted [54], [55], [69]–[74]. Hu et al. [71] and Chia et al. [72] specifically mention the success of this method as home-integrated diagnostic tool for patients with VFDs. Combining the thoughts of these innovations with the promising findings for the gaze training solution of the GazeQuest highlights the potential of VR technology to become a vital multi-purpose tool for patients with peripheral VFDs. Such a tool could not only aid patients in improving their visual capabilities and navigation performance but simultaneously provide an easy solution for frequent and effortless monitoring of the VF, providing clinicians with a detailed record on the progression of visual field loss.

3.3.3 Further gaze training investigations

There are several other research endeavors motivated specifically by the gaze training study. Firstly, no information currently exists on long-term efficacy, both for the training presented here as well as for other comparable gaze training [111], [113], [179]. Considering a potential practical application of gaze training outside of a scientific context, it is pivotal to understand whether permanent improvements can be achieved through a single temporary training period, or if sustained training is required. Secondly, the method of voluntary execution of systematic gaze patterns has proven unsuited for unsupervised home-based training, yielding no significant adoption of the suggested gaze pattern by the patients. However, observations suggest a connection between the application of a personalized systematic gaze pattern and a drastic increase in navigation performance in one of the gaze training patients. While this possible link is based on a single case and does not provide significant validity, it underscores the potential beneficial relationship between gaze training and systematic gaze patterns. This motivates the identification of alternative and individualized systematic gaze patterns, as well as the design of new experimental paradigms better suited to evaluate their effect.

3.3.4 Opportunities in emerging and future technologies

As has been mentioned in the introduction of the thesis, VR is a rapidly evolving field [7], [9], [10], [38]. Novel hardware and software solutions emerge every year, and existing technology becomes more performant, accessible, and compact. This section outlines the potential impact of emerging technologies and anticipated future developments on the capabilities of VR within the field of VFDs.

Many recent advancement or innovations in development target the **optical system** of VR devices, consisting of displays and lenses to focus the image on the retina. For one, several novel approaches aim to reduce the distance required between displays and lenses [206], [207]. This allows for more compact designs of the VR device, bringing its center of mass closer to the head and therefore minimizing slippage as well as physical strain from extended usage periods. Another innovative technology is that of varifocal lenses. In a real visual scenario, our eyes typically adjust their focus based on the distance of the object being viewed - a process called accommodation. However, current optical systems employ static lens designs that refract light in a fixed manner, eliminating the eye's ability to accommodate to varying distances. Varifocal lenses, on the other hand, feature an adjustable focal point [208]. Using precise eye-tracking, it is possible to identify the point or object focused by a user within a virtual scene. The varifocal lens can then be dynamically adjusted to refract the light of the display in a way that mimics the natural effects of light originating from a respective distance. This allows the eyes to naturally accommodate within the virtual scene, improving the realism of the visual experience and facilitating depth perception. This technology may be especially important in the context of peripheral VFDs, since other forms of depth perception - such as binocular vision or parallax effect mentioned in chapter 1.1 - may be impaired by the loss of peripheral vision. Meta has showcased a prototype highlighting the feasibility of this technology to be integrated in consumer-level VR devices [207].

While not limited to the use in VR, **eye trackers** are a crucial component of many VR based setups. As mentioned in the previous point, accurate eye-tracking is required to realize varifocal setups. Similarly, gaze-contingent simulations of VFDs ideally require high accuracy and low latency of the eye tracker, as has been discussed in chapter 3.1.1. Lastly, high eye-tracking accuracy in combination with dynamic classification of regions of interest - using deep neural networks [209], [210] or other algorithms [211] - allows for more detailed and scene-context-aware analysis of gaze behavior, Scanpaths, and obstacle awareness. This could provide additional insights

for designing optimized gaze patterns or for comparing the gaze behavior under influence of simulated and real VFDs. A promising innovation especially for the issue of eye-tracking latency is the use of neural networks over computer vision based algorithm for gaze estimation or pupil detection [212]. Whereas eye-tracking systems integrated in current VR devices have reported latency of around 45-81 ms, neural networks promise latency in sub-millisecond range at comparable accuracy [212]. In terms of accuracy and precision improvements, neural network based eye-tracking shows promise as alternative to current approaches [7], [213], [214], though it does not yet outperform gold standard laboratory eye-tracking devices [215]. Furthermore, integration of calibration-free eye-tracking methods [216] could further facilitate the usability of eye-tracking especially outside of controlled experimental conditions, such as in home-based environments.

As observed in the presented gaze training study and suggested by Harris et al. [88], adaptations in gaze behavior displayed in VR only exhibit limited transfer to real-world settings. This may negatively influence the effectiveness of VR based gaze training, as mentioned previously in chapter 3.2.3. It also represents a major limitation to the validity of results of current VFD simulations. Most experimental setups in vision science ultimately seek to investigate real-world effects. If results obtained within a virtual setting do not accurately reflect real-world behavior, then the proposed method of simulating VFDs to expand study populations becomes impractical. A promising solution to this problem is offered by **Mixed Reality (MR)**. MR describes a technology that merges video capture of the real world with overlayed virtual content. MR devices provide all the functionality of a standard VR device. However, the ability to simultaneously display the real-world surroundings to the user and combine elements of both real and virtual content in a single setup vastly expands that functionality, offering new possibilities in vision research [217], [218]. For gaze training and rehabilitation methods, MR offers the ability to integrate visual training tasks into real environments, bringing the visual experience during training closer to that of real-world scenarios. In the context of VFD simulation, MR allows to replace virtual settings with a display of the real environment. This enables participants to interact with the real world while simultaneously being subject to the simulation of VFDs. For seamless and accurate presentation of MR scenes, it must be determined when virtual scene elements would be partly or fully obscured by real-world objects. Because of this, accurate depth mapping of the real-world environment is required for high-quality MR experiences. Until recently, VR devices capable to provide high-quality MR experiences are scarce, ex-

pensive, and unsuited for mobility tasks or home-based use due to dependency on external hardware [219]. However, the landscape of MR is now rapidly changing. New deep-learning methods promise improved depth mapping quality [220], facilitating the spatially accurate occlusion of real and virtual scene elements. Furthermore, the Meta Quest 3 [221], released in October 2023, marks the first stand-alone device with high-quality MR functionality, followed by the Apple Vision Pro [222] scheduled for release in early 2024. It can be expected that these two releases will popularize MR, including its application in the field of vision science. As a result, the potential of this emergent technology, particularly its applications in VFD research, will represent a main focus of future investigations following this work.

3.4 Outlook and continued development of the GazeQuest

The findings of the described experimental trials have broadened the understanding of the potential of VR in VFD research. However, another promising achievement has emerged from this work: The developed GazeQuest framework has proven to be an effective and practical rehabilitation solution. In a clinical trial, the effectiveness of the GazeQuest as a gaze training tool for RP patients has been clearly demonstrated by the drastic improvement to collision avoidance and walking speed it provided. Furthermore, the feasibility of utilizing the GazeQuest framework for home-based visual exercises has been shown. A work-in-progress version of the software has been shared on the platform GitHub as an open-source project [223].

The significant potential of this technology as well as the demand in effective rehabilitation methods especially for RP supports the idea to transition the GazeQuest framework from an experimental context to a practical application as a consumer-grade rehabilitation tool. Based on the findings, observations, and patient feedback of the presented experimental trials, three key areas have been identified as focus of potential continued development and optimization: Accessibility, sustained motivation, and software robustness.

3.4.1 Accessibility and device compatibility

With the aim of practical application as a training tool for patients, usability and accessibility become a crucial consideration in the design and development of the Gaze-

Quest. This involves addressing two aspects: firstly, it must be ensured that patients have physical access to hardware capable of running the developed software. The current prototype of the VR framework was developed for a specific device – the Pico Neo 2 Eye – and was pre-installed before it was given to users. However, it is crucial that patients who already possess or can access a VR device, for example through family members, can effortlessly install and use the GazeQuest software on their respective devices. Furthermore, patients who consider the purchase of a VR device for gaze training should not face limitations in their buying choices. They should have the flexibility to select a device based on factors such as functionality, affordability, and comfort. Achieving this requires compatibility of the GazeQuest framework with a range of VR devices, with a priority on those popular in the consumer market, such as the HTC Vive series or the Meta Quest series. In addition to ensuring hardware compatibility, accessibility encompasses another critical aspect: users should be able to operate the software autonomously. This necessitates a straightforward installation process, comprehensive tutorials explaining software functions and visual task objectives, and a comprehensive help guide.

3.4.2 Sustained motivation and gamification

A second key area in the context of practical application involves improving the user experience and increasing the patients' motivation for frequent and sustained training. Without extrinsic motivation factors that were present during the experimental trials, such as monetary compensation or drive to support the scientific process, patients' motivation to use the GazeQuest training is tied solely to the personal benefits they see in it. Thus, when designing the GazeQuest for practical application, the factor of fostering motivation and avoiding feelings of boredom and stagnation becomes an even greater priority. In this context, the exploration of gamification will play a crucial role. Gamification, defined by Deterding et al. [224] as "the use of game design elements in non-game contexts", has been well investigated and demonstrated to positively impact learning tasks and behavioral change [225]. Moreover, it has been recognized for its ability to enhance user engagement and enjoyment across various tasks [225]–[227]. Its impact extends to the field of healthcare [227] and has already been studied and applied in various forms of ophthalmic diagnostics, such as in visual field testing [74], [228] or contrast sensitivity [229]. Even the gaze training tasks by Ivanov et al. [111], Roth et al. [179], and the ones presented in this work apply elements of gamification,

such as clearly defined challenges and goals as well as performance scores that quantify user's success. However, these gamification elements only represent the surface of the vast pool of strategies that can be applied to enhance user engagement and sustained motivation. Further exploration of these strategies should be a prime focus in the continued development of the GazeQuest software.

3.4.3 Software robustness

As a last key consideration, a focus must be put on software robustness. Industry-standard methods such as unit testing and integration testing [230], [231] should be applied to systematically isolate and examine individual components of the software and their interaction in order to identify and address potential faults. Additionally, the integration of robust error-handling mechanisms can prevent complete system breaks in cases of unexpected code behavior and instead revert the system to a stable state or provide users with simple instructions that may solve the issue. During the continued development stage, frequent user experience tests with patients should be conducted, allowing for fast iterations and patient-oriented design refinements.

3.4.4 Practical application

In addition to software development, the aim for practical application of the software in a real-life context demands financially realizable strategies for distributing the software. Several institutions and organizations focused on services, information, and networking opportunities for patients with visual impairments, such as Pro Retina [232], the 'Deutsche Blindenstudienanstalt e.V.' (blista) [233], or the 'Berufsbildungswerk für Blinde und Sehbehinderte Stuttgart Nikolauspflege' [234], have declared their interest in cooperating to explore effective strategies to make the GazeQuest training available to patients.

3.5 Conclusion

The work presented in this thesis marks significant steps towards the utilization of Virtual Reality in the rehabilitation of visual field defects. It offers new insights, demonstrating the effectiveness of VR based gaze training solutions for retinitis pigmentosa patients. The thesis also introduces a new, adaptable VR training framework that will

serve as foundation for continued research and development, aiming to offer a novel and engaging rehabilitation tool for individuals living with visual field defects. The tool is available as a work-in-progress open source software [223].

Furthermore, the findings within this thesis reveal a high similarity between performance under simulated and real visual field defects within virtual environments. Visual task performance of visually healthy individuals experiencing simulated peripheral visual field defects reflects the performance displayed by actual patients within a virtual setting to a significant degree. In addition, it is observed that the gaze behavior of individuals experiencing simulated visual field defects gradually adjusts, resembling that of actual patients more closely over time. These results support the practicality of employing VR based simulation tools to facilitate accessibility assessments and experimental trials related to rare visual field defects.

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Appendix

1 Publication A

brain sciences

MDPI

Article

Influence of Systematic Gaze Patterns in Navigation and Search Tasks with Simulated Retinitis Pigmentosa

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Abstract: People living with a degenerative retinal disease such as retinitis pigmentosa are oftentimes faced with difficulties navigating in crowded places and avoiding obstacles due to their severely limited field of view. The study aimed to assess the potential of different patterns of eye movement (scanning patterns) to (i) increase the effective area of perception of participants with simulated retinitis pigmentosa scotoma and (ii) maintain or improve performance in visual tasks. Using a virtual reality headset with eye tracking, we simulated tunnel vision of 20° in diameter in visually healthy participants (n = 9). Employing this setup, we investigated how different scanning patterns influence the dynamic field of view—the average area over time covered by the field of view—of the participants in an obstacle avoidance task and in a search task. One of the two tested scanning patterns showed a significant improvement in both dynamic field of view (navigation 11%, search 7%) and collision avoidance (33%) when compared to trials without the suggested scanning pattern. However, participants took significantly longer (31%) to finish the navigation task when applying this scanning pattern. No significant improvements in search task performance were found when applying scanning patterns.

Keywords: retinitis pigmentosa; visual performance test; visual field loss; vision impairment; goal-directed walking; visual search; virtual reality; gaze training

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1. Introduction

Retinitis pigmentosa (RP) describes a subset of diseases that lead to severe concentric loss of vision ("tunnel vision") in the peripheral field of view (FoV) [1–3]. It affects approximately 0.03% of the world population and is for the majority of cases not curable [4]. Although patients with RP oftentimes retain their normal visual acuity until late stages of the disease [5], the loss of peripheral vision was shown to severely limit the ability of patients to safely navigate and avoid obstacles [6,7]. However, the optic flow and judgement of direction is not affected by the decreased FoV [8,9], leading to the assumption that the decrease in navigation performance is caused mainly by a lack of obstacle awareness. This is further supported by the findings of F. Vargas-Martin and E. Peli [5], who showed that RP patients have a decreased average horizontal gaze amplitude compared to normal-sighted subjects. This seemingly contradictory behavior is assumed to originate from the lack of visual stimuli in the periphery, as gaze movement was shown to be guided by attention [10], and the target of a saccade rarely lies outside of the visual area. It must be noted, however, that other studies such as that of Turano et al. [11] have found contrasting results where the standard deviation of the gaze is significantly higher in RP patients compared to the visually healthy control group. Still, it can be assumed that in order to account for the lack of peripheral sight, larger gaze amplitudes are required in order to recognize obstacles and

navigate safely. Only the area that was covered by gaze within a certain amount of time has the potential to give information to people with tunnel vision in a similar way that the peripheral FoV gives information to visually healthy individuals. This "gaze area over time" will in the following be called "dynamic field of view" (DFoV).

The only approved causal therapy for RP has been available since 2017 in the USA and since 2018 in Europe for retinitis pigmentosa caused by bi-allelic mutations in the gene RPE65 [12]. Although there are promising studies in the field of gene therapy for further genotypes in RP that could prohibit the progressive loss of the peripheral field [13–15], they are still in early research phases and do not guarantee the rehabilitation of the visual field. Most cases of RP are detected only after symptoms already appeared, at which point the damage of the degenerated peripheral photoreceptors is almost always irreversible [13,14]. Other studies have investigated the use of external, head-mounted displays to artificially increase the FoV [16–22] by compressing a larger visual area into the remaining FoV of the patient.

A third approach, which our study focuses on, are methods to guide the gaze through training of voluntary and controlled saccades [23]. These gaze movements are typically slower than "natural" reflex-like saccades, so the question remains whether it can be applied as a neural plasticity training to become as fast and nonintrusive as natural saccades, which is suggested by the effectiveness of neural plasticity training on saccadic adaptation in visually healthy persons [24–27]. In a study carried out by Ivanov et al. [23] it was shown that training with a visual search task on a computer display, designed to demand and encourage larger saccades, could partially lead to navigation improvement in RP patients as they walked longer durations at their preferred walking speed after the course of six weeks of training. These findings are in line with similar studies investigating compensatory training for patients with hemianopia—the loss of the left or right hemisphere of the FoV, usually caused by a stroke—in which gaze training was also found to improve detection and reaction rates in different visual tasks [28–31]. However, the number of collisions with obstacles during the navigation trials did not decrease in Ivanov's study. This shows that the training of saccades has indeed influence on the navigation, but larger saccades alone might not suffice to improve the perception of obstacles, which suggests the addition of a more systematic gaze pattern to the training.

Being able to perceive a larger visible area may not only be important for obstacle awareness but for larger-scale orientation as well. Landmarks are an essential aid to remember a route or navigate unknown routes based on descriptions or maps. The selection of such landmarks is closely connected to the gaze behavior [32], and so an increased DFoV is likely to increase the number of detected landmarks and thus improve orientation and route learning.

When trying to improve the DFoV of patients with tunnel vision through systematic scanning patterns, the question arises as to which type of pattern is most beneficial. It can be assumed that the natural gaze behavior of visually healthy people is already optimal, as it is guided by the stimuli from peripheral vision. This, however, may not be the case for patients with tunnel vision or other conditions that occlude the FoV, as is suggested by previous studies of gaze behavior of people with visual impairments [23,28,30,33]. Here, no stimuli from the periphery of the FoV exist to draw the gaze toward important focus points in the scene. In these cases, the gaze direction is much more crucial for the general awareness of an object or point of interest in the scene.

In our study, we therefore investigated whether systematic scanning patterns have an influence on the DFoV as well as the performance in different visual tasks in participants with simulated tunnel vision and if so, which systematic scanning pattern has most potential to lead to improvements in visual tasks when being applied in training.

2. Materials and Methods

2.1. Ethics

This study was proposed to and approved by the ethics committee of the Institutional Review Board of the Medical Faculty of the University of Tübingen (628/2018802) in accordance with the 2013 Helsinki Declaration. All participants signed informed consent forms.

2.2. Software and Hardware Specifications

The experiment was performed in a virtual reality (VR) environment. By this, larger viewing angles than with a standard screen can be achieved. Furthermore, head rotations can be detected within the simulation to measure the influence of both head and eye movements in the different scanning patterns. The virtual experimental environment and visual tasks as well as the tunnel vision simulation were created for this study using the game engine Unity3D, Version 2019.2.

The VR headset on which the virtual content was displayed was the FOVE 0. It had a 70 Hz screen refresh rate and a 120 Hz eye-tracking refresh rate, eye-tracking accuracy of 1°, and a visual field of 100°, according to its technical data sheet [34]. Manual testing found that the visual field per eye measured 81–85° in horizontal direction and 88–91° in vertical direction. The latency of the eye-tracking of the headset was estimated to be between 20 and 50 ms [35]. The frame rate of the application itself did temporarily drop to ~40 frames per s depending on the number of obstacles on screen and the amount of rapid head movement. The wire connecting the headset to the laptop had a length of 3 m. A wireless Microsoft Xbox One X controller was used as an input device for the visual task execution.

2.3. Scanning Patterns

Two artificial gaze patterns were evaluated by comparing both their DFoV and visual task performance to each other, as well as to a free gaze condition where participants were asked to use their gaze as they normally would. Both scanning patterns were designed with focus on efficient use of the remaining FoV. The first one was the "left–right pattern", where most saccades are of horizontal nature (Figure 1a). This maximized the covered area, as no point of the FoV was covered twice within one pattern. The distance between each gaze line should ideally have been equal to the angular field of view of the participant. This pattern was suggested by Ivanov et al. [23] and was also used in visual training studies for patients with hemianopia [28].

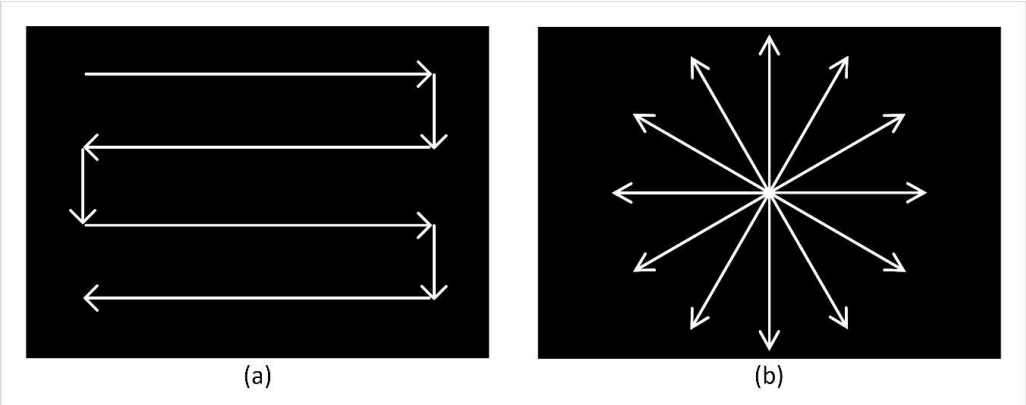

Figure 1. Visual representation of the left–right scanning pattern (**a**) and the radial scanning pattern (**b**) that participants were asked to follow during the visual tasks.

The second gaze pattern (Figure 1b) was a radial pattern in which saccades always occurred between the center view and the periphery. Here, the per-time area coverage was not as optimized as in the left–right pattern. However, it allowed participants to keep track of the area in the center of the FoV, which may have been beneficial especially in navigation

scenarios in order to follow the desired walking direction. It also allowed participants to shift gaze more freely into different directions of the periphery.

The different scanning patterns were shown as lines to participants at the start of the respective session. After showing the scanning pattern, the participants were asked to repeat the pattern, first with guidelines and then again without. This was repeated multiple times until the participants felt confident in being able to repeat the pattern consistently without guidelines. It was explained to the participants that they were not required to continuously follow the scanning patterns at all times and were allowed to fixate points of interest when necessary, but they were instructed to substitute any large gaze movements with the previously studied scanning pattern. The consistent execution of scanning patterns was supervised by the experimenter, who could follow the gaze of the participants on a laptop display. When necessary, participants were reminded between trials to follow the scanning pattern.

2.4. Study Population

The study population consisted of nine participants (four male, five female) between 19 and 27 years of age (average 23.2 $\pm$ 2.49 years) for the main group as well as three participants (all female) in the control group (aged 23 to 27 years, average 24.7 $\pm$ 2.08 years). No additional control participants could be recruited due to restrictions for participant studies introduced in response to the SARS-CoV-2 pandemic. All participants were self-reportedly visually healthy, with two participants stating to occasionally wear glasses in lectures or while driving. Glasses could not be worn during the experiment as they did not fit under the VR headset; however, it was made sure before the experiment that the search task targets could be recognized effortlessly by the participants. Table 1 shows the participants' age, sex, and vision correction as well as their experience with controllers and VR headsets.

Table 1. Participant age, sex, vision correction as well as their previous experience with VR headsets and game controllers. A capital C marks participants of the control group.

Participant	Age	Sex	Vision Correction	VR Experience	Controller Experience
1	23	m	-	no	yes
2	25	m	-	no	yes
3	21	f	-	some	yes
4	24	f	-	no	no
5	27	f	-	no	some
6	20	m	G [1]	no	some
7	23	f	-	some	some
8	19	f	-	some	some
9	23	m	G [1]	some	yes
C1	27	f	-	some	some
C2	23	f	-	some	no
C3	24	f	-	no	some

[1] occasionally wearing glasses.

2.5. Mesasured Parameters

To evaluate the effectiveness of the scanning patterns, both DFoV as well as visual performance were assessed. The DFoV was measured as the average area covered by the restricted FoV of 20° over a moving window of 3 s, measured once per s. We roughly estimated based on the findings of Peli et al. [36] that at normal navigation speed between 1 and 2 $m \cdot s^{-1}$, 3 s was sufficient to react to most obstacles, including pedestrians. However, the number was mostly arbitrary as it was only used to compare the DFoV of different scanning conditions against each other. Results for the DFoV over 1, 5, and 10 s durations can be found in the Supplementary Materials (Tables S1 and S2). The visual performance was measured by the time required to complete a navigation trial and the number of

obstacle collisions within one navigation trial, or as the correctness of the number of targets found in the search task.

We also observed the variability of gaze direction for both eye-only movement and the total gaze, including head rotation. These parameters described the standard deviation of the horizontal and vertical position of the gaze and allowed a more detailed analysis of how different scanning patterns as well as different visual tasks influenced the gaze behavior.

At the end of each session, a study questionnaire was filled out in which the participants were asked to rate their physical and mental strain, their subjectively perceived success in the visual tasks, as well as their expectations for long-term training with the respective scanning pattern.

2.6. Experimental Setup

The study was carried out over the course of three sessions between 60 and 90 min. In each session, one of three different conditions were selected, either the left–right eye scanning pattern, the radial eye scanning pattern, or no systematic scanning pattern. Those three conditions were pseudo-randomized such that all three conditions were equally distributed between the three sessions, thus minimizing the influence of task learning effects.

In each session, the participants were asked to do a total of 20 navigation trials and 40 search trials, split into two sets of 10 navigation and 20 search trials, respectively, and a 15 min break in between. Additionally, in the first session and before the start of the trials, the participants were introduced to the headset and were able to familiarize themselves with the headset and the controls of the navigation task. In both sessions where a scanning pattern was applied, the respective pattern was shown to the participants and trained for 5 to 10 min before the trials began. The participants remained seated during the experiment. The movement in the navigation task was done using the controller; however, participants were required to turn in their swivel chair in order to change the direction they were facing, thus increasing the immersion of navigation. The control group performed the same visual tasks with the same scanning patterns as the main group, with the only difference being that they carried out the tasks with unrestricted FoV.

2.7. Visual Tasks

The navigation task was done by applying a virtual, randomized environment resembling a corridor of 8 m width with parquet floor and white walls, as is seen on the left side of Figure 2a. Each environment consisted of eight 8 × 8 m tiles in randomized order, out of which two were the starting and end tile, two resembled straight corridors, two had left corners and two had right corners, allowing for a total of 120 different corridor layouts (examples being shown in Figure 3). In addition, at the beginning of each new tile, a random obstacle out of a selection of 15 different obstacles was instantiated, such as different walls, low-hanging bars, or simulated pedestrians. Lastly, some low-height obstacles such as barrels or small fences were instantiated at different positions on the tiles. This variety of obstacles encouraged gaze variation both horizontally and vertically and even required participants to adapt to sudden changes of the environment.

The randomized nature of both the layout of the corridor and the obstacles allowed for a near infinite number of environments, precluding the possibility that obstacle courses were repeated and recognized in later trials. Participants were able to virtually walk at a maximum speed of 3 $m \cdot s^{-1}$ or ~10 $km \cdot h^{-1}$ with an acceleration of 3 $m \cdot s^{-2}$. However, participants could freely adjust their walking speed below that limit by not pushing the thumb stick of the controller to full extent. Collisions with walls or obstacles were indicated by a bouncing sound effect and the participant's avatar was knocked back by up to 1 m depending on collision speed, thus preventing movement through obstacles and giving participants space to adjust their course without the risk of repeatedly colliding with the same obstacle. The simulated pedestrians moved in intervals between 4 and 10 s at a speed

of 2 m·s^{-1}, allowing participants to avoid collision as long as they were aware of their presence and movement.

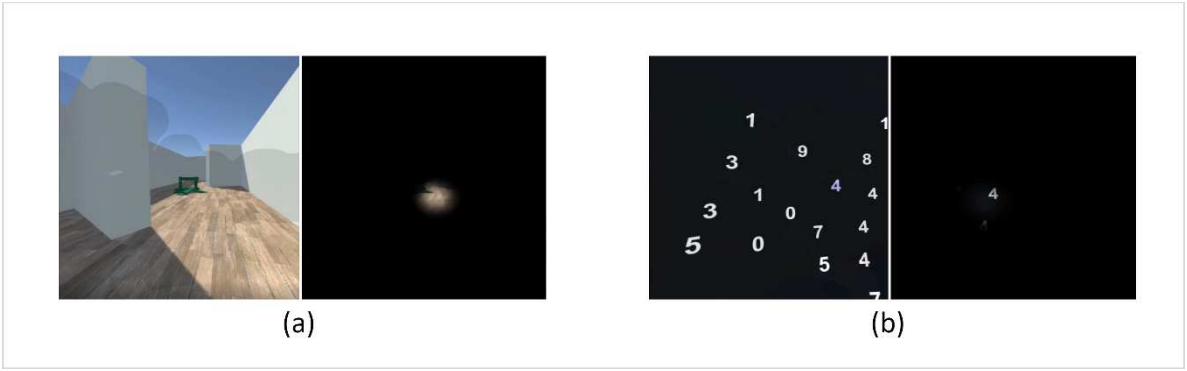

Figure 2. (**a**) Example of a navigation trial from participant's view, without (**left**) and with (**right**) simulated tunnel vision. The slightly darkened area on the left side image indicates the area already covered by gaze for test and presentation purposes but was completely transparent during trials. (**b**) Example of a search trial from participant's view without (**left**) and with (**right**) simulated tunnel vision. The digits are randomly distributed search targets. Both images (**a**,**b**) are captured from the scene render on the laptop screen. The content viewed by the headset user may have varied in proportions due to the influence of the headset's lenses and different screen shapes.

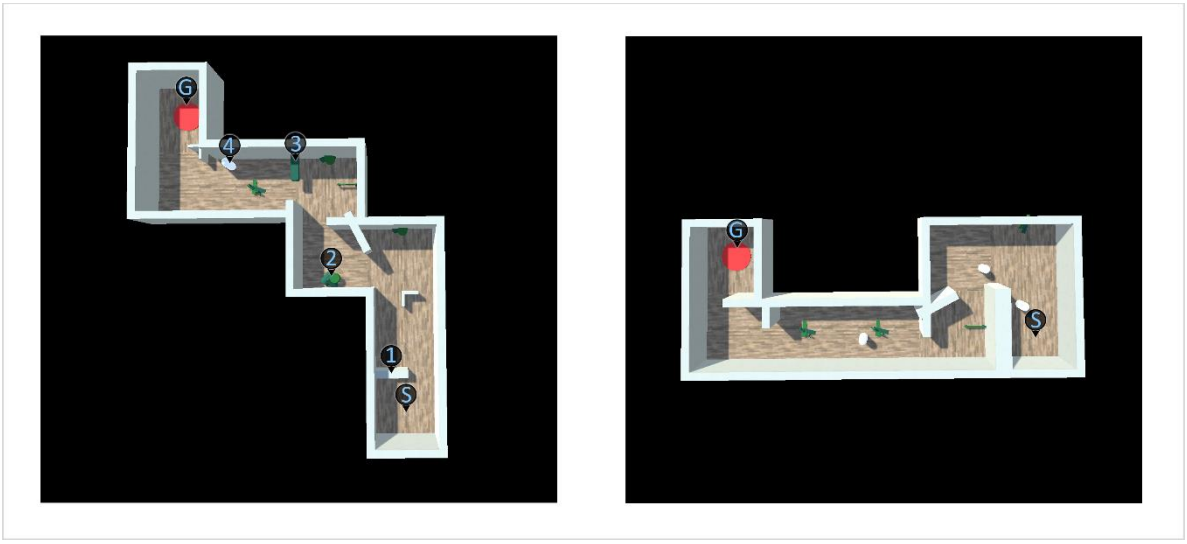

Figure 3. Top-down view of two examples of the randomized obstacle parkour used in the navigation task. The letter S indicates the starting point, the red circle marked with a G indicates the goal of the parkour. The blue digits mark examples of the four different obstacle types: 1 = large static obstacle/wall; 2 = low-height obstacle; 3 = obstacle hanging from ceiling; 4 = pedestrian.

The search task trials started by presenting a random digit to the participant with the additional information to search for this number in the upcoming screen. Then, 30 random digits were instantiated, distributed in a spherical field of 95° × 60° with a 3 m radius (see Figure 2b). The participants were given 20 s to search the scene and were instructed to press a button on the controller whenever they spotted a target with the specified target digit. After 20 s, all digits disappeared, and the next trial started. A trial was marked as correct if after 20 s the number of button presses matched the number of target digits.

2.8. Questionnaire

The questionnaire was structured following the basic layout of a system usability scale by John Brooke [37], however with four instead of five choices (very little, little, high, very

high) in order to prevent indecisive participants from choosing the middle option. The questions were adjusted to fit the research focus.

2.9. Statistical Methods

A total of 545 navigation task trials and 1070 search task trials, split among the nine participants and three different scanning pattern conditions, were evaluated. In the control group, the results of 180 navigation task trials and 358 search task trials were acquired and evaluated. For the analysis of the effects of systematic scanning patterns on DFoV, gaze variability, as well as navigation duration, linear mixed-effect models were applied. This allowed the analysis to account for the varying intrinsic performances of participants as a random factor. The models considered both random intercept and random slope of the random factor, since consistent data across all participants could not be assumed. Additionally, the models considered the trial number as a fixed effect. For the analysis of collisions in the navigation task, a zero-inflated Poisson regression was applied. Both trial number and trial time were considered as fixed effects. The rationale for this will be explained in the Discussion. To analyze the search task performance, a binomial generalized linear mixed-effects model was used, where participants were again considered as a random factor. A detailed summary of the statistical results for the applied models is found in Appendix B, Tables A1–A5. Due to the pseudo-randomized order of scanning pattern conditions, which ensured an equal distribution of the conditions over the three sessions, the session in which a trial took place was not included as a factor in the analysis. All averages are given including the standard deviation. Error bars also show standard deviations. The analysis was done in R using the lme4 and pscl package.

The questionnaire is presented as averages. A statistical test for significance was not feasible due to the small sample size of only one answer per participant and scanning pattern.

3. Results

3.1. Navigation Results

Figure 4 shows the results for DFoV, number of collisions, and time required to finish the task, averaged over all navigation trials of the main participant group and control group, respectively.

All values of DFoV are given as percentage of a $200^\circ \times 150^\circ$ field. This field was used as reference as it roughly describes the horizontal and vertical angle of the FoV of a visually healthy person. The average DFoV of all trials of the main participant group was $4.59 \pm 0.73\%$. Without any suggested scanning pattern, the DFoV was $4.39 \pm 0.73\%$ (control group $4.50 \pm 0.70\%$). With left–right-pattern being applied, the DFoV was $4.82 \pm 0.74\%$ (control group $6.71 \pm 1.85\%$), and, with the radial pattern applied, it was $4.57 \pm 0.73\%$ (control group $6.77 \pm 1.53\%$). If only trials without any collisions are considered for a collision-independent comparison, the DFoV was $4.31 \pm 0.73\%$ for 115 free trials, $4.86 \pm 0.73\%$ for 122 left–right trials, and $4.54 \pm 0.73\%$ for 112 radial trials. In both cases, the left–right pattern increased the DFoV by approximately 10% compared to the no-pattern trials ($p = 0.034$ for all trials; $p = 0.02$ for no-collision trials), and the radial pattern increased the DFoV by approximately 5% ($p = 0.269$ for all trials; $p = 0.096$ for no-collision trials). The average number of collisions per trial without applied scanning pattern was 0.73 ± 0.85 (control group 0.05 ± 0.22). It was significantly lower in both scanning pattern conditions at 0.49 ± 0.70 ($p < 0.001$) (control group 0.1 ± 0.32) in the left–right pattern trials and 0.58 ± 0.75 ($p < 0.001$) (control group 0.12 ± 0.35) in the radial pattern. The average time required for a navigation trial was found to be significantly lower when no scanning pattern was applied (37.3 ± 12.2 s, $p = 0.0011$ for left–right; $p = 0.0017$ for radial; control group 24.4 ± 5.08 s), while trials with applied left–right pattern had an average trial duration of 48.8 ± 15.8 s (control group 28.1 ± 6.70 s) and trials with radial pattern 48.5 ± 16.8 s (control group 28.7 ± 7.95 s).

The number of collisions was decreased for trials with left–right scanning pattern even when accounting for the differences in average trial durations. The zero-inflated Poisson regression of collisions showed an estimate for the count model coefficients of the left–right condition of −1.09 with a standard error of 0.16 and for the radial condition an estimate of −1.10 with a standard error of 0.14. In both conditions, the *p*-values were below 0.001. The implications will be explained in more detail in the Discussion. The lines in Figure 5 show the average number of collisions in each scanning condition for trials of similar duration in a moving average. The moving average was applied only to the plot in Figure 5 to provide more clarity and had no influence on the statistical analysis. A breakdown of DFoV, average collisions, and trial duration for individual participants is found in Appendix A, Figure A1. Summaries of the analysis results for the navigation trials are found in Appendix B, Tables A1–A3. Raw data for DFoV, number of collisions and trial duration in navigation trials is found in the Supplementary Materials, Table S1.

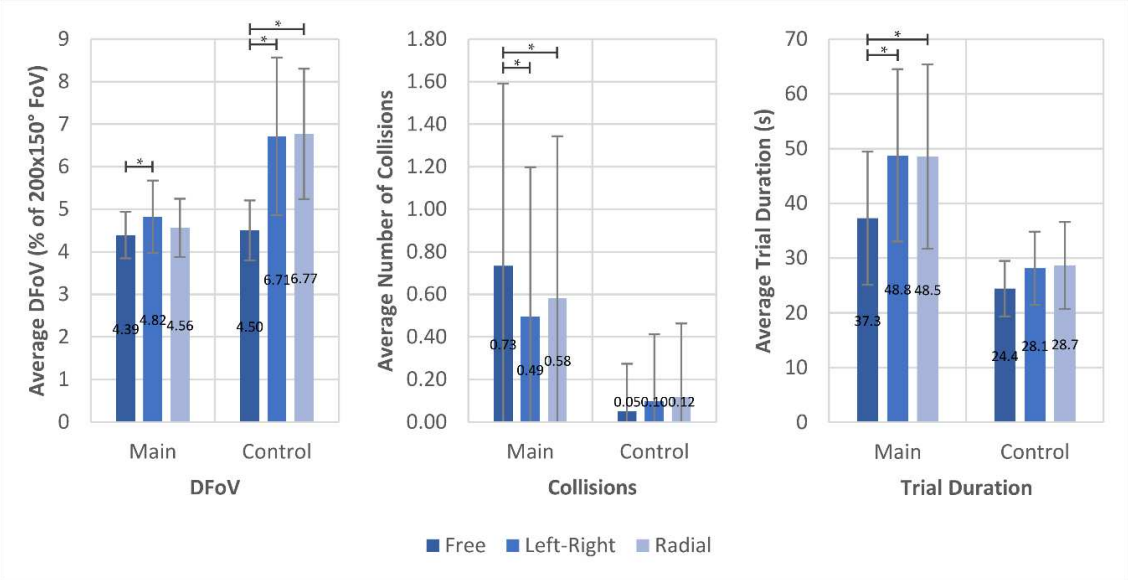

Figure 4. Comparison between average dynamic field of view (DFoV), number of collisions, and trial duration in the three different scanning pattern conditions during navigation for both main group and control group (* $p < 0.05$).

The variability of gaze direction describes the standard deviation of horizontal and vertical gaze angles. Figure 6 displays the variability of the total gaze that describes the actual gaze direction of eye rotation and head rotation combined, compared to body rotation, as well as the variability for only eye movement and head rotation independently. Since the experimental setup only allowed tracking of head rotation and eye position but not full body rotation, the body rotation was estimated as the 3 s average of head rotation, assuming that a person facing in a direction for more than 3 s while walking would turn their body accordingly. Both total gaze variability and head rotation variability were measured in reference to the estimated body rotation.

Horizontal gaze variability was almost 3 times as high as vertical gaze variability in all three scanning pattern conditions, with an average of 18.26 ± 3.44° (control 24.08 ± 4.24°) horizontal gaze variability and 6.37 ± 1.90° (control 7.13 ± 2.66°) vertical gaze variability. Between different gaze pattern conditions, only small differences in both horizontal and vertical gaze variability were found in the main participant group, with the most relevant differences being displayed in the decrease of horizontal head rotation variability in the left–right ($p = 0.072$) and radial ($p < 0.001$) pattern. In the control group, there was a strong increase in vertical gaze variability, with both total gaze and eye position variability increasing by 73.2% to 81.5% in both scanning patterns compared to no-pattern trials. This increase was not found in the main participant group. Raw data for navigation trials can be found in the Supplementary Materials, Table S3.

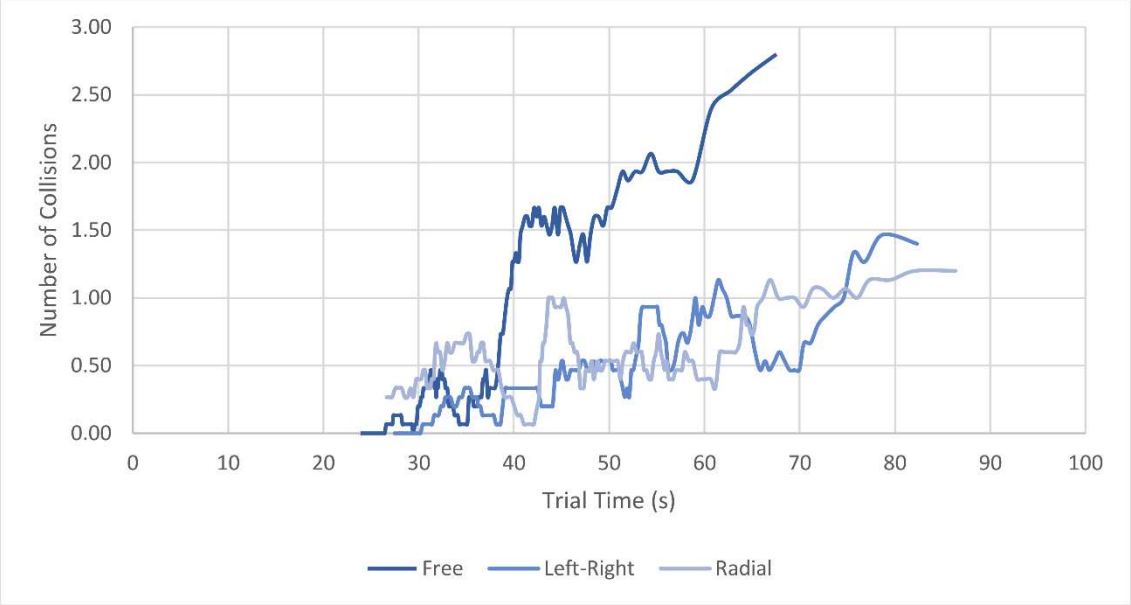

Figure 5. The moving average of the number of collisions by trial duration in the three conditions (period of 15). This visualizes how the number of collisions in trials of similar duration varied between the different scanning pattern conditions. The results shown are from the main participant group.

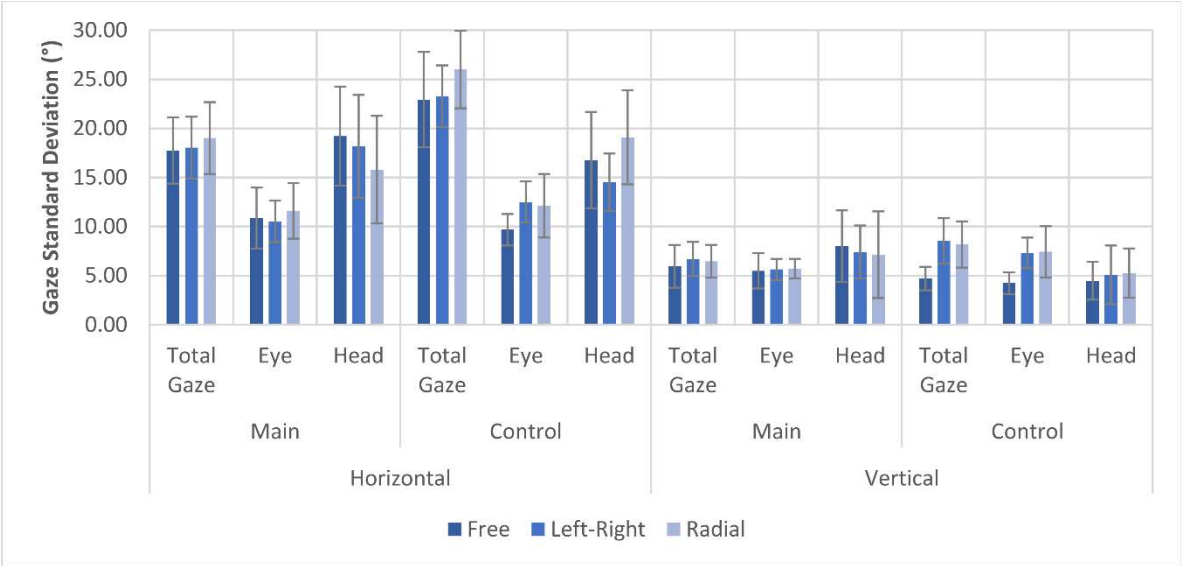

Figure 6. The average standard deviation of total gaze, eye position, and head rotation in the navigation task. Total gaze and head rotation were measured in reference to the estimated facing direction of the body.

3.2. Search Task Results

In the search task, the average DFoV over 3 s was higher in left–right trials ($p = 0.099$) with an average of 3.53 ± 0.75% (control 3.85 ± 1.03%) compared to the trials with no applied scanning pattern with 3.29 ± 0.69% (control 3.37 ± 1.04%) DFoV. The average DFoV of the radial scanning pattern trials was lower ($p = 0.327$) at 3.16 ± 0.66% (control 2.95 ± 0.76%), as can be seen in Figure 7. This trend was found in both main and control group. No significant difference between the left–right scanning pattern trials and the no-pattern-trials could be found in the search performance—the ratio at which the number of targets in the search task was correctly identified—with 75.9% correct trials in the no-pattern-condition and 76.5% in the left–right pattern condition ($p = 0.804$). The radial condition had a lower ratio of correct trials compared to the no-pattern condition ($p = 0.089$)

with only 69.5% correct trials. There was, however, a significant effect between DFoV and search performance ($p = 0.0016$). The results for individual participants are found in the Appendix A, Figure A2. Summaries of the analysis results for search trials are found in Appendix B, Tables A4 and A5. Raw data of DFoV and performance in search trials is found in the Supplementary Materials, Table S2.

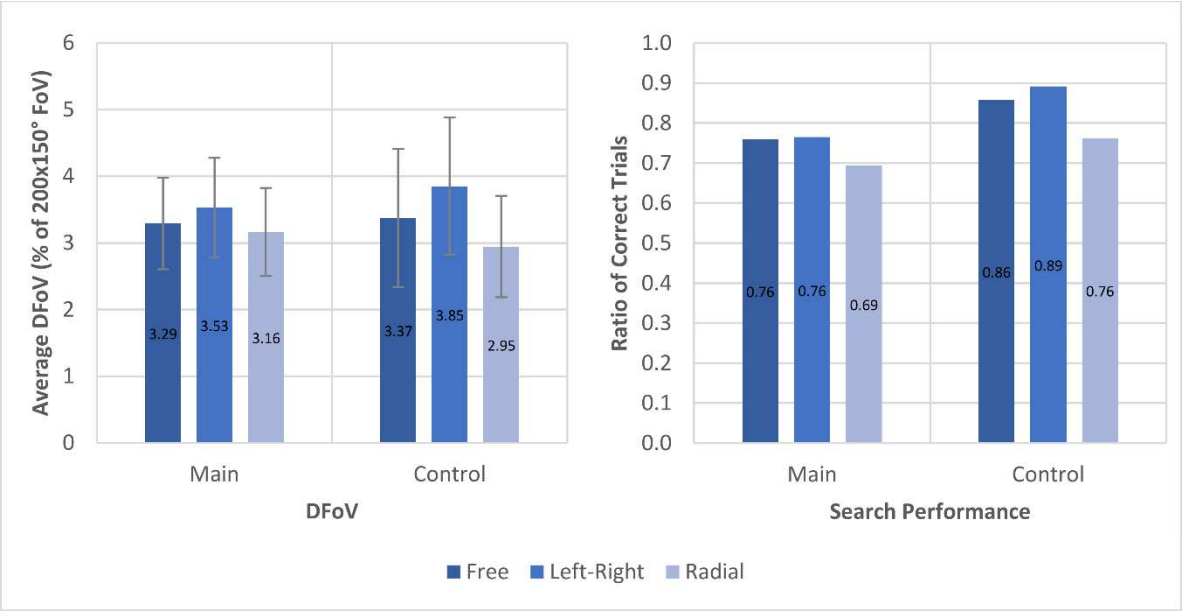

Figure 7. Comparison of average DFoV and ratio of trials in which the correct number of targets were found between the three different scanning pattern conditions during search task for both main group and control group.

The gaze variability in the search task that is displayed in Figure 8 shows larger differences between scanning pattern conditions, but less difference between main and control group compared to the gaze variability during navigation task. Most notable is the difference in eye position and head rotation variability between the radial pattern trials and the two other scanning pattern conditions. The main group shows an increase in horizontal eye position variability in radial patterns of 47.5% compared to the no-pattern trials, but a 57.5% decrease in head rotation variability, with smaller, but similar differences found in vertical direction. This contrasts with the left–right pattern, which is more in line with the no-pattern variability of eye position and head rotation. The raw data for gaze variability in all search trials is found in the Supplementary Materials, Table S4.

3.3. Questionnaire Results

Figure 9 displays the rating reported by the participants on their perceived performance in the two visual tasks, as well as the rating of physical and mental strain, meaning the strain on the eyes as well as required concentration.

Additionally, the question "Which of the two eye scanning patterns is more intuitive?" revealed that all nine participants as well as the three participants of the control group preferred the left–right pattern. To the question "Do you believe that it is possible to adapt to at least one of the scanning patterns in a way that it feels natural and unobtrusive to use?", three participants answered that they could imagine it for both scanning patterns, five participants could only imagine it for the left–right scanning pattern, and one participant could not imagine either of the scanning patterns being perceived as natural and unobtrusive. Two of the participants mentioned that even during the study they felt the effects of adaptation. Individual results for the participants can be found in the Supplementary Materials, Table S5.

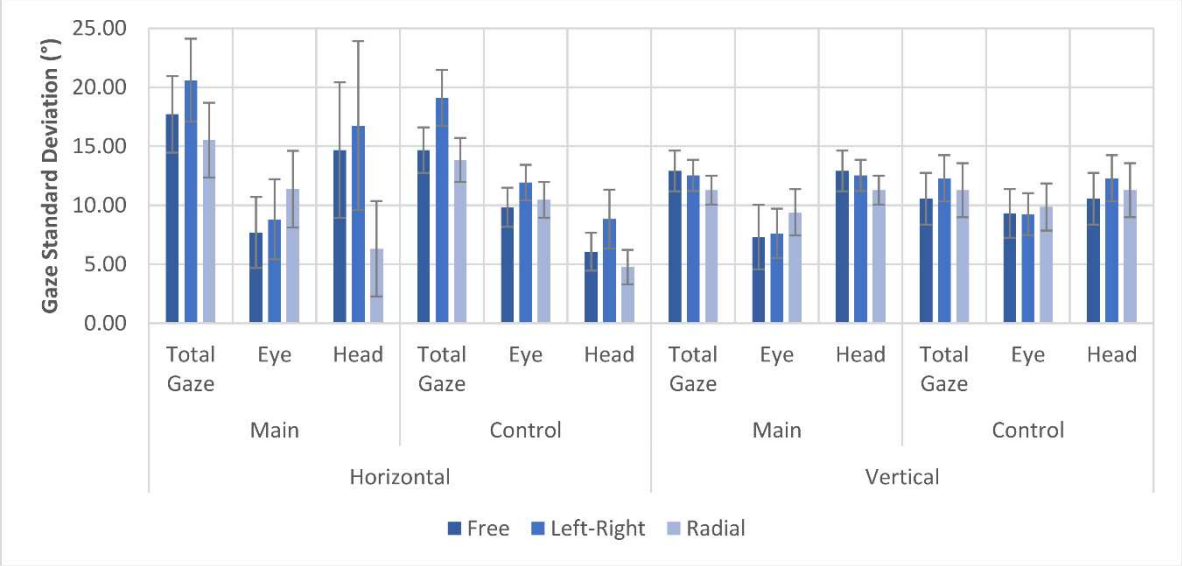

Figure 8. The average standard deviation of total gaze, eye position, and head rotation in the search task. Total gaze and head rotation were measured in reference to the estimated facing direction of the body.

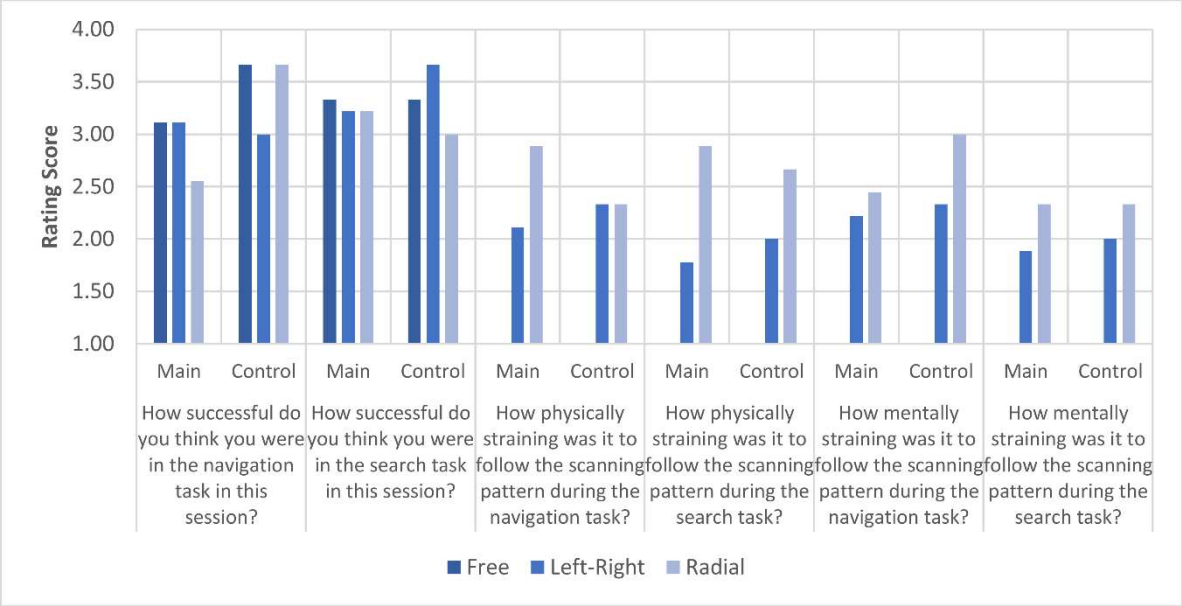

Figure 9. The results of the participant questionnaire, ranked from 1 = very low to 4 = very high.

4. Discussion

We investigated whether it was possible to increase the dynamic field of view of participants with simulated tunnel vision by applying systematic eye scanning patterns and evaluated in which way these eye scanning patterns influenced the performance in two visual tasks—a navigation task and a search task. For that, a software for virtual reality was developed that utilized the built-in eye tracking functionality of the VR headset to simulate a FoV limited to 20° in participants with healthy eyesight.

It was found that applying a systematic "left–right" eye scanning pattern did increase the DFoV of the participants by approximately 10% compared to the DFoV without scanning pattern. Further, the number of collisions with obstacles in a virtual navigation task was significantly reduced with applied scanning patterns, with the left–right pattern reducing them by 32.9% and the radial pattern by 20.5%. The time required to navigate through the obstacle parkour however increased by 30.8% (left–right) and 30.0% (radial)

when applying the scanning patterns. Partially, this can be explained by a shift in the speed–error tradeoff often found in psychophysical experiments. The confrontation with a new task—applying the systematic gaze patterns—and the resulting reduction in confidence compared to the no-pattern trials likely led to a shift toward error prevention at the cost of speed [38]. However, by analyzing the number of collisions in a model that considered the trial duration as a fixed effect, we found that the scanning patterns had an influence on the collision reduction that could not be attributed only to the difference in average trial duration and thus the speed–error tradeoff. Figure 5 further supports this finding, as it shows that in trials of similar duration, the average number of collisions was typically lower in scanning pattern trials—especially the left–right pattern trials—compared to the no-pattern trials.

The performance in the visual search task, measured by the rate of trials in which the correct number of targets was identified by the participants, did not improve with applied scanning patterns and was even decreased for the radial scanning pattern by 9.3% compared to the trials with no scanning pattern. The DFoV in the search task was increased by 7.3% for the left–right pattern but decreased by 4.0% for the radial pattern compared to trials without scanning pattern. The analyses of these effects did not show significance, but the numerical trends suggest that out of the two scanning patterns tested, the left–right pattern may have led to similar or better results than the radial scanning pattern in all aspects. It was also favored by participants in terms of intuitiveness, perceived success, mental and physical strain, as well as expected potential to naturally adapt to this scanning pattern. It can be assumed that the left–right scanning pattern fell more in line with natural eye movements due to the horizontal sweeping motion of the gaze known from other visual tasks, such as reading. Further, the left–right pattern showed improvements or similar results in all aspects except trial duration compared to the no-pattern condition, indicating that scanning patterns were indeed able to increase the performance in visual tasks to a degree.

The results show that the DFoV was on average around 30% higher during the navigation task than during the search task. This can be explained by the fact that it is more difficult to recognize a certain number and distinguish them from other numbers rather than just noticing the existence and dimensions of an obstacle [39]. Furthermore, it is likely that increasing the average distances between the targets of the search task by either reducing the number of targets or increasing the field size would increase the DFoV.

The total gaze variability shows that the increase in DFoV in the left–right scanning pattern seems to have different causes based on the visual task. In the navigation task, the horizontal gaze variability did not increase significantly, whereas the vertical gaze variability showed an increase equal to that of the DFoV. Meanwhile, in the search task, the opposite was found in that only the horizontal gaze variability increased when applying the left–right scanning pattern. It was also found that scanning patterns—especially the radial scanning pattern—decreased the variability of head rotation and in return led to an increase in eye position variability. Kerkhoff et al. [40] found that an increase in head movements does not improve visual performance in patients with visual field disorders and can even reduce the effects of training. This suggests that the scanning patterns could improve the success of visual gaze training even further.

To the best of our knowledge, no other research regarding the influence of suggested eye scanning patterns on the visual performance in navigation and search tasks of participants with tunnel vision has been published to this point, apart from the preceding study by Ivanov et al. [23] that motivated this study. It is interesting to note that Ivanov et al. found a significant improvement of preferred walking speed of the participants after their training—which would be comparable to the navigation trial duration measured in this study—whereas no significant improvements in the number of collisions per trial were found. This contrasts with our findings, where the navigation trial duration increased when applying systematic scanning patterns, but the number of collisions decreased. This can be explained by changes in the speed–error tradeoff of the participants. It can be assumed that

in the study by Ivanov et al., participants adapted to the new gaze behavior introduced to them over the course of the six weeks of daily training. Thus, they became more confident in the simultaneous execution of visual tasks and trained gaze behavior. Contrary to that, our study did not apply any training. Measurements were taken within an hour after the participants were first introduced to the new gaze behavior. This means that participants had very little time to adapt to the new gaze behavior and thus their confidence level likely was lower in the scanning pattern trials compared to the reference (the no-pattern trials). It was found that confidence has a direct influence on the speed-error tradeoff in subjects [38], where higher confidence levels result in a shift toward faster execution times and lower confidence levels result in a shift toward lower error rate. This is in line with the comparison of the results between the study by Ivanov et al. and ours. It further suggests that by applying saccadic search training in combination with systematic scanning patterns, it may be possible to improve both average walking speed and obstacle avoidance in patients with tunnel vision.

Comparison to studies that evaluated visual aiding devices, such as that of Luo et al. [19], Hicks et al. [20] or Angelopoulos et al. [22], is not feasible, since the goal of our study was not to find the full extent of visual performance improvement that was achievable with scanning patterns, which would require a much more extensive training, but only to compare different scanning patterns to each other and the performance without scanning pattern. It is thus unsurprising that our study did not find performance improvements of a similar magnitude to studies with visual aiding devices, such as a reduction of errors of 50% in both search task and obstacle avoidance [22] or an over 50% reduction in navigation trial duration over 10 trials [20] through augmented reality depth mapping.

It has to be noted that the results are not fully representative of patients living with RP, as all study participants were visually healthy, and the limitation of the visual field was only simulated within the VR environment. Although the simulation of visual impairments in visually healthy participants was shown to induce similar behavior as their real counterparts [41], there are multiple aspects due to which results could vary if the experiment were to be repeated with real patients. First is the difference in experience with the condition. The participants of this study were all new to the experience of a limited FoV, and thus they did not have time to develop their own gaze strategies. Second, the use of a VR headset for the simulation brought its own difficulties. The FoV of the VR headset was limited to 100° independent of the limits of the simulated RP scotoma, which means that any viewing angle further than 50° to any side was not possible with eye movement alone. Lastly, the participants had to remain seated during both visual tasks, which especially in the navigation task resulted in further deviation from real-life scenarios. However, eye-tracking is a crucial aspect for both simulating tunnel vision as well as measuring the DFoV, and to our knowledge, wireless VR headsets with reliable eye tracking solution were not publicly available during the time of the experiments. It was thus necessary to use a wired solution combining controller navigation and body rotation. The choice to simulate RP in this way rather than to recruit real patients was made in view of a larger-scale follow-up study in which the effects of long-term scanning pattern training are assessed. We avoided recruiting patients at this point that would then no longer be able to participate in this larger-scale study without having an advantage compared to other participants due to the previous scanning pattern training.

5. Conclusions

Based on a setup simulating tunnel vision in a virtual-reality environment, we showed that the application of systematic gaze patterns can improve obstacle avoidance and dynamic range of the field of view. It was found that the scanning pattern focusing on straight, horizontal, sweeping eye movements (left–right pattern) led to an overall similar or better performance than the pattern based on radial eye movements from the center of the visual field to its periphery and back—and was also better accepted by participants. Based on these findings, the left–right pattern will be applied in a follow-up study. In this

follow-up study, a six-week saccadic gaze training for patients with retinitis pigmentosa will be performed to investigate the effects of scanning pattern training on real-world navigation and obstacle avoidance.

Supplementary Materials: The following are available online at https://www.mdpi.com/2076-3425/11/2/223/s1: Table S1: Navigation Task Results; Table S2: Search Task Results; Table S3: Navigation Task Gaze Variability; Table S4: Search Task Gaze Variability; Table S5: Questionnaire Results.

Author Contributions: Conceptualization, A.N., K.S., I.I., and S.W.; methodology, A.N.; software, A.N.; validation, A.N., I.I., and S.W.; formal analysis, A.N.; investigation, A.N.; resources, S.W.; data curation, A.N.; writing—original draft preparation, A.N.; writing—review and editing, K.S., I.I., and S.W.; visualization, A.N.; supervision, K.S., I.I., and S.W.; project administration, S.W.; funding acquisition, I.I. and S.W. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: This study was proposed to and approved by the ethics committee of the Institutional Review Board of the Medical Faculty of the University of Tübingen (628/2018802) in accordance with the 2013 Helsinki Declaration.

Informed Consent Statement: All participants signed informed consent forms.

Data Availability Statement: The data presented in this study are available in the Supplementary Materials, Tables S1–S5.

Acknowledgments: We thank Katharina Rifai of the ZEISS Vision Science Lab for her support and feedback during the design of the study. Furthermore, for this work, the methodological advice of the Institute for Clinical Epidemiology and Applied Biometry of the University of Tübingen was used. We want to express our appreciation to Johann Jacoby for his kind support in the statistical analysis of our data. Lastly, we want to thank the participants of this study for their positive feedback, their motivation, and patience throughout the experiments.

Conflicts of Interest: We declare that Siegfried Wahl is scientist at the University of Tuebingen and both Siegfried Wahl and Iliya Ivanov are employees of Carl ZEISS Vision International GmbH, as detailed in the affiliations. There were no conflicts of interest regarding this study.

Abbreviations

RP	Retinitis Pigmentosa
FoV	Field of View
DFoV	Dynamic Field of View
VR	Virtual Reality

Appendix A

The results for navigation and search task, separated by participants, are shown in Figures A1 and A2.

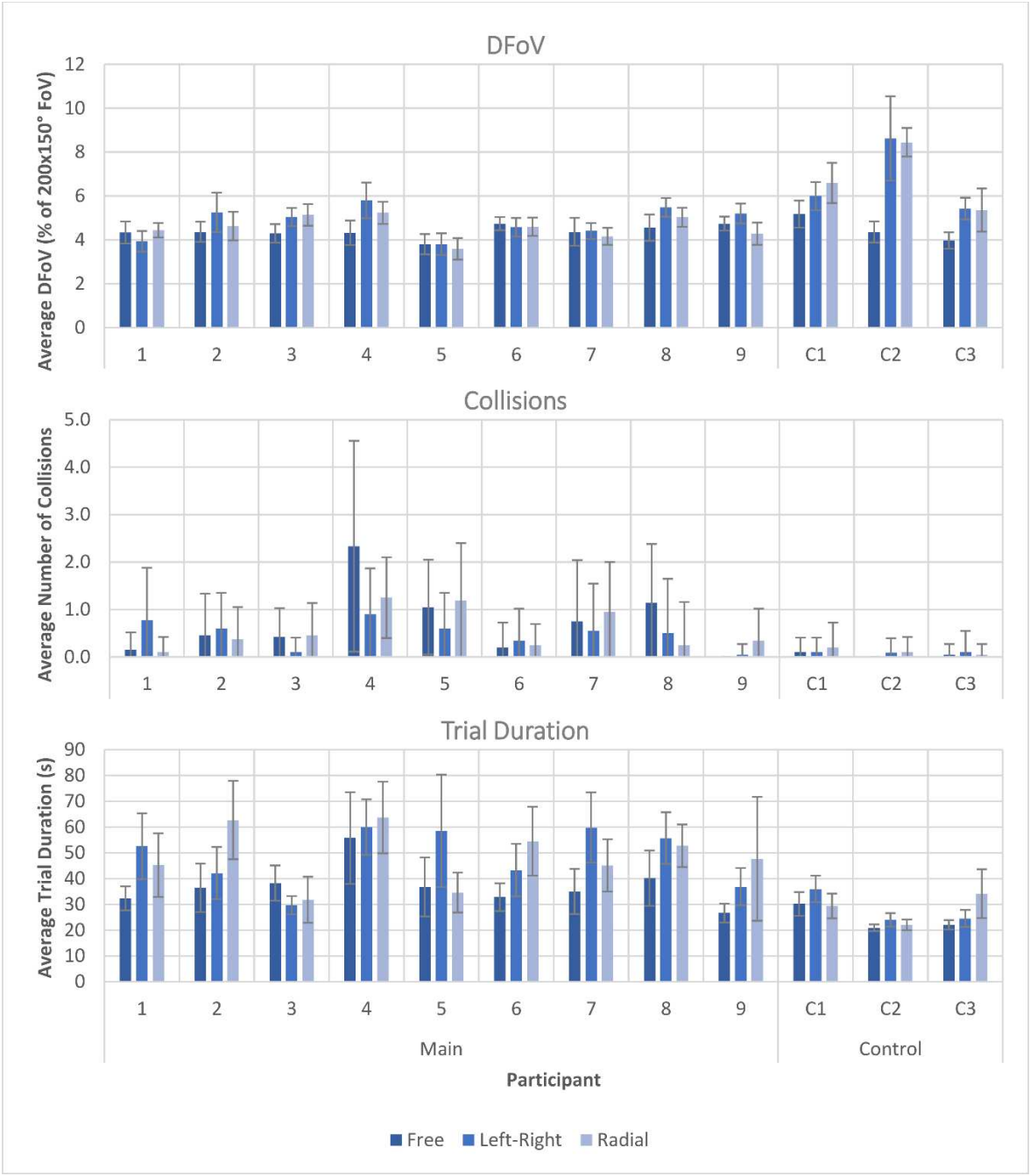

Figure A1. Comparison of DFoV, number of collisions, and trial duration in the navigation task between individual participants. Each bar shows the average of the results of 20 trials.

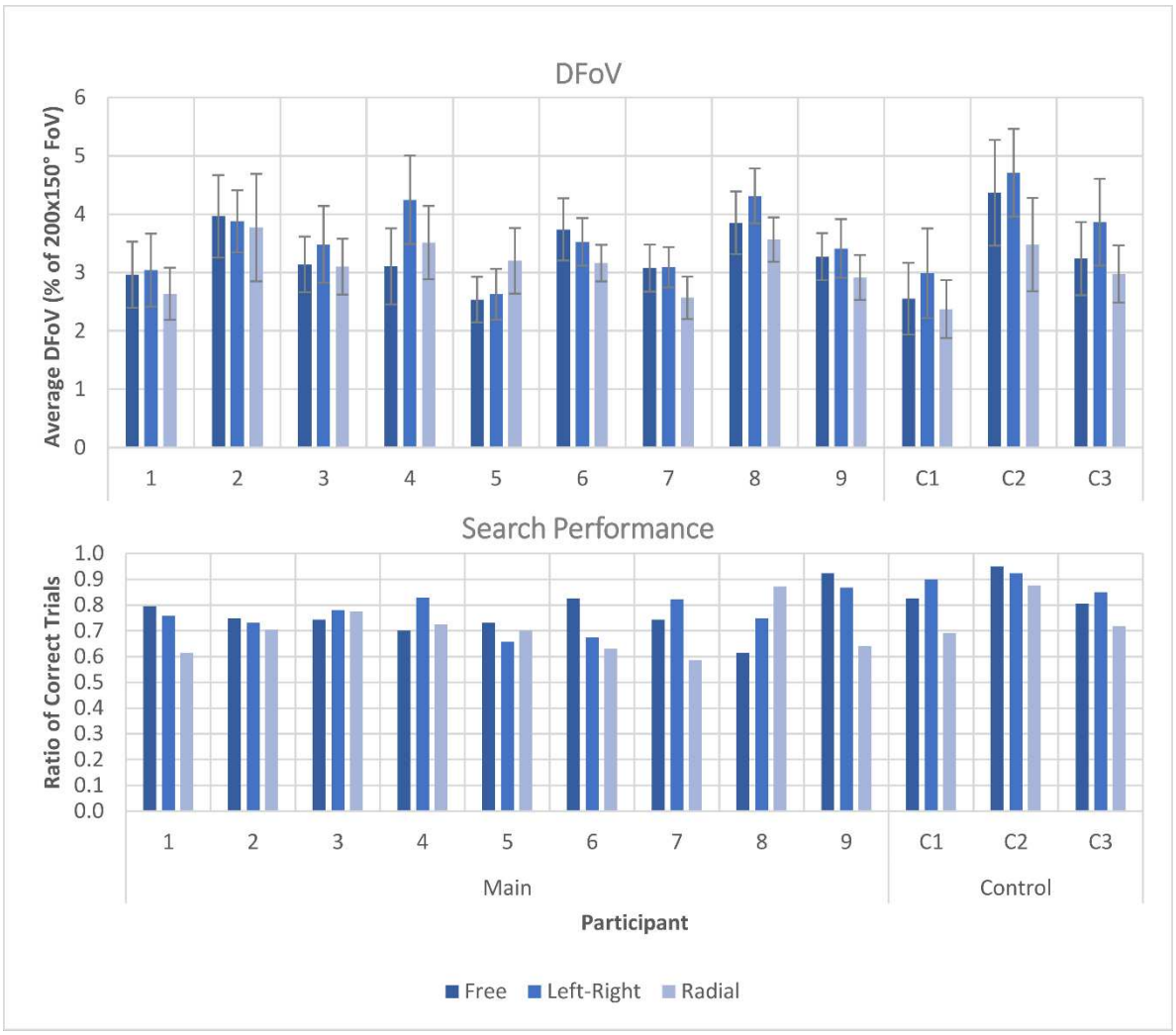

Figure A2. Comparison of DFoV and task performance between individual participants in the search task. Each bar is an average of the results of 40 trials.

Appendix B

The results of the statistical models that were applied for tests of significance are shown in Tables A1–A5.

Table A1. Results of the analysis of DFoV in navigation trials. The applied model was a linear mixed-effects model that considered both random intercept and random slope.

	DFoV in Navigation Trials		
Predictors	**Estimate**	**SE**	***p*-Value**
(Intercept)	4.11	0.1	0.000
Left–right	0.44	0.21	0.340
Radial	0.18	0.16	0.270
Trial	0.027	0.0035	0.000
Number of Observations: 545			

Table A2. Results of the analysis of collisions in navigation trials. The applied model was a zero-inflated Poisson regression model.

	Collisions in Navigation Trials			
Count Model Coeff.	**Estimate**	**SE**	***z*-Value**	***p*-Value**
(Intercept)	−0.89	0.27	−3.3	<0.001
Left–right	−1.09	0.16	−6.9	<0.001
Radial	−1.10	0.14	−7.9	<0.001
Trial	0.018	0.011	1.65	0.099
Trial duration	0.024	0.0035	6.96	<0.001
Zero-inflated Poisson regression model coefficient				
(Intercept)	9.78	2.28	4.28	<0.001
Left–right	0.082	0.82	0.099	0.921
Radial	−11.0	77.18	−0.143	0.886
Trial	−0.031	0.051	−0.612	0.541
Trial duration	−0.26	0.061	−4.35	<0.001
Number of Observations: 545				

Table A3. Results of the analysis of trial duration in navigation trials. The applied model was a linear mixed-effects model that considered both random intercept and random slope.

	Trial Duration in Search Trials		
Predictors	**Estimate**	**SE**	***p*-Value**
(Intercept)	44.1	2.86	0.000
Left–right	11.5	3.52	0.0011
Radial	11.3	3.60	0.0017
Trial	−0.65	0.082	0.000
Number of Observations: 545			

Table A4. Results of the analysis of DFoV in search trials. The applied model was a linear mixed-effects model that considered both random intercept and random slope.

	DFoV in Search Trials		
Predictors	**Estimate**	**SE**	***p*-Value**
(Intercept)	3.12	0.16	0.000
Left–right	0.22	0.13	0.099
Radial	−0.14	0.14	0.327
Trial	0.0084	0.0014	0.000
Number of Observations: 1070			

Table A5. Results of the analysis of search performance. The applied model was a binomial generalized linear mixed-effects model.

	Search Performance			
Predictors	**Estimate**	**SE**	***z*-Value**	***p*-Value**
(Intercept)	2.91	0.64	4.56	0.000
Left–right	0.48	0.65	0.74	0.459
Radial	−0.57	0.57	−1	0.317
Trial	−0.045	0.018	−2.47	0.014
Random Effect:				
Groups	**Name**	**Variance**	**Std. Dev.**	
Participants	(Intercept)	0.102	0.319	
	Left–right	0.036	0.19	
	Radial	0.027	0.16	
Number of Observations: 1070				

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2 Publication B

PLOS ONE

RESEARCH ARTICLE

Influence of open-source virtual-reality based gaze training on navigation performance in Retinitis pigmentosa patients in a crossover randomized controlled trial

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Data Availability Statement: All relevant data are within the manuscript and its Supporting information files.

Abstract

Methods

A group of RP patients (n = 8, aged 20-60) participated in a study consisting of two 4-week-phases, both carried out by the same patient group in randomized order: In the 'training phase', participants carried out a Virtual-Reality gaze training for 30 minutes per day; In the 'control phase', no training occurred. Before and after each phase, participants were tasked to move through a randomized real-world obstacle course. Navigation performance in the obstacle course as well as eye-tracking data during the trials were evaluated. The study is registered at the German Clinical Trials Register (DRKS) with the ID DRKS00032628.

Results

On average, the time required to move through the obstacle course decreased by 17.0% after the training phase, the number of collisions decreased by 50.0%. Both effects are significantly higher than those found in the control phase ($p < 0.001$ for required time, $p = 0.0165$ for number of collisions), with the required time decreasing by 5.9% and number of collisions decreasing by 10.4% after the control phase. The average visual area observed by participants increases by 4.41% after training, however the effect is not found to be significantly higher than in the control phase ($p = 0.394$).

Conclusion

The performance increase over the training phase significantly surpasses the natural learning effect found in the control phase, suggesting that Virtual-Reality based gaze training can have a positive effect on real-world navigation tasks for patients with RP. The training is available as work-in-progress open-source software.

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Competing interests: This work was done in an Industry-on-Campus-cooperation between the University of Tübingen and Carl Zeiss Vision International GmbH. Two of the authors, I.I. and S. W., are employees of Carl Zeiss Vision International GmbH. This does not alter our adherence to PLOS ONE policies on sharing data and materials. There are no competing interests related to employment, consultancy, patents, products in development, or marketed products.

Introduction

Retinitis pigmentosa (RP) is a subset of inherited retinal diseases characterized by progressive loss of the Visual Field (VF) due to the degeneration of the retina [1–3]. This loss of the VF starts at the periphery or middle periphery and leads to blindness in the long-term progression of the degeneration [4, 5]. Other symptoms of RP include blurriness of sight, glare sensitivity, as well as night blindness [1, 6]. RP is estimated to occur in about 1 in 4000 people [5, 7–10].

The condition in which visual information can only be perceived in the center of the VF is known as "tunnel vision". It can have severe impact on the daily lives of those affected by RP [6], especially in visual tasks such as navigation and visual search. At the time of writing there is only one approved gene therapy for retinitis pigmentosa [11]. Despite good results in efficacy of this therapy also on the visual field, in the majority of the patients halting the progression is not consistently possible [6, 8]. It is therefore essential to explore other methods that can improve the visual capabilities of RP patients—and thus improve their quality of life.

One of these approaches is gaze training, which involves teaching patients how to adjust their gaze movements to compensate for their missing visual areas [12, 13]. For patients with limited VF, an important technique for this approach is the use of exploratory saccades. Exploratory saccades are rapid eye movements that help explore the visual environment by quickly shifting the point of fixation to new locations [14]. While these eye movements can not directly improve the biological health of the retina or increase the size of the "static" VF, i.e. the visual area that can be perceived at any one time, they can increase the visual area that is observed over time, facilitating the detection of new visual information. By incorporating exploratory saccades into gaze training, patients can learn to adapt their gaze movements to partly accommodate for their limited VF and observe larger areas around them. This can lead to better obstacle detection, safer navigation, and an overall higher level of independence in everyday visual tasks.

The concept of gaze training for low-vision compensation has been investigated and applied before. Nelles et al. [12] and Pambakian et al. [13] both evaluated the effects of a four-week supervised gaze training in patients with hemianopia, a condition of half-sided visual field loss. In the study of Nelles et al., training included specific instructions for adaptive gaze strategies, whereas patients in the study by Pambakian et al. were free to develop their own gaze strategies. In both studies, it could be shown that after gaze training, patients had a significantly shorter reaction time for visual stimuli in the non-seeing side of the visual field. Additionally, patients reported improvements in several vision-related quality of life aspects after training. Nguyen et al. [15], Roth et al. [16], and Ivanov et al. [14] conducted studies comprised of six weeks of unsupervised at-home training with a screen-based exploratory saccade training in patients with hemianopia (Roth et al.) and RP (Nguyen et al., Ivanov et al.), respectively. They were assessing the training effect on visual search (Roth et al., Ivanov et al.), scene exploration (Roth et al.), and the effect on real-world mobility (Nguyen et al., Ivanov et al.). Similarly, Kuyk et al. [17] investigated the effects of five days of visual search training on both search and real-world mobility tasks in people with different visual field impairments. All three studies with visual search testing paradigm found improvements in reaction time after training, both for digital feature search and for real-world object selection. For the real-world mobility tests, limited effects were reported: Nguyen et al. found significant training effects for real-world navigation in patients with visual field size $<10^{\circ}$. In the study by Ivanov et al., RP patients displayed a significant improvement in walking speed, but no improvements in collision avoidance. In the study by Kuyk et al., no significant effects in walking speed were found, but collision avoidance improved in one of the two tested lighting conditions. A different

study by Hazelton et al. [18] compared the effectiveness of four different eye movement training tools on patients with stroke-induced visual field loss. Quantitatively, no significant improvements were found for any of the four tools, with only individual patients displaying improvements in certain testing paradigms such as visual search or reading speed. Qualitative assessment suggested, however, that patients perceived a positive influence of the training tools on everyday visual tasks. Gunn et al. [19] conducted a study in which patients with visual impairments caused by glaucoma underwent two supervised one-hour training sessions comprised of both general and task-specific gaze strategy training and instructions, including video showcases of 'expert' performers. Effects of the training were evaluated in a foot-placement task and a short obstacle avoidance task, with significant performance improvements found in foot placement accuracy and obstacle avoidance, though at a reduction in movement speed in the obstacle avoidance task. Additionally, changes in the patients' gaze behavior were registered after training. Lastly, Young and Holland [20] tested whether gaze training could improve mobility and reduce risk of falling even in elderly persons with no visual field impairment. After a supervised training in which participants received instructions on gaze behavior, participants were found to show increased foot placement accuracy, with no significant changes on movement speed. It can be noted that all of these training paradigms rely on either personal supervision and instructions (Nelles et al., Pambakian et al., Gunn et al., Young and Holland) or use a screen-based setup for at-home training (Nguyen et al., Roth et al., Ivanov et al., Kuyk et al., Hazelton et al.). With the constant advancements in technology and accessibility of Virtual Reality (VR) headsets, a question is raised about the potential of VR to be applied for gaze training purposes. Compared to conventional, computer display based setups, VR devices offer a number of possible advantages.

- The displays of a VR headset cover larger visual angles than a traditional computer screen, with most commercially available VR headsets featuring visual angles of 90˚ per eye or higher [21]. Assuming the recommended minimal distance from a working screen of 50cm [22], a 45" screen (99.7cm×56.0cm) is required to match the visual angle of a VR headset at least in horizontal dimension, and an 80" computer screen (177cm×99.6cm) would be required to also match the vertical visual angle.
- In addition, VR headsets can measure head rotations and adjust the displayed image in real-time to mimic the effect of "looking around". This further increases the visual angles at which VR headsets can display visual content, allowing for a full 360˚ view.
- Lastly, the use of VR allows the risk-free simulation of immersive, interactive 3D environments that provide a perspective and visual experience much closer to that of the real world.

To the best of our knowledge, at the point of writing there is no Virtual Reality based gaze training for people with visual field deficit apart from the one presented in this work. However, research on the use of Virtual Reality for adjusting gaze behavior in other fields, such as for industry task training [23], medical procedures [24], or as therapeutic intervention for patients with mental health disorders [25], suggests that the use of VR applications is feasible to influence gaze behavior. In addition, it has been shown that skills trained in VR can have sustained transfer effect to real-world performances in tasks such as tire changing [26], golfing [27], simulated electronic assembly [28], or walking with minimal foot clearance [29]. In this work, we are investigating the potential of Virtual Reality to be applied for unsupervised, at-home gaze training, as well as the influence of gaze training in a virtual environment on the navigation performance in real-world tasks.

Materials and methods

The first part of this section will focus on the developed gaze training, its implementation, and the intentions behind its design. Subsequently, an experimental study will be presented to show how the gaze training impacted real-world navigation. A CONSORT flowchart for this study is provided in Fig 1.

Development of a virtual-reality based gaze training tool

The initial phase of our project was dedicated to the development of the gaze training software. The aim was to create a tool that is easy to use, engaging, and that provides visual training

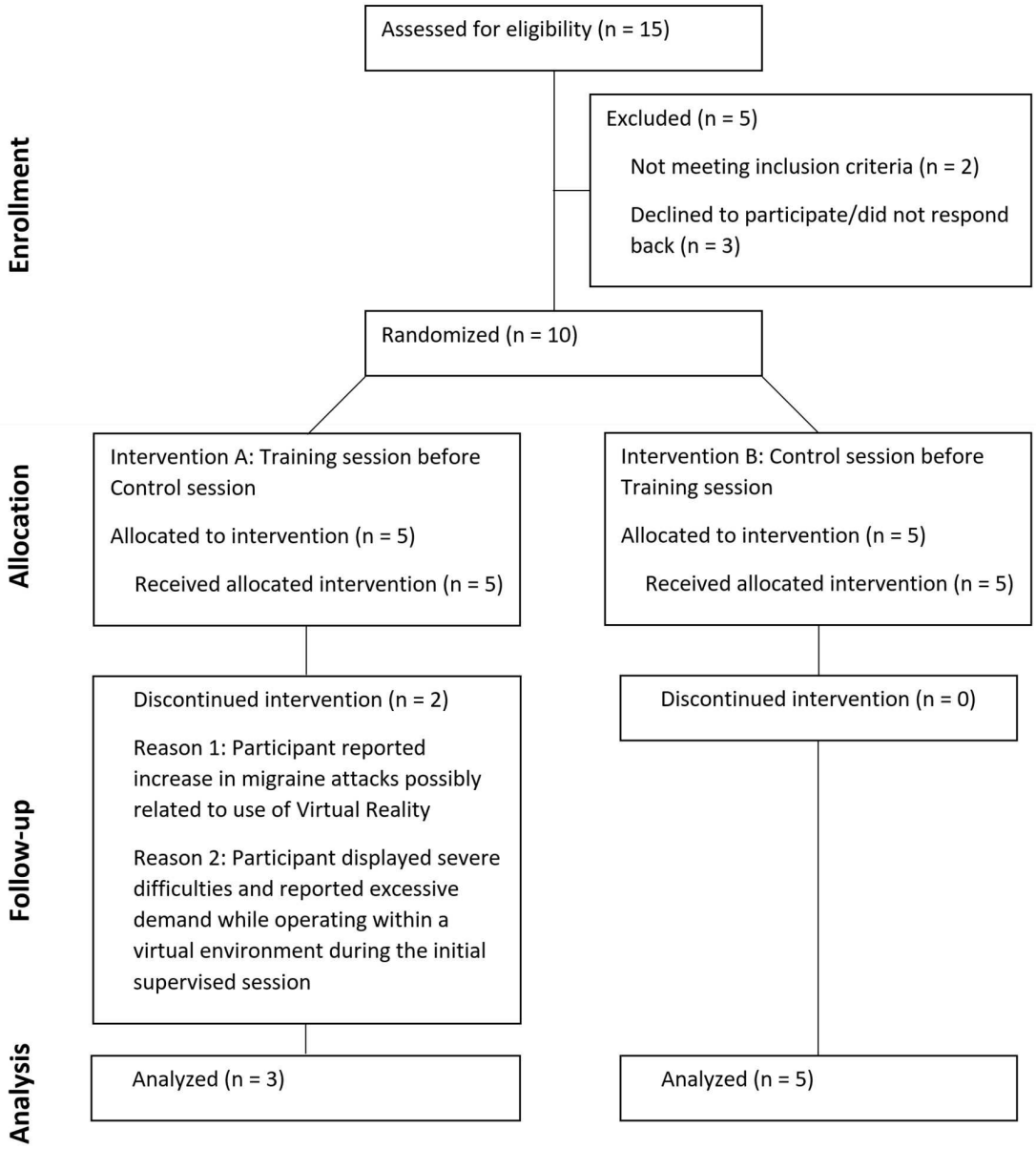

Fig 1. CONSORT flowchart. The CONSORT flowchart for the patient study described in this work.

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tasks to motivate larger and more frequent eye movements. The training should be usable in an unsupervised at-home environment. The realizability and feasibility of this aim was demonstrated in studies such as by Ivanov et al. [14] and Kuyk et al. [17]. However, this unsupervised training approach mandated measurements that ensure risk-free execution of the training. Thus, training was designed such that no physical movement is required that would put the user or their environment at risk of accidents. All tasks were designed to be executed in seated or stationary standing position: While the viewing direction within the VR environment was controlled physically through head and body rotation, any form of locomotion was triggered solely through controller input. The implications of this sacrifice of real-world mobility—in a training specifically designed to improve the mobility of patients—will be further addressed in the discussion.

Software and hardware specifications. The training software was developed in the Unity3D game engine (Version 2021.3LTS), using the Pico XR SDK (version 1.2.4). The Pico Neo 2 Eye VR headset was used for development and training. It provides stand-alone functionality, meaning that no connection to a computer or any external tracking devices is necessary. The device features a 75 Hz display refresh rate and the VF per eye is stated to be 101˚ [30] according to the developer's specifications, though independent measurements have shown a VF per eye of 89˚ both horizontally and vertically [21]. The built-in eye tracker of the Pico Neo 2 Eye has a refresh rate of 90 Hz and an accuracy of 0.5˚ according to the device specifications, with an ideal eye-tracking range of 25˚ horizontally and 20˚ vertically [30]. The use of VR is possible while wearing glasses or contact lenses.

Training tasks. The training software consists of three visual tasks. Considering the unsupervised nature of the training, it wasn't practical to base the training on specific gaze instructions given to patients, as is typically done in supervised experimental training conditions [12, 19]. While patients could have received instructions before training, continuously monitoring patients over the course of the training to ensure that instructions are followed correctly would not have been possible. Acknowledging this, the training tasks were instead designed such that their success criteria naturally promote exploratory saccades and frequent eye movements, encouraging patients to develop own strategies and adaptive behavior. This follows the approach of previously mentioned studies by Nguyen et al. [15], Ivanov et al. [14], or Pambakian et al. [13]. In the following sections, the three visual tasks designed for the training are described:

- **Target tracking** In this task, a varying number of targets (starting at five) move across a two-dimensional area in front of the user in a random pattern (Fig 2A and 2D). To make the task more visually appealing and thematic, targets were displayed as cartoon-styled mice. At the start of training, the area's dimensions are 52˚ horizontally and 39˚ vertically, which roughly represents 30% of the visual angles of a healthy VF at 180˚×135˚. Two of the targets are marked at the start of the trial (visualized as a piece of cheese carried by the mouse, as illustrated in Fig 2A), and the user is asked to follow the marked targets with their gaze in order to not lose track of them. After 8–12 seconds, all targets stop their movements, and the marked targets change their appearance to become indistinguishable from the non-marked targets. At this point, the user is prompted to select the two formerly marked targets through input of the VR controller. Selected targets are revealed to be either correct or incorrect. A trial is considered to be successful if the user selects both correct targets and no or only one incorrect target. When selecting two incorrect targets, the trial fails.
- **Search Task** Inspired by visual search gaze training methods as applied in different previous studies [13, 14, 16], this task requires participants to search an area in front of them for specified visual cues. As in the Target Tracking Task, the default dimensions of this area are 52˚

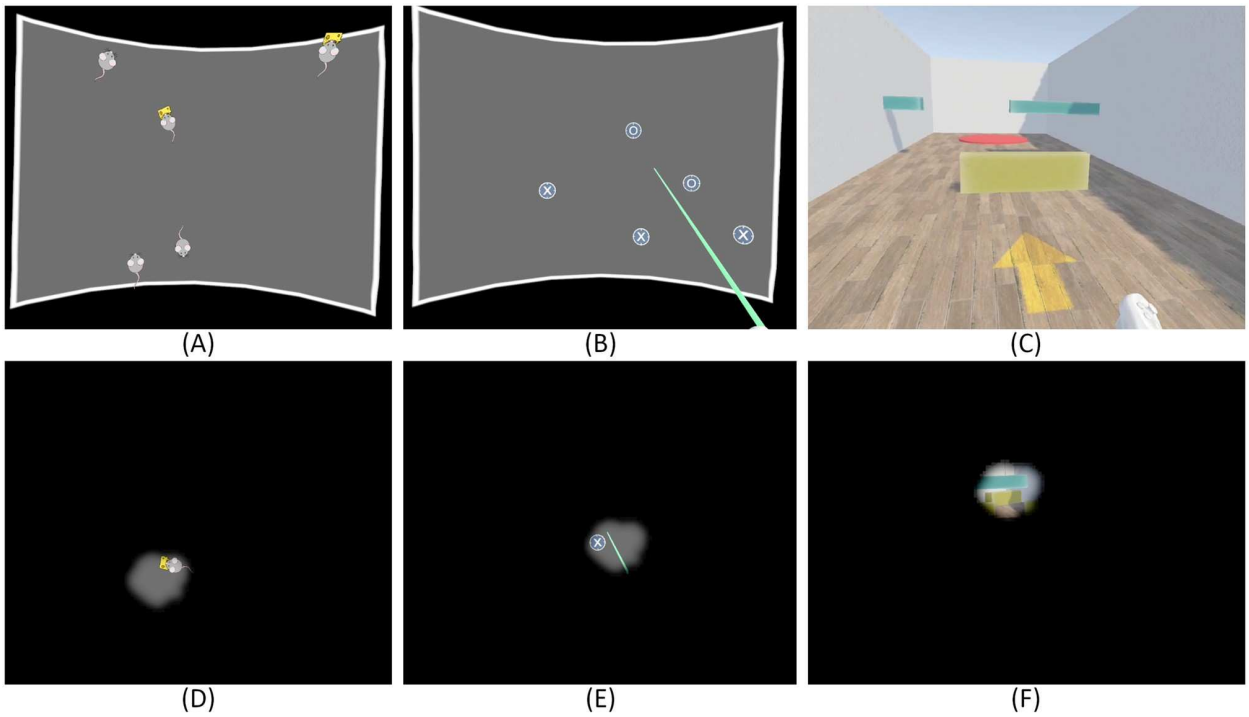

Fig 2. Screen captures of the three visual tasks of the VR gaze training. A: Target Tracking (marked targets are indicated by a piece of cheese); B: Search Task; C: Navigation Task; D: Target Tracking with simulated tunnel vision; E: Search Task with simulated tunnel vision; F: Navigation Task with simulated tunnel vision. The tunnel vision displayed in D-F has a 15˚ diameter. The tunnel vision simulation is added for visualization purposes in this manuscript only and was not present during participants' training. The grey training area has dimensions of 80˚×60˚ in these examples, representing an easy-to-medium difficulty level.

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horizontally and 39˚ vertically. The objective of the task is to search for stationary targets, marked by a prominent cross symbol (Fig 2B and 2E), and to use the controllers to select as many of them as possible within a given time frame of 20 seconds. A total of three marked targets are placed in the defined area and once a target is selected, it is instantly moved to a new position inside the designated area, with a minimum distance of 30˚ from the previous position. This minimum distance is introduced to avoid targets re-appearing directly in the participant's VF, thus further promoting continuous scanning of the area to find additional targets. In addition to the targets marked with a cross, there are similar targets marked with a circle that serve as distractors to ensure that participants fully focus on a target before selecting it. Each trial was rated based on the number of marked targets that are found within the limited time frame.

- **Navigation Task** In the third task, participants are asked to navigate through a randomized obstacle course simulated in a virtual environment (Fig 2C and 2F). Using the controllers of the VR device, the participant is able to move at a dynamic pace, with a set maximum speed of $3\frac{m}{s}$ by default. The movement direction is controlled via the participant's body orientation, which is measured through the VR headset's orientation. The obstacle course is designed as a corridor with two left turn tiles, two right turn tiles and two straight tiles, each measuring 8 meters in both width and length (Fig 3). The six tiles are arranged in randomized order for a total of 90 unique layouts. Along the corridor, 12 randomized obstacles are placed. To motivate adaptive eye movements, obstacles have different height, shape and

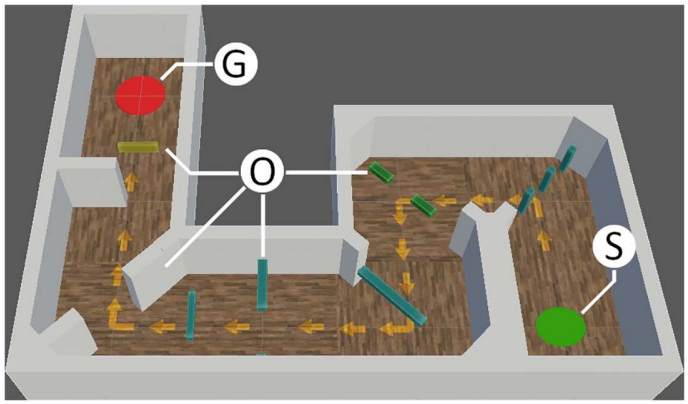

Fig 3. Navigation task visualisation. Top-down view on a randomized obstacle course of the Navigation Task. S: Starting position; O: Obstacles (example selection); G: Goal area.

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movement patterns and can be divided into three categories: Near-ground obstacles require scanning of the lower visual area; Obstacles hanging at head-level require eye movements towards the upper regions of the visual area; Moving obstacles periodically move from one side of the walking corridor to the other and thus require dynamic and frequent eye movements to notice and avoid them. Collisions with obstacles or the walls bordering the walking corridor are indicated through a sound cue as well as a "bouncing" animation that moves the user's avatar back slightly. The goal of the obstacle course is marked with a prominent red circle, which the participant has to reach in order to successfully finish the trial. The trial was rated based on the duration required to move through the obstacle course, as well as the number of collisions during the trial. A trial was considered fully successful if the trial duration was below a specified threshold (default 60 seconds). A trial was considered completely failed if the goal was not reached within twice the duration of the threshold. Collisions reduced the threshold by approximately $\sim$15% of its current value.

After each trial, participants are brought back to a selection menu in which they are able to inspect the rating and result of the trial as well as their overall progress, go back to the main menu or start the next trial. Additionally, participants had the option to mark the previous trial as "invalid", but were instructed to only mark trials as invalid if there were technical or external factors distorting the results. A video showcasing the three training tasks can be found in the S1 Video.

Adaptive difficulty levels. One of the design goals for the gaze training was to keep users engaged and motivated even throughout extended training phases. At the same time, the visual tasks should have low entry levels to make it easy for participants to get started and get used to the training tasks. To follow both premises, adaptive difficulty levels were introduced in all three visual training tasks. This means that the difficulty level of each individual task increases or decreases automatically based on the participant's current performance in that task, with the aim to ensure that the tasks remain at an appropriate level of difficulty to keep the user engaged and motivated. In the selection menu in-between trials, participants are informed about the difficulty level they have reached and about their progress towards the next difficulty level.

For the Target Tracking Task, higher difficulty levels translate to a larger bounding area in which the targets move, higher target movement speed, and a greater number of both marked

and unmarked targets. Similarly, increased difficulty in the Search Task leads to an expansion of the area in which targets are located, and increases the number of distractor targets while keeping the number of correct targets at three. In the Navigation Task, the maximum movement speed of the participant's avatar gradually increases with higher difficulty level, while at the same time reducing the time limit to move through the obstacle course without reducing the performance rating. Additionally, the speed of moving obstacles in the Navigation Task is adjusted to match the participant's increased movement speed, resulting in a faster-paced trial that demands quicker reaction times and heightened situational awareness to avoid obstacles.

Suggested gaze pattern. Preliminary studies [14, 31] suggest the potential of specific systematic eye movements—called gaze patterns—to positively impact gaze training. Following this, participants were encouraged to follow a suggested, systematic gaze pattern (visualized in Fig 4) while executing the training.

The shape of the gaze pattern was selected following the findings of a previous study [31] in which two popular gaze patterns were tested. One of the gaze patterns that were suggested to patients in this study (Fig 4) was found to lead to better results in both navigation as well as search tasks when compared to the competing pattern. However, findings of this and other gaze training studies [19] also suggest that training and application of specific, mandatory gaze patterns can potentially result in a reduction of the subjects' walking speed.

Thus, in this study, patients were given autonomy in choosing if—and to which degree—they want to follow the suggested gaze pattern. The pattern was visually introduced to the patients on a screen prior to the use of the gaze training, explaining its background and potential advantages.

In addition, after each training trial within the VR environment, participants received automated feedback in form of a "similarity value", a quantitative measurement of how closely their real gaze behavior matched the suggested gaze pattern. This quantitative measure of similarity between gaze behavior and suggested gaze pattern is evaluated at run-time using a Multimatch algorithm [32], and is described in detail in Appendix A in S1 Appendix.

Experimental study

To test the influence of gaze training on the navigation performance in the real world, we designed an experimental randomized controlled crossover study. The layout consisted of two phases (Fig 5):

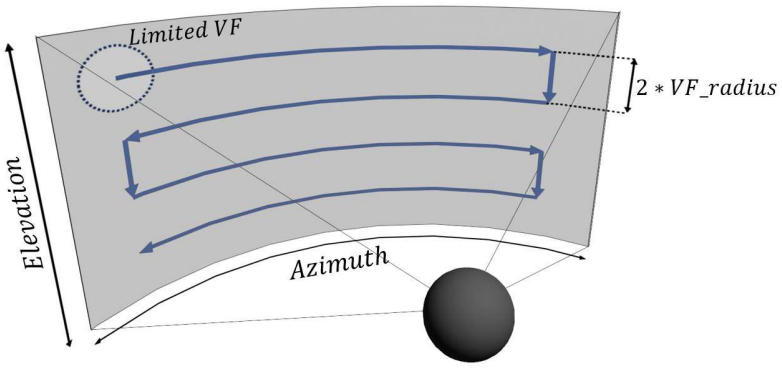

Fig 4. Gaze pattern visualization. Visualization of the pattern presented to the participants. The pattern starts in the upper left (or right) corner, moving along the azimuth axis to the opposite side. Then the pattern moves down along the elevation axis with an angular distance equal to the diameter of the participant's VF. This pattern is continued until the lowest area was scanned. Following this pattern ensures that a large visual area is covered by the limited VF in an efficient manner.

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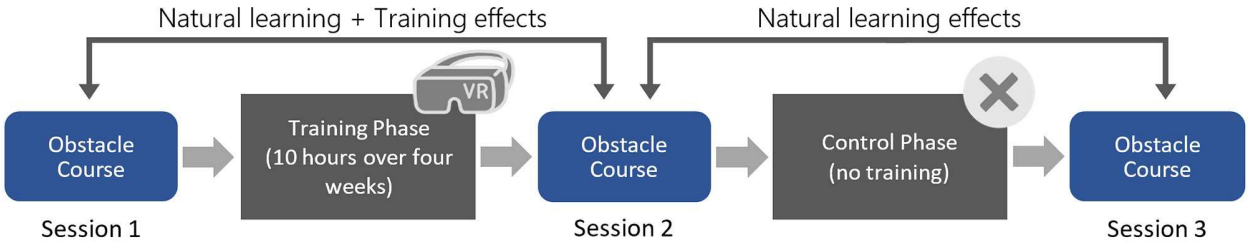

Fig 5. Study structure. Schematic of the study structure, including two phases of 3–4 weeks and the three in-person obstacle course sessions held. The order of training phase and control phase was randomized for each participant.

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- In the training phase, participants used the developed VR gaze training software at home for 10 hours over the course of 3–4 weeks (20 training sessions, 30 minutes per day, 10 minutes per task).
- In the control phase, participants would follow their normal life routine over a similar duration without carrying out any gaze training.

The experimenter randomized the order of the two phases for each participant during scheduling using a random number generator, allocating five participants to the group starting with training and five participants to the group starting with the control phase. Before and after each phase, participants completed an in-person session in which their task was to move through a randomized real-world obstacle course (20 trials per session). Details about the setup and experimental environment for these sessions and the obstacle course trials can be found in Experimental setup. The purpose of the control phase was to account for any improvements that might occur during the task that are not correlated to the gaze training. Despite randomizing the obstacle course setup to minimize memorization effects, participants can still be expected to learn and improve their performance by becoming familiar with the base structure and types of obstacles in the obstacle course. This natural improvement in performance is considered the 'natural learning effect' of the experiment.

The impact of the training can thus be evaluated in three steps:

1. We assess the navigation performance in the real-world obstacle course before and after the training phase to determine the combined effect of both the potential training effect and natural learning effect. At this step, it is not yet possible to distinguish between the two effects.
2. Next, we assess the navigation performance before and after the control phase to find the natural learning effect displayed by participants, with no influence of gaze training.
3. By determining the differences between the "distilled" natural learning effect found in step 2 and the combined effect of training and natural learning found in step 1, it is possible to evaluate the effect that the developed gaze training has on real-world navigation performance. If the effect found after the training phase is significantly higher than the effect after the control phase, the gaze training can be considered successful.

Ethics and clinical trial registry. This study was proposed to and approved by the ethics committee of the Institutional Review Board of the Medical Faculty of the University of Tübingen (628/2018BO2) in accordance with the 2013 Helsinki Declaration. Patients were

recruited in the time from June 9, 2022 to November 22, 2022. All participants signed written informed consent forms. The study is registered as a clinical trial at the German Clinical Trials Register (DRKS) with the registry ID DRKS00032628. The registration was done retrospectively, as the study was originally considered as non-interventional observation study, not as clinical trial. Prompted by later feedback, this decision was reconsidered and the study was registered. The authors confirm that all ongoing and related trials for this intervention are registered.

Study population. 10 patients (one male, nine female), aged between 20 and 60 years (average 49.6 ± 13.0), participated in the study, two of which discontinued the study early on. Details about the reasons for discontinuation are provided in the Discussion. Participation criteria were the diagnosis with Retinitis pigmentosa, a VF between 5˚ and 30˚ diameter, a visual acuity of 0.1 or higher, and unrestricted mobility. It was tested in the first session that the participants are able to effortlessly see and recognize all targets and other visual features used in the gaze training, as well as all interfaces and menus required to operate the VR headset. The sample size was determined following the calculation for sample size in longitudinal studies comparing mean change with two time points, found in Rosner [33], equation 8.30), assuming a standard deviation of 20% (estimated based on Baroudi et al. [34]) of the mean navigation performance and an increase in performance of 25% after training, with an alpha of 0.05 and a power of 0.8.

Table 1 lists information about the eight participants that finished the study. The provided medical data is based on the most recent medical examination of each patient. The medical examinations only provided visual representations of the VF of patients, which are included in Appendix B in S1 Appendix. In addition to these, the VF was measured during the first in-person session using a VR based kinetic perimetry developed for this project. While these

Table 1. Patient data.

Patient (Age / Sex)	Age of diagnose	Visual field (RE / LE)	Visual acuity[1] (RE / LE)	VF notes	Gaze training experience	VR experience	Vision correction
1 (20f)	14	7.62˚ / 8.26˚	0.40 / 0.40	-	-	high	G/C[2]
2 (57f)	27	18.64˚ / 18.18˚	0.20 / 0.05	spots[3]	VisioCoach[4]	-	G
3 (55f)	18	17.64˚ / 16.36˚	0.13 / 0.20	-	-	-	G
4 (47m)	25	24.60˚ / 25.40˚	0.05 / 0.05[5]	-	-	low	G
5 (59f)	50	18.54˚ / 18.34˚	0.32 / 0.25	spots[3]	VisioCoach[4]	-	G
6 (59f)	16	10.92˚ / 9.64˚	0.10 / 0.10	-	-	-	G
7 (40f)	18	12.18˚ / 14.56˚	0.40 / 0.32	spots[3]	VisioCoach[4]	-	G
8 (60f)	20	20.00˚ / 19.48˚	0.50 / 0.40	-	-	-	G

Summary of general patient data. In addition to the displayed data, all patients reported to have undergone Orientation & Mobility training with the white cane and were using the white cane as a navigation aid in everyday life. The column 'Visual field' reports on the average diameter of VF for right eye (RE) and left eye (LE) measured within the VR setup. Visual acuity reports on the Visual Acuity of patients measured during their most recent medical examination.

[1]Visual acuity is notated as decimal score.

[2]G = Glasses, C = Contact lenses. These refer to visual aids used in everyday life. Only contact lenses were worn during experimental trials, as glasses would interfere with the applied eye tracking device.

[3]The patient displays some spots of remaining vision in the peripheral field.

[4]A commercially available screen-based gaze training software for RP patients [35], applied in the previously mentioned studies by Ivanov et al. [14] and Roth et al. [16] and evaluated by Hazelton et al. [18].

[5]It should be noted that participant 4 does not meet the participation criterion of a visual acuity >0.1. This was discovered only after the start of training, since the initially provided medical examination report did not include results for the visual acuity. However, despite not meeting this criterion, the participant was still able to navigate the VR interface and did not exhibit any difficulties in recognizing the visual targets required for the tasks. Consequently, it was decided to continue with the study participation.

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measurements do not have diagnostic validity, they provide a better estimation of the perceived visual area of patients within the VR setup. This approach also ensured consistency in the measurement of VFs between participants.

Experimental setup. The real-world obstacle course was set up in an area with the dimensions of 4.8 meters width and 9.0 meters length. Two static privacy screens (visible in Fig 6) were placed such that an S-shaped corridor is formed. This extended corridor had a length of 18 meters—assuming a pathway exactly along the middle of the corridor—and a width of 3 meters.

Within the path, different obstacles were placed in a semi-randomized layout. Each obstacle arrangement consisted of 12 large carton boxes measuring 120×60×60 centimeters. Six of the boxes were oriented horizontally, six vertically. The set of obstacles also included six low-height obstacles that required participants to step over them, measuring 120×20 centimeters. Lastly, three sheets of cloth of 60 centimeters width were hanging from the ceiling, their lower edge at a height of 150 to 170 centimeters, adjusted to be on participants' eye level. A total of 20 randomized obstacle layouts were created, with each layout being used exactly once per session. An example for one of these layouts is found in Fig 7. All obstacles were colored in blue to increase the contrast against the floor and background. The primary walking direction of the obstacle course was chosen such that participants were always facing away from the windows to avoid glare effects. The room was fully lit during all trials. A video showcasing the obstacle course in an example trial is found in the S2 Video.

During the trials, participants were wearing Pupil Labs Invisible eye tracking glasses [36]. The device provides a 0.5˚ accuracy and a 200Hz refresh rate [36] according to the technical specs provided by the seller. Tonsen et al. [37] find that the mean bias of gaze-estimation ranges from below 0.5˚ up to 2.5˚ based on the VF region, with mean sample errors of 5˚ to 6.5˚. Inertial measurements for tracking of head rotation use Madgwick's algorithm [38], but no specifics are given about their accuracy and precision. Timestamps for start and stop of each trial were measured and automatically stored using a custom smartphone application built with the Unity3D game engine.

Experiment execution. Each session was initiated with four unmeasured trials to familiarize the participant with the task, the types of existing obstacles and the shape of the walking corridor. After that, 20 measured trials were done. Details on the measured parameters within these trials are found in Measurement parameters.

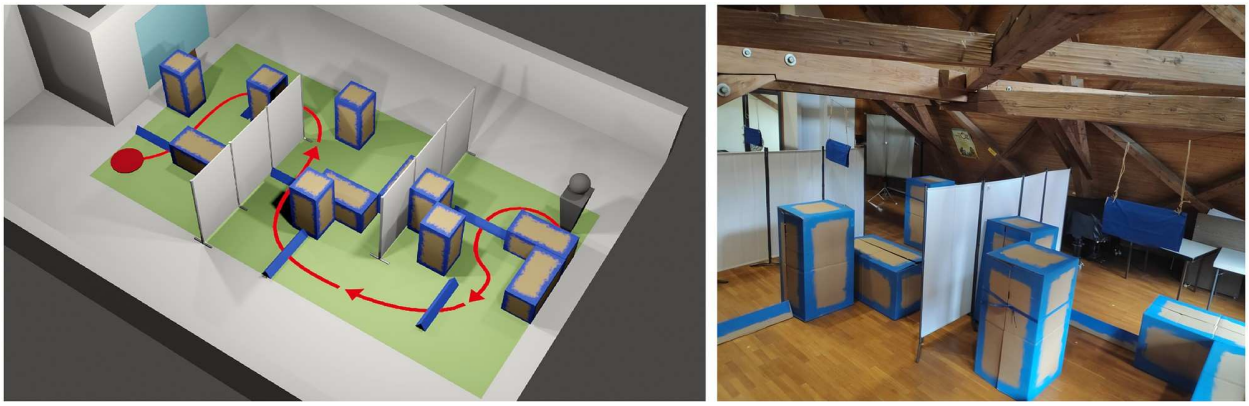

Fig 6. Obstacle course layout. Example of the real-world obstacle course in simulation (left) and actual setup (right). The simulated obstacle course is for presentation purposes only and was not used as part of the study.

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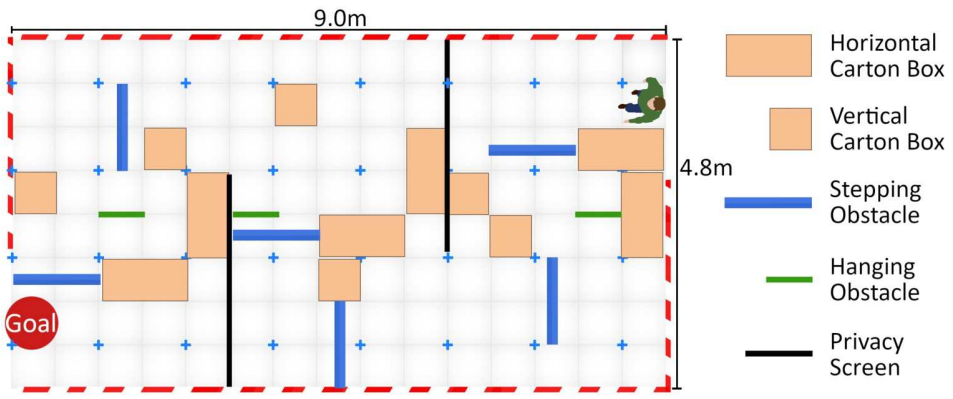

Fig 7. Obstacle course schematic. Example of one of the schematic layouts used to set up the obstacle course before each trial. Participants started each trial at the position that is marked by a person in the layout.

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Prior to each trial, the experimenters positioned the obstacles according to one of 20 different layouts. Once the obstacle course was set up, the participant was guided to the starting position and directed to face forward towards the opposite side of the obstacle course. At this point, the Pupil Labs eye-tracking device was activated using the corresponding smartphone app. During this process, the participant had the opportunity to visually explore the scene, although only the initial third of the obstacle course was visible from the starting point due to the privacy screens. When everything was prepared and the participant confirmed their readiness, a second smartphone was used to start a timer and simultaneously play a sound cue, signaling the participant to start. While the participant navigated through the obstacle course, an experimenter followed them at a distance of approximately 3 meters, monitoring for any collisions that occurred during the trial. Upon reaching the designated goal area, the timer was stopped, accompanied by a second sound cue to indicate the completion of the trial.

During the session prior to the start of the gaze training, which could be either the first or second session, depending on the order of training and control phase, participants were introduced to the VR device and gaze training application. They were given the opportunity to familiarize themselves with the controls of the VR device and were guided through a tutorial of about 30 minutes duration in which the three visual tasks as well as the interface navigation within the gaze training application are explained. During this explanation, participants were also introduced to the suggested gaze pattern.

Measurement parameters. Two sets of measurement parameters were acquired as part of this study. The first set consists of the results of the real-world obstacle course trials, which were acquired during the in-person sessions. The second set consists of the performance and eye tracking information measured within the gaze training application during the four-week training phase. The following list summarizes all measurement parameters that were considered in the evaluation of this work:

Real-world obstacle course measurements

- **Trial duration** Trial duration in the real-world obstacle course trials describes the time required by the participant to move from the starting position to the designated goal area. It was measured with the custom smartphone application described in Experimental setup.
- **Collisions** This parameter describes the number of obstacle collisions that occurred during a trial. Collisions were visually observed and documented by an experimenter who was closely

following the participant during the trials. Collisions were categorized into two types: 'Full collisions' referred to frontal impacts where the obstacle was visibly and audibly struck—typically by the participant's foot -, requiring a complete adjustment or re-evaluation of the movement path. 'Light collisions' referred to situations where obstacles were grazed or lightly touched, without impeding the participant's motion. This distinction was made to acknowledge that patients may limit their efforts on the avoidance of collisions that would—in a real-life scenario—pose risks of accidents or injuries. Given that light collisions would usually not pose such risks, it is possible that patients put less priority on avoiding these types of collisions. Thus, if a shift from 'mostly full collisions' to 'mostly light collisions' is detected between two sessions, it can be considered a positive effect on navigation performance.

- **Dynamic visual field** Using Pupil Labs Invisible eye tracking glasses, both the direction of gaze relative to the head and the orientation of the head itself are measured during the real-world obstacle course trials. Based on these two parameters, the dynamic visual field (DVF) is calculated. We define the DVF as the visual area observed over a specified amount of time. When fixating a single point, a person with tunnel vision would only be able to observe the area within their normal VF—in this context, this could be described as the 'static' visual field. However, as soon as the person starts moving their gaze, they will automatically explore and observe new areas of their visual surroundings. Measuring this observed area over a fixed duration results in the DVF. Notably, the DVF only increases if new visual area is explored that has not already been observed within the specified time frame. In this work, the time frame for the DVF is set to three seconds. This means that the DVF at any point of time is defined as the observed visual area over the last three seconds. Averaging the DVF for all measured samples within a trial provides the average DVF for that trial. The DVF is reported and evaluated as a percentage change, showing how much the DVF increased or decreased over the course of the training or control phase. An increase of average DVF of 10% indicates that the person was able to observe 10% more of their surroundings. DVF is calculated considering all eye tracking samples, both during fixations and during saccades, since detection of potential obstacles or points of interest is possible even during eye movements [39]. A detailed description for how the DVF is calculated and computed is found in Appendix B in S1 Appendix.

- **Saccade characteristics and gaze pattern similarity** In addition to the DVF, the eye tracking data were also used to determine saccades during the trial, following an approach by Nyström et al. [40]. In a first step, the current gaze speed for each sample frame of the captured eye tracking data was calculated, summing both eye movements and head rotation angles. The data was smoothed out by applying a moving window average over five frames ($\sim$25ms). Next, the mean μ and standard deviation σ of the noise of the eye tracking samples were determined. For this, only samples with angular gaze speed below 100˚/s were considered. Following the approach of Nyström et al., a saccade was detected when a peak in the gaze speed surpassed a threshold $v_{max} = \mu + 6 * \sigma$. If a saccade was detected like that, the start- and end point of the saccade were determined based on a second threshold $v_{onset} = \mu + 3 * \sigma$. Appendix C in S1 Appendix shows an example graphic that visualizes saccade detection using this approach. The saccades were analyzed for different characteristics. The first characteristic was the ratio of exploratory saccades, defined as the number of saccades larger than the average visual field radius divided by the total number of saccades per trial. Next, the saccade frequency was determined as the average number of saccades per second. The average ratio between the horizontal and vertical components of saccades was determined to assess whether patients move their gaze more vertically or horizontally. Following an approach by

David et al. [41], we analyzed the direction of each saccade relative to its preceding saccade. This provides additional insight into the patients' gaze behavior. Lastly, the saccades were used to calculate the gaze pattern similarity value as described in Suggested gaze pattern. Saccades were determined by considering world-centric gaze, meaning that both the direction of the eyes as well as the rotation of the head were considered.

Gaze training measurements.

- **Target tracking task performance** The performance of the Target Tracking Task—the task in which participants had to track and select a number of marked targets—was evaluated based on the number of incorrectly selected targets per trial. Each trial's performance was measured on a point scale, where trials with no incorrect targets selected were rated with two points, and trials with one incorrect target equated to one point. However, due to the gradual change in difficulty levels of the task—described in Training tasks—rating each trial in the same way would not result in a good approximation of a participant's total performance, as higher difficulty levels are likely to result in lower success rates. For the Target Tracking Task, the main factor that influences the difficulty of a task is the number of marked targets that must be tracked simultaneously. It is not feasible to compare a trial with only two marked targets to a trial with three or even four marked targets. Thus, to achieve a balanced approximation of task performance, only trials with four marked targets were considered, which is 45.1% of all measured trials.
- **Search task performance** In the Search Task, the base performance can simply be measured as the number of targets found and selected during the fixed 20-second time period of a trial. However, this again does not consider the change in difficulty level, which results in a larger or smaller area that has to be scanned to find the targets. To account for this, the Search Task performance score was adjusted based on the size of the search area in which targets would be placed, such that $P_{adj} = n * (w_{area} * h_{area})$, where P_{adj} is the adjusted performance score, n is the number of targets found and w_{area} and h_{area} being width and height (in visual angles) of the search area. In other words, to achieve the same performance score in a search area four times larger, the participant would have to find four times fewer targets.
- **Navigation task performance** The performance of the Navigation Task consists of two measurement parameters, both of which are reported on separately. The first parameter is the trial duration, which is the time taken from start to finish of the navigation course. The second parameter is the number of collisions during a trial. The layout of the obstacle course did not change with varying difficulty levels, making trials of different levels of difficulty more comparable to each other than in the other two tasks.
- **Gaze direction and dynamic visual field** Similar to the real-world course trials, both head-centered gaze direction and head rotation were measured in all three visual tasks of the gaze training, using the VR headset's built-in Tobii eye tracking device. This data was used to calculate the DVF on a frame-by-frame basis, using the combined gaze direction.

It must be noted that the performance scores calculated for the visual tasks of the gaze training are just an approximation of a participant's actual skill level at different stages of the training, and are influenced by the methods that are applied to consider and eliminate the impact of varying difficulty levels on the performance.

Questionnaire. Five times during the training phase—following the initial training session and subsequently after every five training sessions -, participants were requested to complete a questionnaire to assess subjective ratings of enjoyment, motivation, stress, eye strain and other related factors. The questionnaire always featured the same questions, with seven of

the questions following a 10-point Likert scale format and four questions allowing for free-form answers:

Questions to rank from 1 to 10:

- **Enjoyment**—To what extent do you find each of the visual tasks enjoyable?
- **Motivation**—How motivated are you to improve your performance in each of the visual tasks?
- **Easiness**—How would you rate the ease of carrying out each of the visual tasks?
- **Stress**—To what degree do you experience stress while executing each of the visual tasks?
- **Eye Strain**—How straining is each visual task on your eyes?
- **Intuitiveness**—How intuitive is the use of the gaze training software?
- **Discomfort**—How much physical discomfort do you experience while wearing the VR headset?

Questions with free-form answers:

- **Feedback for gaze training**—Which aspects of the gaze training application did you perceive as especially positive or negative?
- **Feedback for VR device**—Which aspects of the Virtual Reality headset did you perceive as especially positive or negative?
- **Feedback and suggestions**—What changes or improvements would you like to see implemented in the gaze training application?
- **Technical issues**—Did you encounter any technical issues during the training? If so, please describe.

Evaluation process and statistical methods

In the real-world obstacle course tasks, effects for the four measurement parameters were tested. Each parameter was tested using two different paradigms: First, the effects of training- and control phase were assessed individually by testing the data acquired in the session before the respective phase against data acquired in the session after the phase (Pre-Post test). Second, the two effect sizes from training and control phase are tested directly against each other to determine if training effects significantly surpass effects of the control phase (Training-Control test). For this test, delta values for each trial are calculated: For example, the difference between the first trial of the session before the training/control phase and the first trial of the session after the training/control phase is calculated. This way, the effects for each phase can be expressed as a set of delta values. By testing the set of delta values from the training phase against the delta values from the control phase, statistical significance between effect sizes can be evaluated. The following sections describe the statistical models and pre-processing steps for each measurement parameter.

- **Trial duration** For the Pre-Post test, a Linear Mixed Model (LMM) with trial duration as dependent variable is used. As a fixed factor, the 'pre-post condition' is applied. This binary parameter signifies whether a respective trial originates from the real-world session before or after the relevant phase. In addition to the fixed effect, participants were included as a random factor in the model, considering both random intercept (to consider different innate

skills) and random slope (to consider different learning rates). Since trial duration results were not normally distributed and instead followed a right-skewed distribution, a logarithmic transformation was applied to the data to better meet the requirements of an LMM. A QQ-plot for the results with logarithm taken is found in (Appendix D in S1 Appendix). The Training-Control test was tested mostly analogous to the Pre-Post test, again using an LMM. Delta trial duration was used as dependent variable, with the respective phase (training or control) as fixed factor.

- **Collisions** The collision parameter does not meet the requirements of a standard LMM, as its values are discrete count data, rather than continuous and normally-distributed. In addition, data was highly zero-inflated, with more than half of all trials (64.0%) showing zero collisions. Thus, for the Pre-Post test, we applied a negative binomial Generalized Linear Mixed Model (nbGLMM) which is suited for this type of data [42, 43]. As before, the pre-post condition was considered as a fixed effect and participants were considered as a random effect, with one model testing the effects over the training phase and a second model testing the effects over the control phase. For the Training-Control test, values were no longer zero-inflated, as the delta values could be both positive and negative. Thus, a Generalized Linear Mixed Model (GLMM) was applied.
- **Dynamic visual field** The DVF was found to follow normal distribution quite well (the QQ-plot is found in Appendix D in S1 Appendix) and data is continuous, allowing the use of an LMM for both Pre-Post test and Training-Control test with no additional transformations. Analogous to the other measurement parameters, the Pre-Post test uses absolute DVF values as dependent variable and the pre-post condition as fixed factor, whereas the Training-Control test uses delta values of the DVF as dependent variable and the respective phase as fixed effect.
- **Gaze pattern similarity** The different saccade characteristics—ratio of exploratory saccades, saccade frequency, ratio of vertical to horizontal gaze movements, as well as the change in directions of saccades, were evaluated analogous to the DVF. The same is true for the gaze pattern similarity.

While the order of the obstacle trials was changed between sessions, each of the 20 obstacle trial layouts was used exactly once per session. This ensures that the effect of different layouts on the performance within the obstacle course does not have to be considered in the statistical models.

Regarding the results of the Virtual Reality gaze training, it was modeled and analyzed how the task performance as well as the DVF in all three visual tasks changes over the course of the training.

- **Target Tracking Performance** As described in Measurement parameters, the performance in the Target Tracking Task is based on the number of incorrectly selected targets at the end of a trial. To measure this, a point scoring system was employed, where a score of 2 points was assigned for trials with zero errors, 1 point for trials with one error, and 0 points for trials with two or more errors. This means that the Tracking Task Performance can be treated as count data, and thus a Generalized Linear Mixed Model (GLMM) was employed for the analysis. Fixed factors of the model are the training session number (from 1 to 20) as well as the number of the current trial within the training session, as both can be assumed to have an influence on the task performance. Once again, participants were considered as random factor with both random intercept and random slope.

- **Search Task Performance** Search Task Performance was measured as the number of stationary targets found in a 20 second interval. QQ-plots found it to roughly follow normal distribution, making the use of an LMM suitable for analysis. As before, fixed factors of the model included training session and trial number, participants are considered as random factor.
- **Navigation Trial Duration** Similar to the real-world obstacle course trials, the trial duration of the Navigation Task trials was found to be right-skewed, thus the logarithm was taken for the analysis. An LMM was employed analogues to the previous analysis of the Search Task Performance.
- **Navigation Trial Collisions** The number of collisions per trial can be treated as zero-inflated count data, similar to the collisions in the real-world obstacle course. This indicates the need for a nbGLMM, where training session and trial number are treated as fixed factors, participants as random factor.
- **Dynamic visual field** The DVF was analyzed the same for all three visual tasks using an LMM. No transformation was required, as DVF followed normal distribution in all three tasks according to QQ-plots. Following the previous models, the DVF was tested against the training session and trial number as fixed factors, with participants being considered as random factor.

The alpha level that determines the threshold for statistical significance was chosen as 0.05 for all models. All errors are reported as the standard deviation of results. Analysis was done using R and the RStudio graphical interface with the nlme and lme4 library. The detailed models and results of the statistical analyses can be found in Appendix D in S1 Appendix. The results of the questionnaires are reported on qualitatively, as the number of samples is too low for statistical analysis.

For the real-world obstacle course results, it must be mentioned that 61 out of 480 measured trials did not include complete gaze-tracking data (25 of these trials included head-centric gaze data but no head rotations, 36 trials were missing both eye- and head-tracking data) and thus had to be discarded from the analysis of DVF. This loss of data was likely caused by a shaky contact of the eye tracking device and was only detected late in the experiment phase. The data loss affected three sessions in particular: The eye-tracking data was lost or incomplete in 15 out of 20 trials in the second session of participant 4, 18 out of 20 trials in the second session of participant 6, and all 20 trials in the first session of participant 1. Thus, for participant 1, no results for the change of DVF over the control phase could be evaluated.

Deviations from original study protocol

This chapter lists the deviations of the actual methods from the original study protocol:

- The initial proposal outlined the use of a Fove-0 VR headset for the study. In the time between the ethics application and the start of the study, new VR devices became available that were better suited for at-home training, notably the Pico Neo 2 Eye, which ultimately became the chosen hardware for this study. The main advantage of the Pico Neo 2 Eye compared to the Fove-0 is its self-contained hardware, as it does not require any external hardware setups.
- The protocol allocated a total of 30 RP patients for the study, divided into two groups of 15 patients each: A training group and a control group. During the patient acquisition phase it became clear that the number of RP patients interested in study participation would not

allow for this study population size. Thus, the design was changed to a crossover study, with all patients carrying out both training and control phase in randomized order, as is described in Experimental study. Additionally, the protocol provided for inclusion of an additional group of visually healthy participants as control. This plan was discarded because the low relevance of the results to be obtained from this group would not have justified the additional time and material effort.

- The setup of the real-world obstacle course used in the study deviates from the one described in the protocol. The protocol outlined a 68m long and 1.3m wide corridor. At the time of the study, no location was available that would have allowed for a course of these dimensions. Thus, the course was adjusted to the dimensions described in Experimental setup.
- The protocol planned for a mandatory 'eye motion' task as part of the gaze training. As was mentioned in Suggested gaze pattern and will be further addressed in Discussion, the part was instead included as a voluntary task, following the findings of a preliminary study focused on the effects of gaze patterns in gaze training [31].
- In addition to the real-world obstacle course, the protocol provided for a performance evaluation in a realistic city environment within the virtual world. This plan was discarded because the development of a realistic 3D city environment would have been beyond the available time and expertise for the study.
- Lastly, the methods for statistical analysis were changed. The original protocol outlined the use of t-tests and mixed model repeated measures ANOVA analysis. Over the course of the study assessment, it was decided that Linear Mixed Models as well as negative binomial Linear Mixed Models are more suitable for the statistical evaluation of the acquired data.

Results

Real-world obstacle course

A total of 480 real-world obstacle course trials were absolved, split among 8 participants with three sessions each. The raw result tables for the trials are found in the supplementary material of this work. Fig 8 shows the results for navigation performances and the DVF of the eight participants.

Navigation performance: Trial duration and number of collisions. After the training phase, participants displayed a significant improvement in trial duration by 17.0% compared to the performance before the training ($p < 0.001$), decreasing the average trial duration from 37.2 (±12.3) seconds to 30.9 (±8.68) seconds. The average number of collisions per trial decreased by 50.0% after training ($p < 0.001$), from 0.513 collisions per trial to 0.256 collisions per trial. A comparison with the results before and after the control phase shows that the training phase was significantly more effective in improving the average trial duration ($p < 0.001$) and reducing the number of collisions ($p = 0.0165$) than the control phase. The average trial duration had improved by 5.9% after the control phase, from 34.8 (±12.7) seconds to 32.7 (±9.87) seconds. The average number of collisions per trial improved by 10.4% after the control phase, from 0.391 to 0.350 collisions per trial. Overall, the results suggest that the training phase was significantly more effective in improving navigation performance compared to the control phase.

Out of the four obstacle types in the real-world obstacle course—horizontal box, vertical box, stepping obstacle and hanging obstacle—the type that caused most collisions is the stepping obstacle with a total of 76 full collisions and 53 light collisions in all 480 trials. However, it

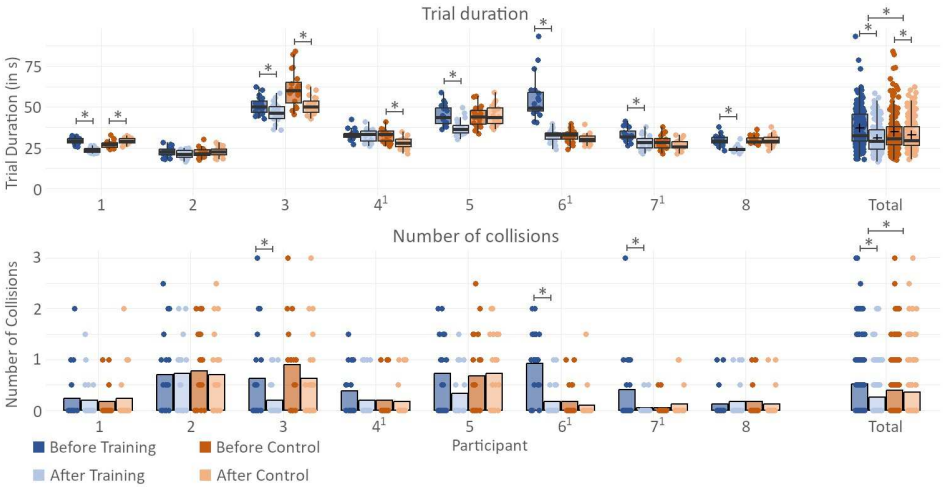

Fig 8. Obstacle course results. Participants' performance in the real-world obstacle course trials before and after each of the two phases. *indicates significance ($p < 0.05$). P-values for individual patients were evaluated by applying the statistical models to a subset of the data containing only trials of the respective patient. [1]marks participants who carried out the training phase before the control phase; all other participants started with the control phase and carried out the training phase afterward.

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is shortly followed by the hanging obstacle at 75 full collisions and 52 light collisions. Considering that each obstacle course layout features six stepping obstacles, but only three hanging obstacles, it can be stated that the hanging obstacles pose the highest risk for collisions. Very few collisions were tracked for the horizontal and vertical boxes, with 6 full collisions and 8 light collisions for horizontal boxes and 3 full collisions and 13 light collisions for vertical boxes.

Visual performance: Dynamic visual field and gaze patterns. Using the eye-tracking data collected during the real-world obstacle course trials, it is possible to evaluate how the average DVF of participants—the visual area observed over time—changed over the course of training and control phase, as shown in Fig 9. Although the average increase in world-centric DVF of 4.41% is found to be significant ($p < 0.001$) when evaluating the data before and after training, the effect is not significantly larger than the increase in DVF displayed after control ($p = 0.394$) at 2.06%. Three of eight participants (1,3,6) display a notable increase in world-centric DVF after the training phase, with two participants (4,8) showing decreases. When considering only head-centric eye movements, no significant change in DVF is found for the average DVF after either phase, with a change of -0.052% ($p = 0.175$) after training phase and 0.108% ($p = 0.383$) after control phase and no significant effect between training and control ($p = 0.148$). While this suggest that the increase in DVF originates mainly from a change in head movements, rather than eye movements, two of the three participants (3, 6) with notable increase in world-centric DVF also show similar increase in gaze-centric DVF.

The results of the evaluation of the gaze pattern similarity—the value describing how closely the participants' displayed gaze movements match the suggested gaze pattern that was presented in Fig 4—is shown in Fig 10. There is no significant increase found after either of the two phases ($p = 0.168$ for training phase, $p = 0.147$ for control phase), and the similarity values give no indication that participants were actively following the suggested gaze pattern.

Similar to the results of DVF and gaze pattern, a direct comparison between effects of training and control phase on different saccade characteristics does not show significance. Saccade

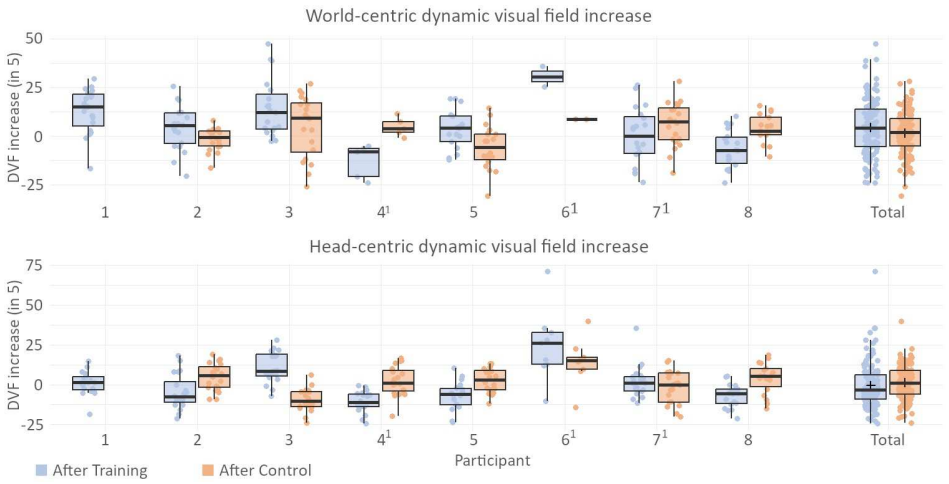

Fig 9. Dynamic visual field. Increase of the dynamic visual field in the real-world task after training phase or control phase respectively. Top graph shows the results based on world-centric gaze data (considers both head- and eye movements) whereas the bottom graph shows results based on head-centric gaze data (only eye movements, no head rotation considered). DVF was calculated over a 3 second rolling window. [1]denotes participants that carried out the training phase before the control phase.

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frequency was found to increase by 3.20% after training and decrease by 1.73% after the control phase ($p = 0.36$). Exploratory saccade ratio decreased by 1.32% after training and increased by 0.69% after control ($p = 0.44$). 6.5% more vertical eye movements were displayed after training, 0.39% more after the control phase ($p = 0.09$). No significant changes are found in the direction of saccades relative to the preceding saccade ($p = 0.068$ for angles of 45˚-135˚, $p = 0.53$ for angles of at least 135˚). It can be noted that a strong variation between individual patients was found for the results, which is further elaborated in the Discussion.

Virtual-reality gaze training

For the gaze training, a total of 3125 Target Tracking trials, 3205 Search Task trials, and 2583 Navigation trials were evaluated, distributed across the eight participants and ∼20 training

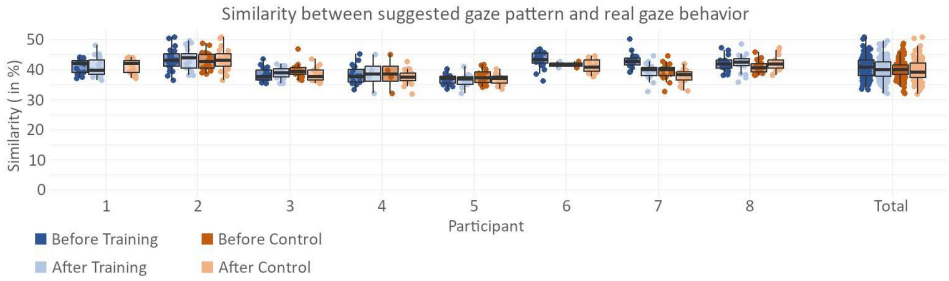

Fig 10. Gaze pattern results. The figure shows the similarity between the gaze pattern displayed by participants and the suggested systematic gaze pattern described in Suggested gaze pattern. Values between 0.3 and 0.5 are common for naive gaze behavior, whereas values between 0.6 and 0.8 can be expected when a subject is actively following the gaze pattern.

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sessions per participant. Fig 11 shows the visual task performance and DVF within the virtual environment over the course of the 20 training sessions.

Most participants improved both in performance and in average DVF in all three tasks. In the Search Task, the average task performance increased by 35.5% ($p < 0.001$). In the Target Tracking Task, performance increased by 13.9% ($p < 0.0032$). The average trial duration in the Navigation Task decreases by 61.0% ($p < 0.001$), the number of collisions is reduced by 80.3% ($p < 0.001$). Despite showing the lowest task performance increase, the Target Tracking Task evoked the highest increase in average DVF over the course of training, with an increase of 43.4% from beginning to end of training ($p < 0.001$). The Search Task followed with an increase in DVF of 29.9% ($p < 0.001$), and the Navigation Task resulted in the lowest average DVF increase out of the three tasks at 19.8% ($p < 0.001$).

Questionnaire. The questionnaires filled by participants over the course of the gaze training give insight into qualitative results. Fig 12 shows the average results of all five questionnaires for the seven ranking questions related to the VR gaze training shown in Questionnaire.

Overall, the Search Task was rated most positively, with high enjoyment and motivation for improvement, as well as low perceived stress and low eye strain reported. On the opposite side, the Target Tracking Task was rated most negatively, with the lowest task enjoyment and motivation to improve upon previous results, and highest stress and eye strain reported out of the three tasks. The questionnaire ratings show high standard deviation between participants, with scores oftentimes ranging from 1 to 10 within the same conditions. Some of the scores of individual patients do not align with verbal feedback given after the study and may thus be a result of misinterpretation of the question. Still, these consistently high standard deviations indicate that the different aspects of the training tasks, such as motivation, perceived difficulty, and enjoyment, are highly subjective. In addition to the score ranking, participants also gave general feedback for the gaze training, both in the questionnaires and in the in-person training sessions. Some participants stated minor technical issues both with the VR headset and the developed software. Additional suggestions included more variety in tasks or task

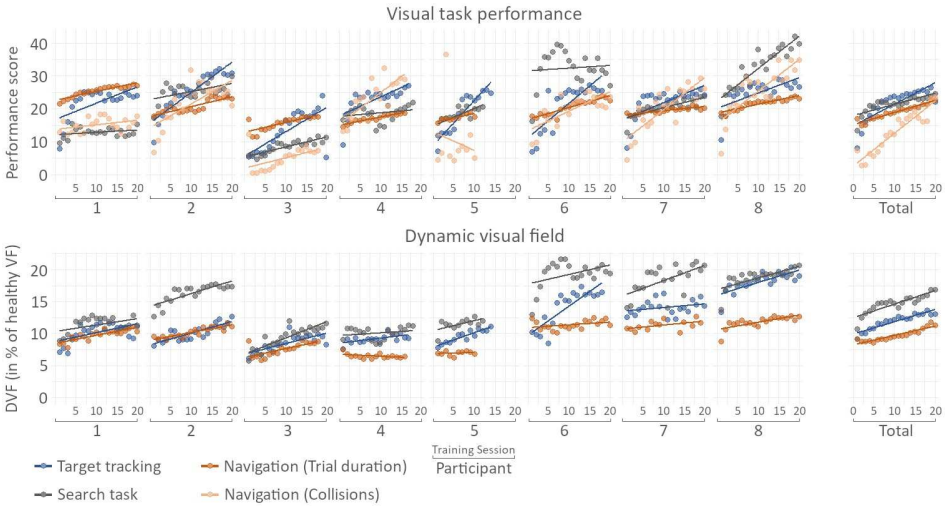

Fig 11. Gaze training results. Task performance score (top) and DVF (bottom) of the three visual training tasks. The Performance score for trial duration was calculated based on the logarithm of the trial duration. The reported DVF is world-centric, measured over a 3 second rolling window and given as percentage of a 180˚x135˚ area (approximately the dimensions of a healthy VF).

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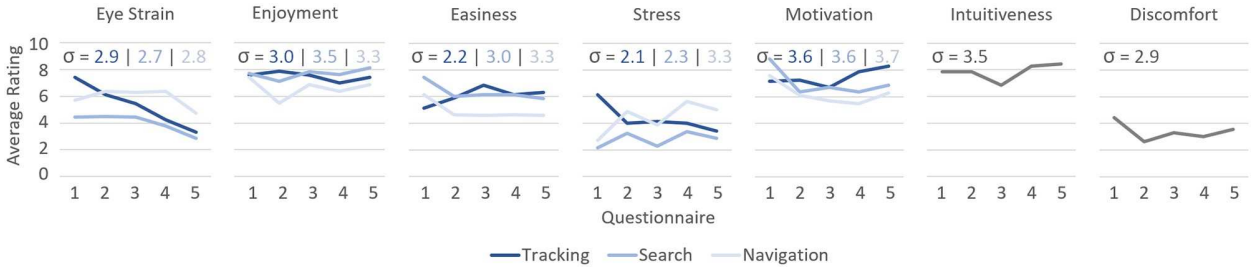

Fig 12. Questionnaire results. Average rating of different aspects of the gaze training. Questionnaires 1–5 were filled after 1, 5, 10, 15 and 20 training sessions. A rating of 10 equals "very high", a rating of 1 equals "very low". The σ-values indicate the average standard deviation over all five questionnaires of the respective task.

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visualization, such as adding different backgrounds; As well as quality-of-life changes, such as more fluent turn animations for the moving targets in the Target Tracking Task, or a better indication before the application switches to the selection menu at the end of a trial.

The raw data results for the obstacle course trials, the VR gaze training, as well as the questionnaires are found in the S1 File.

Discussion

In this study, the effects of 10 hours of training with a VR based gaze training on the navigation performance in a real-world obstacle course task was evaluated in eight Retinitis pigmentosa patients. It is found that the navigation performance increase over the training phase significantly surpasses the natural learning effect found after the control phase, suggesting that Virtual-Reality based gaze training can improve navigation performance of patients with Retinitis pigmentosa. While notable changes in DVF are found in individual patients, the group's average DVF increase after training was not found to significantly surpass the effect of the control phase.

Analysis of the real-world obstacle course results for each individual participant reveals a significant variability in the impact of gaze training on the DVF. Among the eight participants whose results were evaluated, three demonstrated a prominent increase in DVF during the real-world task after training (Fig 9). Notably, two of these participants (participant 3 and 6) also exhibited significant improvements in both trial duration and collision avoidance (Fig 8), with the third participant (participant 1) showing a significant improvement only in trial duration, with no corresponding increase in collision avoidance. These findings imply a positive correlation between an expanded DVF and improved navigation performance. However, it is worth noting that improvements in trial duration and collision avoidance were also observed in participants who did not experience any changes in DVF following training. Participants 5 and 7 exhibited significant improvements in trial duration and noticeable improvements in collision avoidance, despite no discernible change in DVF. Likewise, participants 4 and 8—the only participants to display a decrease in DVF after training—did not exhibit any negative effect on trial duration or collision avoidance, which would be expected when assuming a direct correlation between DVF and navigation performance.

In summary, it is possible that an increased DVF has a positive effect on navigation performance, indicated by the fact that all three patients displaying such increase in DVF also display improvements in navigation performance. However, the opposite statement cannot be made: A lack of increase in DVF—or even a decrease in DVF—in a patient does not imply the absence of improvements in performance, showing that improved trial duration and collision

avoidance are not a direct indicator for changed gaze behavior. This further suggests the presence of other factors through which gaze training influences navigation performance. Participants 4 and 5, for instance, both demonstrated improvements in the Navigation Task over the course of the training despite minimal changes in their DVF (Fig 11). This aligns with the results obtained from the real-world obstacle course (Figs 8 and 9), where participants also displayed improved navigation performance with no increase or even with decrease in DVF. Based on these findings, it is plausible to speculate that the Navigation Task facilitated the development of spatial awareness in these and maybe other participants. It is also possible that through the Navigation Task, participants adapted to previously less familiar types of obstacles, such as obstacles hanging from the ceiling.

In Suggested gaze pattern, a preliminary study was mentioned [31]. Here, we assessed whether systematic gaze patterns could assist people with tunnel vision condition in navigation and obstacle avoidance. For that, a gaze-contingent simulation of a 20˚ diameter tunnel vision condition was employed on visually healthy participants within a Virtual Reality environment, and the participants navigated through a virtual obstacle course while following different gaze patterns in a supervised experimental setup. One of the tested gaze patterns—a mostly horizontal, serpentine scanning motion—was found to significantly reduce obstacle collisions by 32.9% and increase the DVF by 8.9% compared to trials without systematic gaze movements. This came at the cost of a significantly lower movement speed, resulting in an average of 24.6% longer trial duration when following the gaze pattern. The study concluded that the gaze pattern has the potential to enhance visual performance in the presence of tunnel vision and suggests that introducing the gaze pattern in gaze training for individuals with tunnel vision could have beneficial effects. This is in line with a study by Nelles et al. [12], in which hemianopia patients were introduced to a similar gaze pattern in supervised training, displaying significant improvements in visual search after training. However, it is important to note that our preliminary gaze pattern study did not involve any real RP patients and no effect of the execution of gaze patterns in a real-world setting were evaluated in this study. Given the non-conclusive nature of the results of this previous study, the execution of the suggested gaze pattern was included as a voluntary task for the gaze training presented in this work.

As the evaluation of the gaze pattern similarity before and after the training phase indicates, the participants have not adapted this gaze pattern. This is also reflected in participants' statements after the training. Six out of the eight participants (1, 2, 3, 4, 5, 8) reported that they did not follow any specific gaze movement strategies. The predominant reason stated was that they "didn't think of it" during the trials. Participants 6 and 7 reported to follow individual gaze patterns. Participant 6 described a radial gaze pattern, moving the gaze in a small circle at first and then in a second, larger circle. She reported to have adapted this gaze pattern strategy during the Target Tracking Task of the gaze training and is now using it successfully even in everyday life. Participant 7 reported to follow a cross-like gaze pattern, moving the gaze vertically from bottom to top, then left to right. However, she reported to have adapted this gaze pattern only for the real-world obstacle course trials and not during the gaze training. Overall, the outcome implies that systematic gaze patterns are not easily and voluntarily adapted in practical application by the majority of patients. Still, the fact that participant 6—as one of two participants reporting to follow a gaze pattern during trials and the only participant stating to also follow the gaze pattern in everyday life now—displayed the highest increase in both DVF and navigation performance in the real-world obstacle course suggests further research towards the training of individualized gaze patterns in people with limited VF.

Saccade characteristics such as frequency of saccades, saccade directions, or ratio of exploratory saccades did not show significant effects between training and control phase over all patients. However, unlike the gaze pattern similarity, which was mostly consistent across all

patients, changes in gaze characteristics differ dramatically between patients. Notably, participant 4, who was mentioned already to have displayed unusual DVF results both during training and in the real-world task, was found to continue this trend in the gaze characteristics. Both in saccade frequency and in the ratio of "side-facing" relative saccade angles between 45˚ and 135˚ (which can be assumed to be the most effective in scanning the visual area), participant 4 displayed the highest decrease after the training phase and the highest increase after control phase. Similarly, patients with DVF results that suggest positive training effects, such as participant 3 and 6, display mostly positive trends in the gaze characteristics as well.

The influence of patient-related parameters, such as age, previous experience with VR, or experience with other gaze training, can not feasibly be analyzed given the small study population. It can be assumed that younger individuals and those with more VR experience may initially perform better in the gaze training, resulting in a lower entry barrier. However, the effectiveness of training is not expected to be influenced by initial gaze training performance, but rather by the strategies and behavior developed during training. Thus, a study with a much larger population is required to determine whether factors like age and previous VR experience may influence the effectiveness of training positively, negatively, or not at all.

There are several aspects of the gaze training itself that could not be tested within the scope of this project, but hold important research questions for future studies. For one, the design of the training phase did not provide for individual evaluation of the three different tasks. As all tasks were carried out concurrently and real-world task performance was assessed only before and after the full training phase comprised of all three tasks, we cannot draw conclusions about the individual effects that each training task has on real-world navigation performance or gaze behavior. For optimization of the gaze training and to further understand how different virtual tasks can influence real-world performance, the analysis of individual tasks is suggested as a future research topic. Additionally, our study focused on patients with Retinitis pigmentosa to maintain a homogeneous study group and avoid introducing additional variables that could affect the results. Nevertheless, the positive outcomes of our study highly suggest the exploration of the training application in other conditions involving peripheral visual field loss, such as glaucoma or Bardet-Biedl syndrome [44].

The feedback received by participants was overall positive. During the study, six participants (participant 3, 4, 5, 6, 7 and 8) expressed their interest and willingness to continue the gaze training if it becomes available, though participant 8 specified she would prefer to only do the Search Task if training continued. Two participants mentioned to have recommended the training software to friends and acquaintances, and two participants stated to regularly notice improvements in visual and navigation performance in everyday life since the training phase started. Questionnaire results support the overall positive reception of the gaze training, with consistently high ratings in task enjoyment (average 7.26/10) and intuitiveness and ease of use of the software (average 7.85/10). Participants reported some eye strain in the beginning of the training (average 5.86/10) which decreased towards the end of training (average 3.61/10).

To our knowledge, only two other studies were published that investigate the effect of gaze training on the real-world navigation performance in Retinitis pigmentosa patients [14, 15]. It must be noted that quantitative comparison between the results of different gaze trainings is feasible only to a very limited degree due to the different experimental setups in which they were acquired. In their study investigating the effect of a computer display based gaze training application on navigation performance, Ivanov et al. developed a gaze training that consists of an exploratory search task very similar to the Search Task of our work. It was found that a group of RP patients (n = 14) displayed a significant increase in their preferred percentage walking speed by $\sim$6% in a real-world obstacle course after a six-week training period (total of 15 hours), with no significant improvements in obstacle avoidance in the trials. It was already

suggested by Ivanov et al. that the application of VR devices may impact the effect of gaze training positively. Considering the notably larger improvements found after the VR training —compared to those found after training with a screen-based setup—it can be assumed that VR based gaze training shows higher potential to improve navigation performance in real-world tasks. No numeric performance results are reported by Nguyen et al., who used a very similar training setup to that of Ivanov et al. in a group of n = 14 RP patients. It is reported that significant improvements in navigation performance were found only in patients with VF $\leq$20˚ diameter. Our results have shown significant improvements in either trial duration or collision avoidance after training in six out of eight patients. The two patients not showing any significant improvements are participants 2 and 4, who have some of the largest measured average VF diameters of the patient group at 18.41˚ and 25.0˚, respectively. This aligns with the findings by Nguyen et al. suggesting that gaze training may be more effective in patients with VF diameter under 20˚. A larger study population is required to statistically validate this hypothesis. Gunn et al. [19] assessed the influence of a short, supervised gaze training consisting of two one-hour sessions of general scanning techniques and explicit instructions on optimized gaze behavior. The study population consisted of 13 elderly glaucoma patients. The training was found to drastically reduce collisions in a mobility task by up to 88%, with a reduction in walking speed of 10%. Additionally, significant changes in gaze behavior were reported. While the reduction in collisions surpasses the average of 50% reduction found in our study, it has to be considered that the 10% slower movement speed provides patients with more time to plan their walking path and react to obstacles. Furthermore, the study by Gunn et al. lacks a control group, thus it does not distinguish between actual training effects and the improvements in performance that occur naturally from repeating the evaluation task.

One of the most common training methods for low vision patients is Orientation & Mobility (O&M) training. While it is no gaze training, it does fulfill a similar purpose in that it aims to improve walking speed and reduce the number of collisions. Surprisingly, despite the popularity of O&M training, controlled studies evaluating its quantitative effects on low vision patients by comparing navigation performance before and after training are scarce. Soong et al. [45] have conducted such a study, testing the navigation performance of 19 elderly patients with varying low vision conditions after one or multiple sessions of supervised, standardized O&M training. However, patients were not found to have significantly improved in either walking speed or collision avoidance directly after the training. Overall, the results found in our study seem promising compared to literature, seeing how—unlike most previous training methods—significant improvements in both walking speed and collision avoidance were found. It is however unclear to which degree this result can be attributed to the training paradigm, rather than to differences in other factors such as evaluation methods, study population, or training duration.

Despite these promising findings for VR gaze training, the VR based setup also introduces certain limitations: As mentioned in Study population, two participants, in addition to the eight who completed the study, withdrew from the study at an early stage. The primary reason for their discontinuation was directly associated with the use of a VR headset for the training sessions. The first of the two patients reported an increase in migraine attacks when carrying out the training. Virtual Reality is known to cause motion sickness or headaches in some users [46, 47] and it is thus likely that the use of the VR headset did have an effect on the increase in migraine attacks. It was decided to stop the study participation after three training sessions to avoid any risk and discomfort for the participant. The second participant who discontinued the study displayed severe difficulties in navigating within the VR environment when first being introduced to the gaze training. They reported feeling completely disoriented and unable to complete the tasks on their own, and it was thus decided that carrying out the training in an

unsupervised at-home scenario would not be feasible. These two cases highlight that VR gaze training may not be suited for all patients—or, at the very least, requires additional improvements towards the mitigation of motion sickness and the optimization of intuitive tutorials, interfaces, and task design.

A common feedback from participants was that the starting difficulty of the Navigation Task as well as the threshold to advance to higher difficulty levels was too high. Three out of eight participants were not able to advance to a higher difficulty level over the entire duration of the study. They still displayed improvements in performance, but they did not reach the threshold—calculated based on a combination of trial duration and number of collisions—at which the difficulty level would increase. This suggests lowering the starting difficulty of the Navigation Task by decreasing the length of the course as well as the number of obstacles.

Contrary to the Navigation Task, the Target Tracking Task has a low entry difficulty, however participants reported a steep increase in both difficulty and resulting stress at higher difficulty levels. The main factor is the increase of targets that must be tracked simultaneously in order to be successful in the task. Tracking two targets did not prove a big challenge for any of the participants, however once a third target is introduced, difficulty and stress are drastically increased, and none of the participants were able to consistently track more than three targets at the same time. This lead to a stagnation at the difficulty levels around the threshold between three and four marked targets for many participants. To avoid this issue, it may help to limit the number of marked targets to three and instead purely focus on the increase of other difficulty parameters, such as the movement speed of the targets or the area in which targets are free to move around.

Despite these limitations, the developed gaze training shows very promising results, and the use of Virtual Reality as a medium for gaze training seems feasible. Furthermore, it can be emphasized that the training has led to significant improvements in navigation performance despite the VR training itself being fully carried out in seated or stationary standing positions. It can be assumed that the inclusion of real-world mobility would improve training effects further. However, one of our primary goals was to develop a gaze training protocol that could be conveniently and risk-free carried out from home with no need for supervision. We see this as an important measure to enhance user acceptance, especially when considering the practical application of the training beyond controlled research settings. Thus, it was important to show that even with stationary VR training setup, significant improvements in navigation performance in real-world tasks could be achieved. However, the comparison of effects between seated and mobile training conditions provides an interesting research question for subsequent studies, prompting a discussion about the risk-benefit ratio of the inclusion of real-world mobility in Virtual Reality gaze training setups.

The gaze training is currently published as a 'work-in-progress' open-source software on GitHub [48]. This will allow everyone with access to one of the supported VR devices to test and use the gaze training for free once the changes are implemented.

Conclusion

The results after four weeks of training with the developed gaze training software are promising, showing that Virtual Reality gaze training has the potential to improve the navigation performance of people living with Retinitis pigmentosa in real-world tasks. The majority of participants reported the training software—along with the Virtual Reality device—to be intuitive and easy to use, making it suitable for at-home training with no supervision and with minimal introduction time. However, while VR proves to be a viable medium for a gaze training tool, it can also act as an entry barrier for people being susceptible to motion sickness or people

facing difficulties with orienting and navigating in virtual environments. Still, the developed gaze training shows potential to have a significant positive impact on real-world navigation performance and is currently available as work-in-progress open-source software (link: https://github.com/ANCoral05/VR-GT---Virtual-Reality-Gaze-Training).

Supporting information

S1 File. Measurement data. The raw measurements for the real-world obstacle course, the three gaze training tasks as well as the participant questionnaires.
(XLSX)

S1 Video. Visual training tasks. A screen recording of the three visual training tasks of the gaze training.
(ZIP)

S2 Video. Obstacle course trial. Example of one of the trials in the real-world obstacle course, captured by the scene camera of the Pupil Labs Invisible eye tracker.
(ZIP)

S1 Appendix. Additional information regarding the gaze pattern evaluation, VF data and the results of the statistical methods applied in this study.
(PDF)

S1 Checklist. CONSORT checklist.
(PDF)

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Supervision: Siegfried Wahl.

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Appendices

Appendix A - Gaze pattern evaluation and Multimatch-algorithm

As was described in the 'Suggested gaze pattern' section, the patients' gaze movements during training were measured, and the similarity between this gaze movement and the suggested gaze pattern was calculated at run-time. To do so, the first step is to analyze the eye-tracking data captured by the VR device to determine saccades, as described in the section 'Saccade characteristics and gaze pattern similarity'. Using a modified Multimatch-Algorithm [32] , sections of multiple saccades executed by the participant are compared to a saccade representation of the suggested gaze pattern (Fig. 12) to calculate a similarity value based on how well the two saccade patterns match. This similarity value was displayed to participants after each trial of the Gaze Training, giving them a quantitative measure of how closely their gaze movements match the suggested gaze pattern.

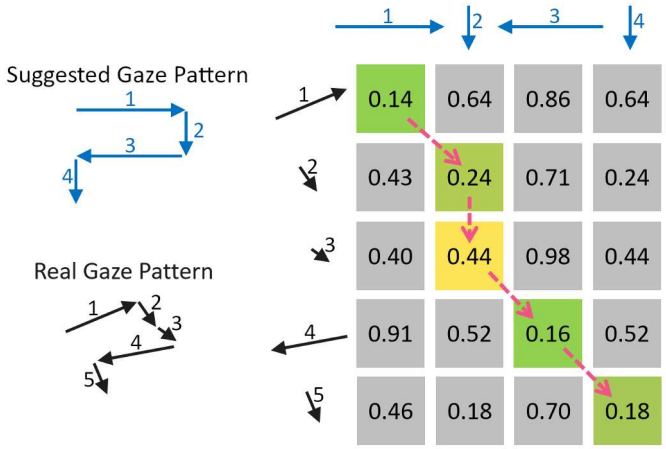

Figure 12: Visualization of a Multimatch-based comparison between a gaze pattern displayed by a participant (Real Gaze Pattern) and an ideal representation of the suggested gaze pattern. Each square displays the difference in angle and amplitude between the respective saccade vectors, with 0.0 meaning saccades are identical and 1.0 meaning saccades are complete opposites. Colorized squares indicate the "path of the least resistance" determined by the Multimatch-algorithm, which describes the best match between the two patterns.

Appendix B - Patients' visual fields

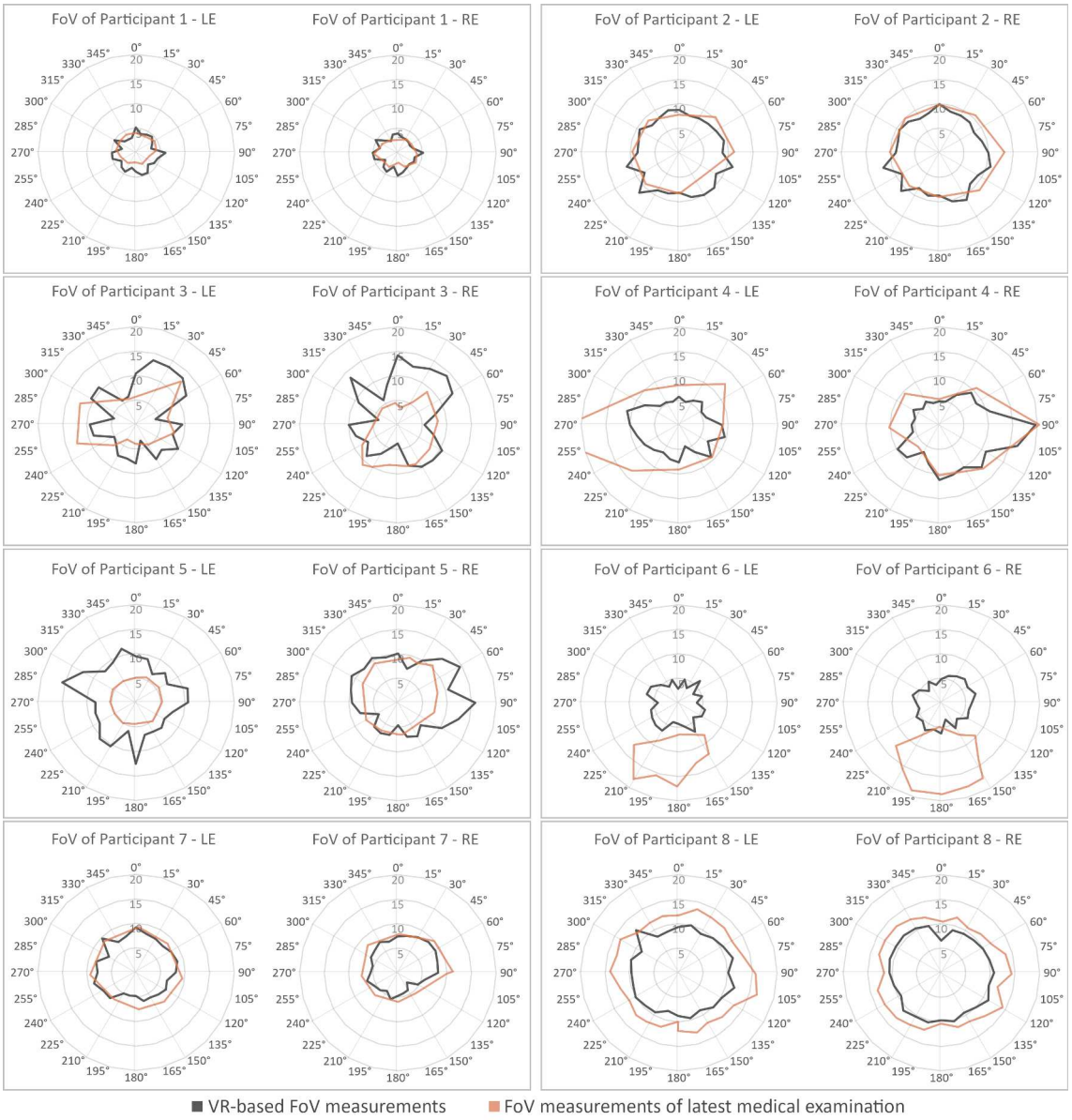

Figure 13: Visualization of the visual field dimensions of the eight participants who completed the study. Grey indicates the VF measured by the self-developed, VR-based kinetic perimetry tool as described in section 3.2.2, orange indicates the participants' VF based on their most recent medical examination.

Appendix C - Dynamic visual field calculation, saccade detection, and saccade characteristics

Calculaton of the dynamic visual field The dynamic visual field (DVF) served as important measurement parameter to explore the visual performance of participants in this study. As outlined in the section 'Real-world obstacle course measurements', the DVF describes the visual area that a person with VFD observes within a specific time interval utilizing their head- and eye movements. This section will provide a detailed explanation of the process for calculating and computing the DVF.

Initially in the computational analysis of the DVF, a virtual spherical grid is defined around the user, with the eye tracker in its center. The grid is subdivided into sections of

1° horizontal and vertical angle, resulting a two-dimensional array consisting of $360 * 180$ individual sections. Next, the eye tacking data, which was captured both within the VR training as well as in real-world trials, is analyzed. For the calculation of the DVF, three parameters are extracted from each eye tracking sample: The time stamp at which the sample was captured, the elevation angle and azimuth angle of the gaze direction measured at that specific time. In addition to these parameters, the static VF size of the respective participant, as reported in table 1, is required for the calculation of the DVF. For each eye tracking sample, the current gaze direction is projected onto a point (x, y) within the two-dimensional array. If the participant's gaze is directed forward, the gaze direction would be mapped exactly in the center of the array at position $(180, 90)$. If the gaze then shifts, for example, by 10° to the right or left, the projected position on the array would change to $(190, 90)$ or $(170, 90)$, respectively. If the gaze shifts upwards or downwards by 10°, the resulting projected position in the array would be $(180, 100)$ or $(180, 80)$. The next step is to project not just the gaze direction to the grid, but the entire VF of the participant. In other words, it must be determined which sections in the array are currently covered by the participant's VF. To achieve this, the following formula is utilized: $\sqrt{(x_{grid} - x_{gaze})^2 + (y_{grid} - y_{gaze})^2} \leq r_{VF}$. Here, x_{grid} and y_{grid} describe the horizontal and vertical position of the section in the grid, x_{gaze} and y_{gaze} describe the projected position of the gaze in the grid, and r_{VF} is the average VF radius of the participant. Each section that is identified to be within the participants VF is annotated with the time stamp of the current eye tracking sample. If the section already contains a time stamp, the old time stamp is overwritten with the newer one. This results in each section of the array containing information about the last time stamp at which it was covered by the VF - or, in other words, the last time it was observed by the participant. The subsequent step to determine the DVF involves iterating through each individual section in the two-dimensional array, counting the number $n_{observed}$ of sections annotated with a time stamp that falls within the specified time interval. For example, with a specified interval of three seconds, $n_{observed}$ would include all sections with time stamps less than three seconds old. To enhance the interpretability of the DVF output, it is reported as a percentage of the visual area that could be observed by a static healthy VF with approximated dimensions of $180 * 135$. In summary, the DVF is calculated as $DVF = \frac{n_{observed}}{180*135} * 100\%$. This calculation is performed for every eye tracking sample measured within a trial. The average of all calculated values yields the DVF for the respective trial, reported in the supplementary file S1.

Saccade detection Fig. 14 visualizes the saccade detection approach described in the section 'Real-world obstacle course measurements' in the point 'Saccade characteristics and gaze pattern similarity'.

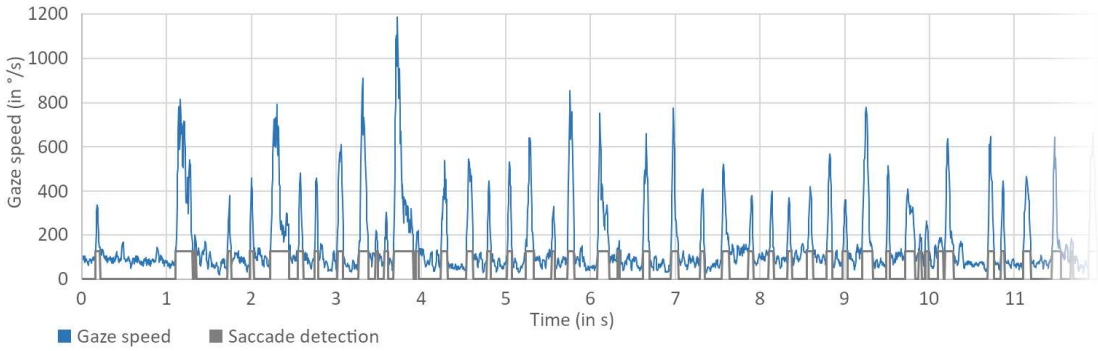

Figure 14: Visualization of the saccade detection following the algorithm of Nyström et al. [40]. The displayed data is taken from one of the real-world obstacle course trials, measured with the Pupil Labs Invisible eye tracker [36].

Saccade characteristics The results for the different saccade characteristics described in this section are shown in Fig. 15.

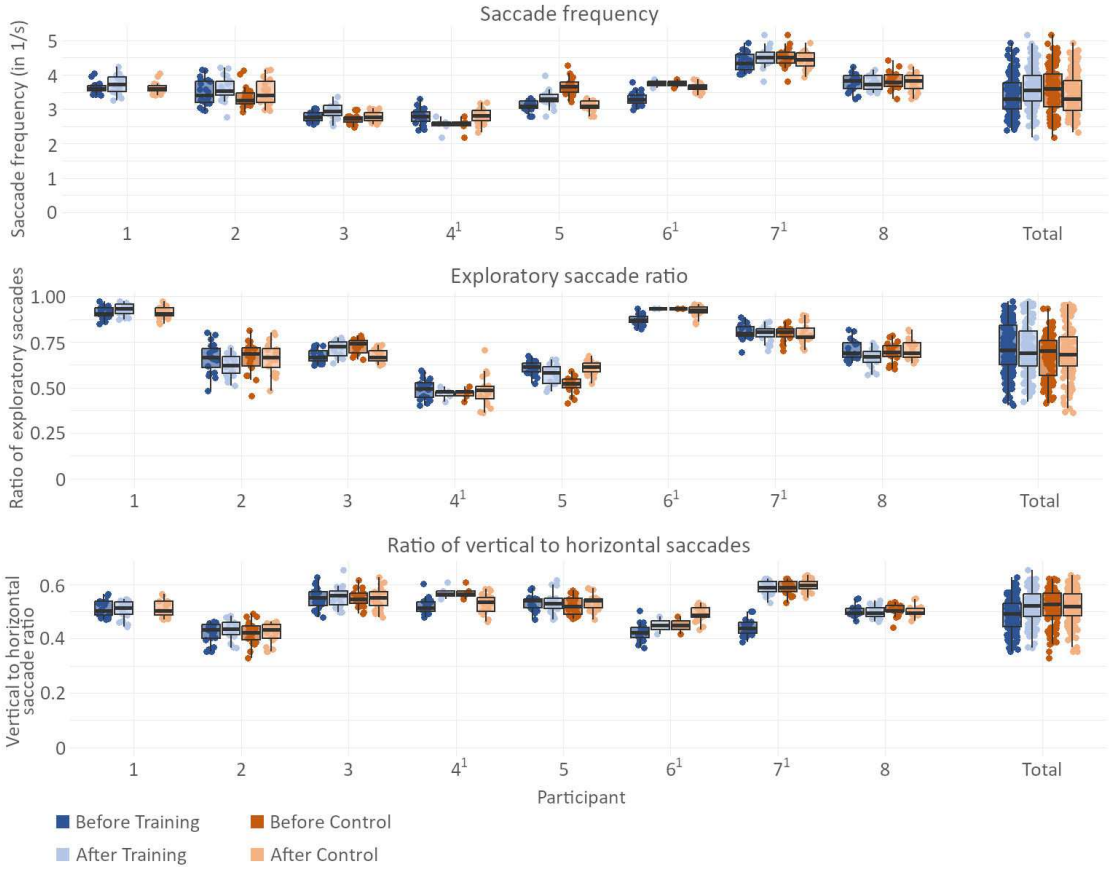

Figure 15: Results of the three parameters saccade frequency, ratio of exploratory saccades, and ratio between vertical and horizontal saccades. Exploratory saccade ratio shows the number of exploratory saccades divided by the total number of saccades per trial. Vertical to horizontal saccade ratio is calculated as the average y-components of a saccade divided by the average x-component. A ratio of 1 would indicate an equal amount of vertical and horizontal eye movements.

Appendix D - Statistical models and QQ-plots

This section lists full details on the models used for the statistical analysis of the real-world obstacle course results, as well as the QQ-plots used to visualize normal distribution of results.

Effect of Gaze Training (pre/post training condition) on trial duration

Model Specification:

- Model: Linear Mixed Model (lme)
- Dependent Variable: log(TrialDuration)
- Fixed Effects: PrePostTrainingCondition
- Random Effects: $\sim 1 + \text{Participant} \mid \text{Participant}$
- Model Fit Statistics: AIC = -285.7289, BIC = -263.1566, logLik = 148.8645

Results:

- Intercept: Estimate = 3.567655, SE = 0.09670653, t-value = 36.89157, $p - value < 0.001$
- PrePostTrainingCondition: Estimate = -0.177829, SE = 0.01577808, t-value = -11.27062, $p - value < 0.001$

Effects:

- Participant (Intercept): StdDev = 2.717010e-01
- Participant: StdDev (Intercept) correlation = 0
- Residual: StdDev = 1.411235e-01

Data Samples:

- Number of Observations: 320
- Number of Groups: 8

Effect of control phase (pre/post control condition) on trial duration

Model Specification:

- Model: Linear Mixed Model (lme)
- Dependent Variable: log(TrialDuration)
- Fixed Effects: PrePostControlCondition
- Random Effects: $\sim 1 + \text{Participant} \mid \text{Participant}$
- Model Fit Statistics: AIC = -349.665, BIC = -327.0927, logLik = 180.8325

Results:

- Intercept: Estimate = 3.490358, SE = 0.10280603, t-value = 33.95090, $p - value < 0.001$
- PrePostControlCondition: Estimate = -0.041963, SE = 0.01421692, t-value = -2.95161, $p - value = 0.0034$

Effects:

- Participant (Intercept): StdDev = 2.893858e-01
- Participant: StdDev (Intercept) correlation = 0
- Residual: StdDev = 1.271600e-01

Data Samples:

- Number of Observations: 320
- Number of Groups: 8

Effect of training phase (pre/post training condition) on number of collisions

Model Specification:

- Model: Negative Binomial Regression (glm.nb)
- Dependent Variable: Collisions
- Fixed Effects: PrePostTrainingCondition
- Random Effects: $\sim 1 + \text{ParticipantID} \mid \text{ParticipantID}$

- Model Fit Statistics: Null Deviance: 291.34 on 319 degrees of freedom, Residual Deviance: 278.05 on 318 degrees of freedom, AIC: 762.19

Results:

- Intercept: Estimate = 0.02469, Std. Error = 0.12360, z value = 0.200, $p - value = 0.841657$
- PrePostTrainingCondition: Estimate = -0.69315, Std. Error = 0.19145, z value = -3.621, $p - value = 0.000294$
- Random Effects: $\sim 1 + Participant \mid Participant$ (Not defined due to singularities)

Additional Information:

- Theta: Estimate = 0.681, Std. Error = 0.147
- Number of Fisher Scoring iterations: 1
- 2 x log-likelihood: -756.191

No estimates can be given for the random effect for this model. This is likely caused due to the number of subjects being too small.

Effect of control phase (pre/post control condition) on number of collisions

Model Specification:

- Model: Negative Binomial Regression (glm.nb)
- Dependent Variable: Collisions
- Fixed Effects: PrePostControlCondition
- Random Effects: $\sim 1 +$ Participant | Participant
- Model Fit Statistics: Null Deviance: 251.63 on 319 degrees of freedom, Residual Deviance: 251.37 on 318 degrees of freedom, AIC: 749.11

Results:

- Intercept: Estimate = -0.2469, Std. Error = 0.1500, z value = -1.645, $p - value = 0.0999$
- PrePostControlCondition: Estimate = -0.1098, Std. Error = 0.2144, z value = -0.512, $p - value = 0.6085$
- Random Effects: $\sim 1 +$ ParticipantID | ParticipantID

Additional Information:

- Theta: Estimate = 0.4307, Std. Error = 0.0814
- Number of Fisher Scoring iterations: 1
- 2 x log-likelihood: -743.1110

No estimates can be given for the random effect for this model. This is likely caused due to the number of subjects being too small.

Effect of training phase (pre/post training condition) on head-centric DFoV

Model Specification:

- Model: Linear Mixed Model (lme)
- Dependent Variable: HeadCentricDFoV
- Fixed Effects: PrePostTrainingCondition
- Random Effects: $\sim 1 +$ Participant | Participant
- Model Fit Statistics: AIC = -345.4398, BIC = -324.6062, logLik = 178.7199

Results:

- Intercept: Estimate = 1.0161667, Std.Error = 0.01021678, DF = 231, t-value = 99.46056, $p - value < 0.001$
- PrePostTrainingCondition: Estimate = -0.0196667, Std.Error = 0.01444871, DF = 231, t-value = -1.36114, $p - value = 0.1748$

Effects:

- participant (Intercept): StdDev = 1.301521e-06
- participant: StdDev (Intercept) correlation = 0
- Residual: StdDev = 1.119192e-01

Data Samples:
- Number of Observations: 240
- Number of Groups: 8

Effect of control phase (pre/post training condition) on head-centric DFoV

Model Specification:
- Model: Linear Mixed Model (lme)
- Dependent Variable: HeadCentricDFoV
- Fixed Effects: PrePostControlCondition
- Random Effects: $\sim 1 + \text{Participant} \mid \text{Participant}$
- Model Fit Statistics: AIC = -225.9001, BIC = -206.1403, logLik = 118.95

Results:
- Intercept: Estimate = 1.0163366, Std.Error = 0.01294036, DF = 193, t-value = 78.54007, $p - value < 0.001$
- PrePostControlCondition: Estimate = -0.0160366, Std.Error = 0.01834613, DF = 193, t-value = -0.87412, $p - value = 0.3831$

Effects:
- Participant (Intercept): StdDev = 1.442753e-06
- Participant: StdDev (Intercept) correlation = 0
- Residual: StdDev = 1.300490e-01

Data Samples:
- Number of Observations: 201
- Number of Groups: 7

Effect of training phase (pre/post training condition) on world-centric DFoV

Model Specification:
- Model: Linear Mixed Model (lme)
- Dependent Variable: WorldCentricDFoV
- Fixed Effects: PrePostTrainingCondition
- Random Effects: $\sim 1 + \text{Participant} \mid \text{Participant}$
- Model Fit Statistics: AIC = -221.0613, BIC = -200.2277, logLik = 116.5307

Results:
- Intercept: Estimate = 0.97800, Std.Error = 0.01326768, DF = 231, t-value = 73.71298, $p - value < 0.001$
- PrePostTrainingCondition: Estimate = 0.06625, Std.Error = 0.01876333, DF = 231, t-value = 3.53082, $p - value = 0.0005$

Effects:
- Participant (Intercept): StdDev = $2.303544e - 06$
- Participant: StdDev (Intercept) correlation = 0
- Residual: StdDev = 0.1453401

Data Samples:
- Number of Observations: 240
- Number of Groups: 8

Effect of control phase (pre/post control condition) on world-centric DFoV

Model Specification:
- Model: Linear Mixed Model (lme)
- Dependent Variable: WorldCentricDFoV
- Fixed Effects: PrePostControlCondition
- Random Effects: $\sim 1 + \text{Participant} \mid \text{Participant}$
- Model Fit Statistics: AIC = -90.34245, BIC = -70.58262, logLik = 51.17122

Results:

- Intercept: Estimate = 0.9865347, Std.Error = 0.01819139, DF = 193, t-value = 54.23087, $p - value < 0.001$
- PrePostControlCondition: Estimate = 0.0448653, Std.Error = 0.02579074, DF = 193, t-value = 1.73959, $p - value = 0.0835$

Effects:

- Participant (Intercept): StdDev = $4.234727e - 06$
- Participant: StdDev (Intercept) correlation = 0
- Residual: StdDev = 0.1828212

Data Samples:

- Number of Observations: 201
- Number of Groups: 7

QQ-plots

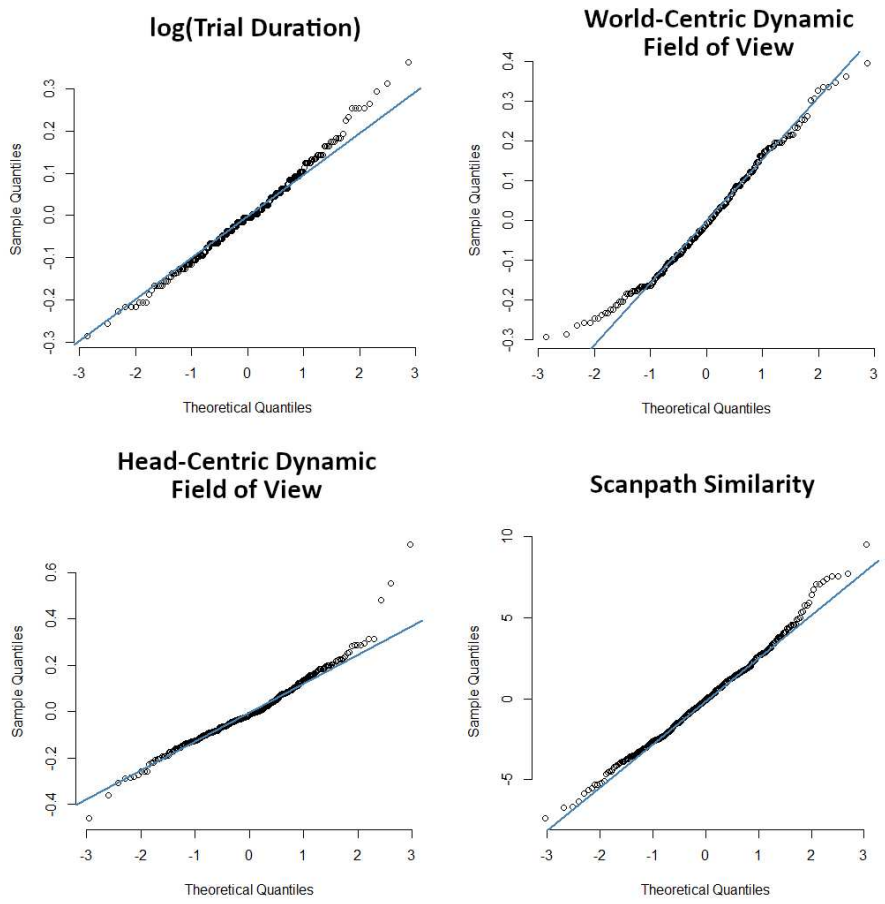

Figure 16: QQ-plots of the residuals of different result parameters of the real-world obstacle course.

3 Publication C

Simulating Vision Impairment in Virtual Reality - A Comparison of Visual Task Performance with Real and Simulated Tunnel Vision

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Abstract

Purpose: In this work, we explore the potential and limitations of simulating gaze-contingent tunnel vision conditions using Virtual Reality (VR) with built-in eye tracking technology. This approach promises an easy and accessible way of expanding study populations and test groups for visual training, visual aids, or accessibility evaluations. However, it is crucial to assess the validity and reliability of simulating these types of visual impairments and evaluate the extend to which participants with simulated tunnel vision can represent real patients.
Methods: Two age-matched participant groups were acquired: The first group (n=8, aged 20-60, average 49.1±13.2) consisted of patients diagnosed with Retinitis pigmentosa (RP). The second group (n=8, aged 27-59, average 46.5±10.8) consisted of visually healthy participants with simulated tunnel vision. Both groups carried out different visual tasks in a virtual environment for 30 minutes per day over the course of four weeks. Task performances as well as gaze characteristics were evaluated in both groups over the course of the study.
Results: Using the 'two one-sided tests for equivalence' method, the two groups were found to perform similar in all three visual tasks. Significant differences between groups were found in different aspects of their gaze behavior, though most of these aspects seem to converge over time.
Conclusion: Our study evaluates the potential and limitations of using Virtual Reality technology to simulate the effects of tunnel vision within controlled virtual environments. We find that the simulation accurately represents performance of RP patients in the context of group averages, but fails to fully replicate effects on gaze behavior.

Keywords: Virtual Reality, Retinitis pigmentosa, Vision Impairment Simulation, Tunnel Vision, Disability

1 Introduction

Virtual Reality (VR) has emerged as a powerful and increasingly popular tool in the field of vision research in recent years. The number of published research articles in the database of PubMed that incorporate the key words 'Virtual Reality' and 'Ophthalmology' have almost tripled in the time since 2019. The reasons for this growing interest and utilization of VR are readily apparent. VR offers a unique platform to investigate various aspects of human vision, perception, and gaze behavior, providing a multitude of advantages compared to other psychophysical experimental setups. Compared to computer-screen based setups (Hecht et al., 2015, Ivanov et al., 2016), VR setups provide larger viewing angles - typically between 90-100° (Sauer et al., 2022). They additionally allow to expand the displayed visual area even further by considering the head rotation of the user, potentially allowing for a full 360° visual scene. Both the stereoscopic view, provided by separate screens per eye, as well as the parallax effect that occurs when shifting the head allow for natural and realistic depth perception. With that, VR provides overall visual experiences close to real life (Hibbard, 2023). Meanwhile, the fully simulated nature of the environments within a VR-based setting allows for much higher flexibility and control compared to actual real-life setups. Experimental environments can be randomized or modified with the press of a button, and each detail and parameter can be individually adjusted without physical or material restraints. Furthermore, with the increasing availability of eye-tracking in VR-headsets (Adhanom et al., 2023), the use of VR for studies on gaze behavior or simulation of specific visual conditions expands even further.

One potential use for VR in vision research is the simulation of visual impairments (Hibbard, 2023, Jones and Ometto, 2018, Jones et al., 2020, Krösl et al., 2018, 2019). An accurate simulation of visual impairments can have various fields of application. It could aid in the evaluation of accessibility of devices, software interfaces or environment architecture (Creem-Regehr et al., 2021, Jones and Ometto, 2018, Krösl et al., 2019). It could provide doctors, family members, caregivers, employers, or colleagues better insights into the experience with - and limitations caused by - visual impairments (Jones and Ometto, 2018, Krösl et al., 2023, Väyrynen et al., 2016). Lastly, it could allow researchers and developers of visual aid systems and low vision training tools to expand a relatively small study population of real patients by including visually healthy participants with simulated visual conditions (Acevedo et al., 2022). This becomes especially relevant for rare conditions, as acquisition of sufficient study populations can be problematic in these cases (Mitani and Haneuse, 2020).

Several studies have explored ways to design simulations for visual field defects to be as visually accurate as possible (Geisler and Perry, 2002, Lewis et al., 2011, Stock et al., 2018), providing visual experiences similar to real conditions. However, visual representation is only part of the simulation. While VR provides a solid theoretical basis, there are many factors related to visual impairments that cannot be replicated even with the use of VR (Hibbard, 2023). These factors include experience and adaptive behavior: Patients with visual impairments often develop specific behaviors over years to cope with their condition, whereas visually healthy participants using a simulation lack this adaptive experience. Moreover, cognitive distinctions exist between actual and simulated visual field defects. Individuals with these defects often initially lack awareness of their condition, especially in cases of gradual onset due to inherited retinal diseases (Fletcher et al., 2012, Hoste, 2003). Even when aware of the diagnosis, affected patients typically do not describe the missing visual fields as actively perceived phenomena (Hoste, 2003); instead, they tend to recognize them only through a decline in everyday visual task performance. Consequently, representing visual field defects as black areas, which is a common practice when visualizing or simulating them using VR or other methods, will never fully capture the lived reality, as the participants will actively notice the visual limitations.

Acknowledging that simulations of visual field defects will - with current technological possibilities - never be perfect, it becomes essential to understand the extent to which these simulations can still accurately mirror real visual field impairments across various types of visual tasks and behaviors. Thus, this work aims to evaluate the performance and gaze behavior in participants with simulated tunnel vision in three different

Virtual-Reality-based tasks. The results are compared to those of an age-matched group of actual patients with peripheral visual field defects (tunnel vision) caused by Retinitis pigmentosa (RP). The results of both groups are collected within the same experimental setup, allowing to evaluate the similarities and differences of task-specific performance parameters and gaze characteristics between the groups. To the best of our knowledge, this is the first study to directly investigate and compare results between patients with visual field defects and participants with simulations of these same defects. The findings of this work will provide an overview of the criteria that studies and test setups should consider when utilizing VR-simulated tunnel vision, and possibly provide a baseline for the evaluation of simulations of other types of visual field defects.

2 Methods

2.1 Ethics

This study was proposed to and approved by the ethics committee of the Institutional Review Board of the Medical Faculty of the University of Tübingen (628/2018BO2) in accordance with the 2013 Helsinki Declaration. All participants signed written informed consent forms.

2.2 Obtaining research data

To evaluate and compare the performance and gaze behavior displayed by both real patients and participants with simulated conditions, two sets of data are required - one for the group of RP patients and one for the group of participants with simulated tunnel vision. In the following, the patient group will be called 'Group A', the group of participants with simulated tunnel vision will be referred to as 'Group B'.

The data for Group A originates from a study by Neugebauer et al. (Neugebauer et al., 2023) examining the effects of VR gaze training on visual performance and navigation performance of Retinitis pigmentosa patients. As part of this study, patients underwent four weeks of training with a Virtual-Reality based gaze training, consisting of different visual tasks, as will be described in section 2.4.3. The work by Neugebauer et al. mainly discusses the effects of the training on the performance and gaze behavior of patients in a real-world setting. However, eye-tracking data and data about the performance displayed by RP patients within the VR training were acquired as part of the results and thus provide a solid basis for the comparison targeted in this work. To acquire the second data set, a group of visually healthy participants (Group B) was acquired. To ensure compatibility and comparability between both data sets, participants of Group B were age-matched to the existing dataset of Group A.

2.3 Study population

Group A consists of eight RP patients (1 male, 7 female) with ages ranging from 20 to 60 years (average 49.6 ± 13.0) and VF sizes of 7° - 25° diameter. Group B comprises of eight participants with healthy or corrected vision (3 male, 5 female), aged between 27 and 59 (average 46.5 ± 10.8). The two groups were matched based on their age and their experience with VR devices, with a standard deviation of ±8.4 years between the two groups. Short-term adjustments in patient scheduling resulted in a notable age disparity in one particular pair (57 and 37), warranting consideration of potential age-related differences in this specific pairing.

Table 1 lists information about the participants of both groups. Information on the patients' age of diagnosis, their level of experience with VR, and their used vision correction are based on participants' reports. The visual acuity of patients was provided based on their most recent medical examination. It was ensured at the start of the training that all participants were able to effortlessly recognize all relevant elements within the virtual environment. The reported visual fields (VFs) were measured independently, as described in section 2.4.2. However, the VFs as reported in the official medical examination can be found in Appendix A.

2.4 Experimental design

In this section, we will describe the Virtual Reality software applied to test the performance, learning rate, and gaze characteristics of participants. The setup - both hardware and software - used for Group B within this study is identical to that used for Group A in the preliminary study. The only difference is the addition of a tunnel vision

Table 1: List of participant data, matched pairs being indicated by the same number. For Group B, the Visual Field Diameter describes the simulated VF.

Participant (Age|Sex)	Age of diagnosis	Visual Field Diameter (RE / LE)	Visual Acuity (RE / LE)	VF notes	VR Experience	Vis. Cor.[1]
Group A - Retinitis pigmentosa patients						
1 (20f)	14	7.62° / 8.26°	0.40 / 0.40	-	high	G/C
2 (57f)	27	18.64° / 18.18°	0.20 / 0.05	spots[2]	-	G
3 (55f)	18	17.64° / 16.36°	0.13 / 0.20	-	-	G
4 (47m)	25	24.60° / 25.40°	0.05 / 0.05	-	low	G
5 (59f)	50	18.54° / 18.34°	0.32 / 0.25	spots[2]	-	G
6 (59f)	16	10.92° / 9.64°	0.10 / 0.10	-	-	G
7 (40f)	18	12.18° / 14.56°	0.40 / 0.32	spots[2]	-	G
8 (60f)	20	20.00° / 19.48°	0.50 / 0.40	-	-	G
Group B - Participants with simulated tunnel vision						
1b (27m)	-	7.62° / 8.26°	-	-	med.	G
2b (37m)	-	18.64° / 18.18°	-	-	low	-
3b (55f)	-	17.64° / 16.36°	-	-	-	G[3]
4b (37f)	-	24.60° / 25.40°	-	-	-	-
5b (56m)	-	18.54° / 18.34°	-	-	-	-
6b (59f)	-	10.92° / 9.64°	-	-	-	G
7b (47f)	-	12.18° / 14.56°	-	-	-	G[3]
8b (54f)	-	20.00° / 19.48°	-	-	-	G

[1]Vision correction used by the participant; G: Glasses; C: Contact lenses.
[2]The patient displays some spots of remaining vision in the peripheral field.
[3]Did not wear glasses during VR training.

simulation in the setup for Group B, as will be elaborated further in section 2.4.2

2.4.1 Software and hardware specifications

The Virtual-Reality environment and the visual tasks applied in this study were developed with the Unity 3D game engine (Version 2021.3LTS) using the Pico XR SDK (Version 1.2.4). The software was installed on the Pico Neo 2 Eye Virtual Reality headset, which features an 89° Field of View according to Sauer et al. (Sauer et al., 2022) at a 75Hz refresh rate.

The Pico Neo 2 Eye uses the tobii eye tracking system with 90Hz frequency and 0.5° accuracy, according to official technical specifications (Tobii., 2023). Stein et al. (Stein et al., 2021) determined the latency of eye-tracking for this system to be 50ms, with an additional 29ms display latency, for an end-to-end latency of 79ms.

2.4.2 Visual field measurement and implementation of simulated visual field defects

To achieve comparable conditions for both groups, the tunnel vision simulation applied for Group B was directly based on the actual VF size of the age-matched patient from Group A. While VF data was available in the medical examination reports provided by patients in Group A, it was determined that conducting a separate VF test within the virtual environment used for the study would be more practical for simulation purposes. This decision was motivated by two key factors. Firstly, for comparability it is essential to have a uniform VF measurement with standardized settings for all patients. The VF reports in the medical examinations came from different examiners and were conducted using varying setups, with no consistent reporting of the specific testing methods and perimetry settings. Additionally, visual angles are difficult to align between virtual environment and real world, as they are influenced

by the distance between the user's eyes and the lenses and screens of the VR device. Therefore, to achieve an accurate simulation of the patients' vision within the virtual environment, it is recommended to measure the VF directly within this virtual setting.

To achieve this goal, a customized kinetic perimetry test was developed. In this test, a white target with a radius of 0.72° is presented on a black background. The target starts at the outer periphery of the VF at 45° and moves toward the center at a constant speed of 3° per second. Patients were instructed to press a key on the VR controller as soon as they registered the target entering their VF. In the center of the field of view, a marker is displayed, and patients are instructed to focus their gaze on this central marker. During the perimetry process, the direction of the patients' gaze is continuously monitored. If the gaze deviates from the central marker, the moving target disappears. This precautionary measure is taken to prevent patients from unintentionally or intentionally exploring the scene in search of the target, which could compromise the accuracy of the results. The perimetry test was conducted at the maximum display brightness available on the Pico Neo 2 Eye, which, as noted in Sauer et al. (Sauer et al., 2022), corresponds to a luminance of $60\frac{cd}{m^2}$. The angular resolution of the perimetry test was set at 15°, resulting in the acquisition of a total of 24 data points per trial. Each eye was tested individually by displaying the target on one screen at a time, making it visible in only one eye. The results of this perimetry test and a comparison with the VF sizes reported in the patients' most recent medical diagnoses are presented in Appendix A. It is important to note that this perimetry test is not diagnostically validated. However, it provides a close estimation of the dimensions of the patients' VFs within the VR setup. As such, these results serve as a suitable parameter for simulating the corresponding visual field defects.

Based on the measured VF dimensions, alpha masks were created using the image editing software Gimp (version 2.10). The peripheral regions of this mask were colored in black, with the VF area being left transparent. The edges of the VF mask were blurred, resulting in a gradual transition from transparent to black over an edge of ∼2° visual angle. The alpha masks were then implemented in the VR software setups for Group B, using eye tracking data such that the masks move in a gaze-contingent manner.

2.4.3 Virtual Reality setup

The VR software applied both in the preliminary study (Neugebauer et al., 2023) and in this study consists of three different visual tasks. Each task focuses on a different issue related to the lack of peripheral vision: Motion perception and tracking, visual search, and navigation. A short video demonstrating the three tasks is found in the supplementary files (Video S1).

Target tracking The peripheral VF is a crucial component in motion perception (Finlay, 1982). Not only does it allow for the initial perception of movement outside of the foveated area; it also enables a person to consistently track movement and estimate motion paths, thus determining potential risks and the danger of collision. A lack of the peripheral VF greatly impairs this ability. While a single moving object can be tracked by keeping the gaze directed at it, tracking multiple moving objects within a scene simultaneously becomes impossible without switching focus between them. The target tracking task (Fig. 1 a and d) aims to test and improve the participants' ability to estimate motion paths of moving targets and to frequently, accurately, and quickly switch focus between targets. In the beginning of the task, a number of identical-looking targets (visualized as mice for higher visual appeal) are spawned at the center of a defined 'play area'. A subset of these targets is marked by a visually distinct indicator (a piece of cheese) (Fig. 1 a). During the trial, all targets move randomly across the play area at a fixed speed, changing directions over time, and the participant is tasked to track all marked targets. In order to prevent one target being occluded by another, targets adjust their direction when getting close to a different target, avoiding collisions. Similarly, when targets approach the boundary of the play area, they adjust their movement towards a point within the area. After a random time interval of 8-12 seconds, all targets stop their movement and the visual markers disappear, rendering all targets in the area visually identical. At this point, the participant is tasked to select all previously

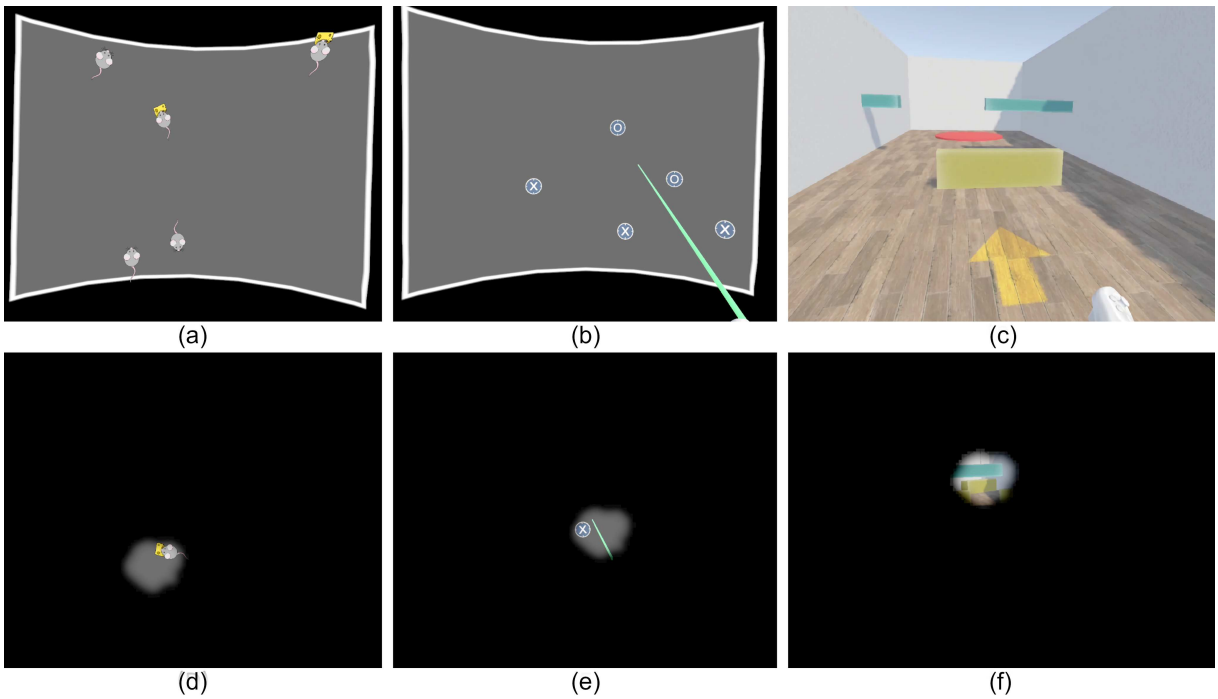

Fig. 1: Examples of the three visual tasks carried out by the participants, from (Neugebauer et al., 2023). (a-c) show the tasks without tunnel vision simulation. (d-f) show the tasks with an exemplary simulated deficient visual field of ∼15° diameter, giving an impression of the visuals displayed to the participant group with simulated tunnel vision. (a,d) Target Tracking; (b,e) Search task; (c,f) Navigation task. The interactive area in the Target Tracking and Search task (visbile in a and b) have dimensions of 80° horizontally and 60° vertically.

marked targets. Based on the number of incorrectly selected targets, the task is rated as full success (zero incorrect targets), half success (one incorrect target) or failure (two or more incorrect targets). The number of marked and unmarked targets, the movement speed of targets as well as the dimensions of the play area are all based on a variable difficulty level. The number of targets starts at five, with two marked targets. The VF dimensions start at 52° horizontally and 39° vertically (approximately 30% of the dimensions of a healthy VF) and the movement speed of mice starts at 3° per second. If the participant's performance reaches a specified threshold, the difficulty level will increase, which leads to higher numbers of targets, higher target movement speed and larger play area. If the participant performs below the threshold, it is also possible that the difficulty level is reduced. This paradigm ensures that the task remains challenging even when participants become more experienced with it. Difficulty levels range from 1 to 100, with each level increasing the adjustable parameters by approximately 3-5% of the starting value.

Search task Visual search is another aspect greatly influenced by the peripheral VF (David et al., 2021). Visual stimuli from the periphery inform us about potential regions of interest, which incentivizes gaze movements towards these areas. While a lack of the peripheral field does not impact the ability to recognize search targets as soon as they enter the VF, it prevents visual stimuli that would guide the gaze towards areas where the target might be located. Thus, people living with severe tunnel vision depend on a more consciously controlled gaze movement to 'scan' their surroundings for any visual cue or target. The search task, based on a similar approach by Ivanov et al. (Ivanov et al., 2016), aims to test and improve this consciously controlled gaze movement. A number of targets (visible in Fig. 1 b and e) with a radius of 2° visual angle are spawned

within the play area. Three targets are marked visually distinct from the others through a large X symbol in the center of the target. Participants are tasked to scan the play area over the course of a 20 second time window in search for these targets marked with an X, selecting them when found. Meanwhile, distractor targets are marked with an O and are not to be selected. Once a target is selected, it is removed and a new target is generated within the play area, but outside of the participant's VF. This ensures that there are always exactly three marked targets within the play area. The goal of the task is to find and select as many marked targets as possible over the duration. Similar to the tracking task, the difficulty of the search task is adaptable, increasing or decreasing in difficulty gradually based on the participant's performance. A higher difficulty level results in a larger play area and a higher ratio of distractor targets.

Navigation task A third task known to often cause difficulties for people with peripheral VF loss is navigation (Barhorst-Cates et al., 2016). Severe VF restrictions not only increase the risk of collision due to not spotting an obstacle in time, it can also impair efficient movement path planning and spatial memory (Barhorst-Cates et al., 2016). Thus, the third task of the gaze training (Fig. 1 c and f) focuses on testing and improving the navigation and obstacle awareness of participants. For each trial, a randomized obstacle course is generated within the virtual environment (Fig. 2).

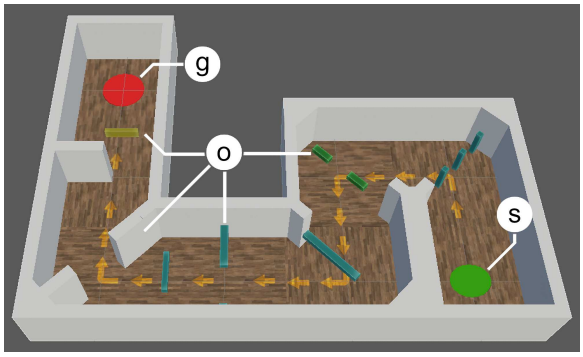

Fig. 2: Example image of one of the obstacle course layouts used in the navigation task, from (Neugebauer et al., 2023). s: Starting position; o: Obstacles (example selection); g: Goal area.

The course consists of an 8m wide and approximately 56m long corridor. Each corridor features two straight tiles, two right corners and two left corners, all in randomized order, for a total of 90 unique layouts. Within the course, a randomized selection of 12 different obstacles are placed. These obstacles consist of walls, near-ground obstacles, obstacles hanging from the ceiling, and obstacles moving from one side of the corridor to the other in a repetitive motion. The participant is tasked to navigate through this obstacle course using their body orientation for direction and controller input for walking speed. Their goal is to reach a zone at the end of the obstacle course (Fig. 2 g) while avoiding collisions, and in as short an amount of time as possible. The different types of obstacles encourage varying gaze behavior, such as scanning both on ground level as well as on head level. A collision is indicated to the participant through an audio cue. A higher difficulty level reduces the time available to participants to move through the obstacle course, though it also increases the movement speed of the avatar. Thus, in order to perform well on higher difficulty levels, participants are required to move and react faster to avoid obstacles.

Once a trial is completed, participants are brought back into a menu screen in which they receive information on their performance within the trial, as well as information on their overall progress, such as the number of daily completed trials and the current difficulty level for the task. Participants were able to mark a trial as 'invalid' using a specified option in this menu. This option was implemented for cases where technical difficulties or outside distractions interrupted the trial execution.

2.5 Study design

For both groups, the study layout consists of three sections (Fig. 3): It starts with an introductory session - analogous to the introductory session given to patients of Group A in the preliminary study by Neugebauer et al. (Neugebauer et al., 2023) - in which the participants are introduced to the VR headset and shown how to operate within the virtual reality environment. The built-in eye tracking device was calibrated

using the pre-implemented tobii eye tracking calibration tool, and after successful calibration, the task execution software was started. Participants went through a guided task execution session, carrying out all tasks for around 5-10 minutes. The experimenter explained the goals and controls for the three visual tasks as well as general menu controls. In addition, a gaze movement pattern was visualized and suggested to participants. This pattern describes a boustrophedon movement - a reading-like motion where the horizontal direction of movement alternates between left-right and right-left - and was based on findings of a previous study (Neugebauer et al., 2021) in which the pattern was found to have a mostly positive effect on visual performance.

Following that, participants were provided with a VR device and would execute the three visual tasks over the course of four weeks in an unsupervised at-home setting. Over the duration, a total of 20 sessions of 30 minutes each were carried out. Performance and eye tracking data were automatically tracked and stored on the device. In the concluding in-person session at the end of the task execution phase, participants returned the VR device to the experimenter.

2.5.1 Questionnaire

During the task execution phase, participants were asked to fill out questionnaires to assess subjective ratings of enjoyment, motivation, stress, eye strain, and other factors of the task execution. The questionnaires had the format of a 10-point Likert scale (Sullivan and Artino, 2013) and were filled after the first training session and after every five training sessions, for a total of 5 questionnaires filled over the course of the training. All five questionnaires featured the same seven questions:

- **Enjoyment** To what extent do you find each of the visual tasks enjoyable?
- **Motivation** How motivated are you to improve your performance in each of the visual tasks?
- **Easiness** How would you rate the ease of carrying out each of the visual tasks?
- **Stress** To what degree do you experience stress while executing each of the visual tasks?
- **Eye Strain** How straining is each visual task on your eyes?
- **Intuitiveness** How intuitive is the use of the gaze training software?
- **Discomfort** How much physical discomfort do you experience while wearing the VR headset?

2.6 Measurement parameters

During training, different parameters were measured in both groups in order to evaluate the participants' performance in the individual visual tasks as well as their gaze behavior during these tasks. The parameters were stored on the VR headset and were evaluated after the training was finished. Parts of the results of the RP patient group have been reported before (Neugebauer et al., 2023).

2.6.1 Performance parameters

- **Target tracking task performance** The target tracking task required participants to select previously marked targets at the end of a trial. The number of incorrectly selected targets - i.e. targets that were not marked during the trial - was measured and used to determine a score for this trial. If no incorrect target was selected before all correct targets are found, the trial was rated with a score of 2. If only one incorrect target was selected, the trial was rated with a score of 1. All other trials were rated with a score of 0.
- **Search task performance** In the search task, performance was measured by the number of static targets found and selected during the trial duration of 20 seconds.
- **Navigation task performance** In the navigation task, both trial duration and number of collisions were measured and individually assessed. Trial duration was defined as the duration from the start of a trial until the defined goal area was reached. Collisions were detected when a bounding capsule that was vertically attached to the user's avatar collided with any surface in the scene, either obstacles or the walls bounding the course. The capsule collider had a diameter of 0.4m and was always positioned exactly at the x- and y-coordinates of the scene camera, oriented vertical to the ground to simulate the body of a standing/walking human.

When assessing performance using these parameters, the variable difficulty level of the

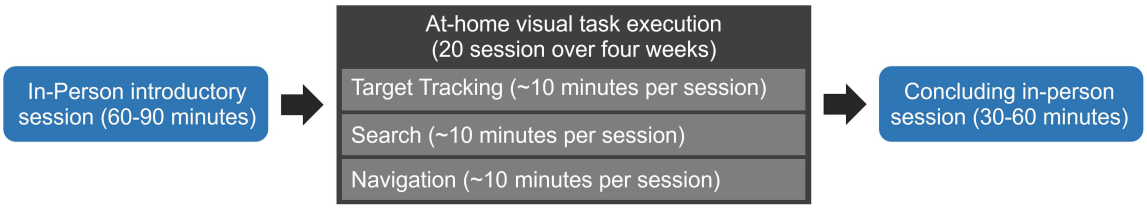

Fig. 3: Schematic of the study layout, showing the introductory in-person session, the task execution phase of 20 sessions of 30 minutes each over four weeks, and a concluding in-person session.

tasks introduced an extra layer of complexity in evaluating participants' performance. As the difficulty increased, it was natural for participants to exhibit a decrease in absolute performance, as more challenging tasks inherently resulted in a higher number of failures. To address this challenge, additional measures were implemented. In the target tracking task, the difficulty level itself proved to be a suitable measure of patient performance. Due to the gradual increase or decrease of the difficulty level based on participants' performance, the difficulty level will usually converge towards a 'saturation' at which the participant will neither win nor lose a predominant number of trials. This saturated difficulty level can be seen as indicator for the current performance of the participant. However, in the two other tasks, this method was not feasible, as in both cases difficulty levels did not reach natural saturation for all participants. This was partly caused by participants improving at a constant rate over the entire duration of the study, or by participants reaching the lower limit of the difficulty range. Thus, for the search task, the performance score was instead adjusted in relation to the size of the play area in which targets were placed. This adjustment was calculated as follows: $P_{adj} = t * (w_{area} * h_{area})$, where P_{adj} represents the adjusted performance score, t denotes the number of targets found, and w_{area} and h_{area} represent the width and height (measured in visual angles) of the play area, respectively. This way, the increasing size of the play area and the resulting increased challenge to find targets within the area is considered in the score. For the navigation task, no specific measures were taken to adjust for changes in difficulty, as changes in difficulty had only minor effects on the measured parameters, and trials of different difficulty levels still remained largely comparable to each other.

2.6.2 Gaze parameters

Using the raw eye tracking data, saccades were detected based on an algorithm suggested by Nyström et al. (Nyström and Holmqvist, 2010). To reduce noise, a moving average over five samples (∼55ms) was applied to the eye tracking data. Then, after applying a low-pass filter of $50°/s$ to the data, the mean (μ) and standard deviation (σ) of the angular velocity of the gaze was calculated for each individual trial. Saccades were registered when gaze velocity surpassed $v_{max} = \mu + 6 * \sigma$, with onset and end of the saccade being detected at a threshold of $v_{onset} = \mu + 3 * \sigma$.

- **Dynamic Visual Field** The Dynamic Visual Field (DVF) serves as the main indicator for visual performance in this work. It describes the area observed by a participant over a specified shifting time window (Fig. 4) - in case of this study, a three-second time window. The DVF is calculated every 0.5 seconds and averaged at the end of a trial. The gaze direction used to calculate the DVF considers both head movements and eye movements. DVF can be measured in square degree of visual angle, however for better comprehension, the DVF in this work is reported as percentage of a healthy VF at approximately $180° * 135°$. In other words: a DVF of 10 indicates that a participant observed a total of 10% of the visual area of a visually healthy subject over the course of the three seconds.
- **Exploratory saccades** Exploratory saccades are defined as saccades that end in a fixation point that lies outside of the area that is visible during the onset of the saccade (Ivanov et al., 2016). The parameter is reported as the ratio of exploratory saccades to the total number of saccades within a trial.

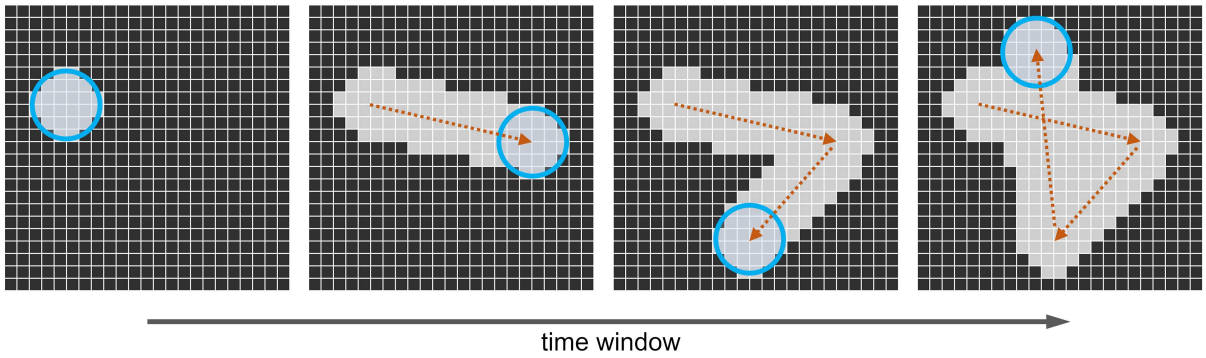

Fig. 4: Visualization of the concept of the Dynamic Visual Field. The array of black pixels marks a large visual area that could potentially be observed by the participant. The blue circle marks the VF of the patient. Orange arrows indicate gaze movement over a specified time window. Light-grey pixels mark the area that has been observed at any point during the moving time window. The Dynamic Visual Field is defined as the ratio between light-grey pixels and total number of pixels at the end of the time window, meaning in the right-most image.

- **Saccade frequency** Saccade frequency describes the number of saccades per second carried out by the participants.
- **Ratio of head-related to eye-related gaze** This parameter describes the ratio by which eye movements and head rotation contribute to the total amplitude of the saccade, respectively. A value of 1 indicates that head movements and eye movements contributed equally to the saccade, a value lower than one indicates that eye movements had a higher contribution, values above 1 indicate higher contribution of head rotation.
- **Ratio of horizontal to vertical gaze movements** Here, the ratio of direction of saccades is reported. A value lower than one indicates that saccades were predominantly horizontally oriented, values higher than one indicate a predominantly vertical orientation of saccades.

2.7 Evaluation and statistical methods

2.7.1 Data samples

Over the course of the study, a total of 6329 Target Tracking trials (3125 from Group A, 3204 from Group B), 6444 Search trials (3205 from Group A, 3239 from Group B), and 5401 Navigation trials (2583 from Group A, 2818 from Group B) have been captured. Due to missing or invalid eye tracking data, some trials had to be excluded from analysis of gaze-related parameters. Trials were excluded from analysis if more than 10% of eye tracking samples were invalid. Table 2 shows the number and reason of excluded trials. In the remaining trials, the average ratio of invalid eye tracking frames varies between 0.45% and 0.6% based on the visual task. Reasons for missing or invalid eye tracking data can include blinking, gaze angles outside of the suggested eye tracking range of 25° from the center of the VF, or temporary hardware failure of the eye tracking device.

Table 2: This table shows the total number of trials per group, the number of trials that had missing eye tracking data, and the number of trials that were excluded from eye tracking analysis due to the ratio of invalid eye tracking frames being above the threshold of 10%. The values are given for Group A and Group B individually.

Visual Task	Trials		Missing		Invalid	
	A	B	A	B	A	B
Tracking	3125	3204	5	0	86	4
Search	3205	3239	0	2	107	1
Navigation	2583	2818	42	0	143	3

Outliers in the dataset have been adjusted by limiting their values to within three times the

standard deviation from the mean (Sullivan et al., 2021).

2.7.2 Statistical analysis

The data analysis in this study was conducted using the R programming language, facilitated by the RStudio graphical interface with the 'nlme' and 'lme4' libraries. The primary objective of this study was to evaluate the similarity of parameters between two groups. Traditional statistical tests like Anova or Linear Mixed Models, while effective at detecting significant differences between groups, fall short in demonstrating equivalence between them. Instances where these models fail to reject the null hypothesis only describe the absence of significant effect, which does not necessarily confirm the equivalence between the groups. To address this, we employed a statistical approach known as 'two one-sided tests for equivalence' (TOST) (Schuirmann, 1987). The TOST method involves two one-sided hypothesis tests. The first test assesses whether the mean difference between Group A and Group B is greater than a pre-defined delta value (upper equivalence limit). The second test assesses whether the mean difference is less than negative delta (lower equivalence limit). If both one-sided tests fail to reject their respective null hypotheses, it provides evidence that the two groups are within the specified delta range.

Each analysis starts by fitting a linear regression model to the data, using the respective measurement parameter as dependent variable and the parameters 'training session' and 'trial number' as fixed effects. By including these factors, the model minimizes the effects of learning-related effects from its residuals, leaving mainly participant-dependent effects as well as stochastic noise. Next, a delta value for the TOST has to be defined. Following an approach by Ng et al. (Ng, 2001), the delta value δ is set to 0.2 times the standard deviation of the samples. Confidence level is set to 0.95 following statistical conventions. With all parameters in place, the TOST is conducted for each investigated parameter on each of the three visual task results.

When the TOST fails to establish significant equivalence between two groups for a given parameter, it prompts the question about whether there is a significant effect between the two groups or if the results are inconclusive. The latter suggests that the sample size does not provide sufficient statistical power to draw clear conclusions about the relation between the two groups regarding the respective parameter. To test for significant effects between the groups, Linear Mixed Models (LMMs) are applied for all continuous parameters. An exception is the 'Number of Collisions' parameter in the navigation task, which has discrete values and exhibits a high zero-inflation. Here, a negative-binomial Generalized Linear Mixed Model (nbGLMM) was employed, as it is particularly suitable for such data types (Bates et al., 2015). Additionally, the 'Trial duration' parameter of the navigation task was transformed using a logarithmic function to improve normal distribution of samples. The general structure of the LMMs was comprised of the same components. The respective measurement parameter was included as dependent variable. Fixed effects included Trial Number as well as the interaction term between Training Session and Group. The interaction term allows to test whether the average learning rate of the two groups significantly differs. Lastly, the individual participant parameter was included as random factor, taking into account both random intercepts and random slopes. This approach recognizes that each participant has unique inherent performance levels and gaze characteristics (random intercept), as well as distinct learning patterns over the course of the study (random slope). To ensure the appropriateness of these models, the normal distribution of residuals was assessed using QQ-plots as a visual indicator.

Finally, the relationship between task performance and VF size is investigated using LMMs. For these, the performance parameters were used as dependent variable, Training Session and VF size are included as interacting fixed factors, and the individual participant parameter was again included as random factor. Notably, only a random intercept was taken into account for the random factor due to the models failing to converge when considering a random slope.

Statistical evaluation of the questionnaires is not feasible due to the low number of samples. Results are reported as raw data.

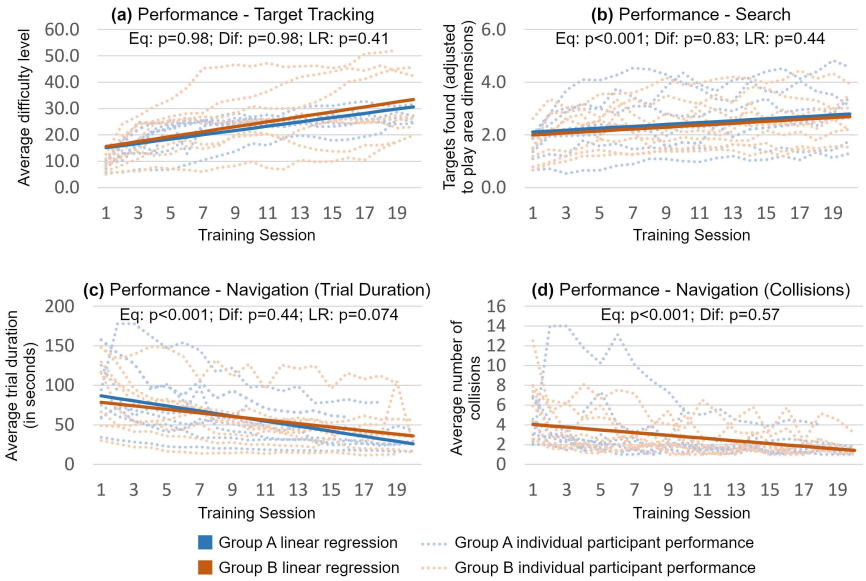

Fig. 5: Results for the task performance in the three visual tasks. Dotted lines show the average results for each individual participant, continuous lines show the average regression of all trials. Results for trial duration and number of collisions in the navigation task are shown separately. Non-logarithmic trial duration values are shown for better visualization despite statistical evaluation only considering the logarithm of trial duration for better normal distribution. Each plot includes the resulting p-values of the statistical models conducted: Eq describes the equivalence between groups found with TOST, Dif describes the effect between groups found with an LMM, and LR describes the interaction effect between the Training Session and Group parameter, meaning differences in the learning rate between groups. Interaction terms are not feasible in the nbGLMM, thus no p-value for LR is reported under (d).

3 Results

3.1 Equivalence and statistical effects between groups

In this first section, we will compare the results of Group A and Group B with each other across all measurement parameters and for all three visual tasks. The objective is to assess the extent to which the simulation of tunnel vision in visually healthy participants captures various aspects of the condition. For each condition, three statistical findings are reported:

1. Equivalence (Eq): This indicates the p-value obtained from the TOST analysis. A p-value < 0.05 signifies significant equivalence between both groups, implying that their results in the given condition are comparable.
2. Difference (Dif): This reflects the p-value derived from the LMM or nbGLMM, as applicable. A p-value < 0.05 suggests significant differences between the results of Group A and Group B for the specific condition.
3. Learning Rate (LR): This assesses whether the two groups exhibit significantly different effects in relation to the dependent variable and the Training Session parameter. This comparison is evaluated within the same LMM or nbGLMM models as before. In this context, a p-value < 0.05 indicates that the two groups display divergent changes in average performance or gaze behavior over the duration of the study, which can be interpreted as one group improving or adapting faster than the other.

3.1.1 Performance

Fig. 5 shows the performance displayed by both groups in the different tasks over the course of training. Raw data of the results is found in the supplementary files (File S1)

Both groups show significant improvements in performance over the course of the study in all

visual tasks ($p < 0.001$ for all four conditions). For equivalence, it is found that in the target tracking task, null hypothesis of statistical difference is not rejected ($p = 0.98$), indicating that the results of the two groups are not equivalent. For the three other parameters, however, null hypothesis of statistical difference is rejected ($p < 0.001$ for all three parameters), thus the performance of both groups can be assumed equivalent in both the search task and the navigation task. As a second step, the parameters were analyzed regarding statistically significant differences using an LMM or nbGLMM, respectively. However, no significant differences between Group A and Group B were found for any of the performance parameters, both regarding the mean of results as well as learning rates.

3.1.2 Gaze characteristics

The results of the five gaze characteristic parameters tested within this work are displayed in Fig. 6. Information about statistical significance of both equivalence and difference between results of both groups is noted within the figure. The null hypothesis for statistical difference is rejected in three conditions: the DVF in the target tracking task, the saccade frequency in the search task, and the ratio between horizontal and vertical gaze direction in the navigation task. As for conditions where significant effects are found between the results of Group A and B, these include the ratio of exploratory saccades in the search task, the saccade frequency in the navigation task, as well as the ratio of head-related gaze movements to eye-related gaze movements in all three tasks. In the other condition, neither significant equivalence nor difference can be concluded from the statistical tests. Regarding differences in the learning rate between the groups, noticeable parameters are the ratio of exploratory saccades as well as the head-to-eye ratio, both of which show a convergence between groups over the course of the study in almost all tasks.

3.2 Influence of visual field size

In this section, it is investigated how the size of the VF of patients from Group A - and respectively the size of the simulated tunnel vision of the matched participant in Group B - affects the performance. Fig. 7 shows the relationships between these parameters. The performance values displayed in these graphs are based on the predicted performance for the 1^{st} and 20^{th} training session, calculated using the results of linear regression.

While some trends are visible in the graphs, no statistically significant effects between VF radius and task performance were found for any of the visual tasks.

3.3 Questionnaires

The questionnaires that were filled by both groups after the course of the study give insight into the qualitative results for the gaze training. The average rankings as well as the distribution of individual scores are shown in Fig. 8. The results show a high variance between different participants even within the same group and condition, indicating high influence of subjective perception and preference. Despite this, it is noticeable that Group A's rating is generally higher regarding task enjoyment and motivation, and lower regarding stress and eye strain. The trend is especially noticeable towards the end of the study. No clearly noticeable differences between groups are found in the ratings regarding easiness, intuitiveness, and discomfort.

4 Discussion

In this study, we have investigated the degree by which the simulation of visual field defects - specifically the simulation of tunnel vision scotoma - in visually healthy participants within a virtual environment can represent the effects of real visual field defects. We have analyzed and compared the results of two age-matched groups consisting of eight Retinitis pigmentosa patients and eight visually healthy participants, respectively, in three visual tasks over the course of four weeks. The findings allow to draw conclusions about which aspects of vision and vision-related task performance can feasibly be reproduced through VR-based simulation, which aspects show clear differences, and how this relation changes over the duration of the study.

Our findings suggest that the simulation of tunnel vision in visually healthy participants is well suited to accurately represent performance within different vision-based VR tasks. Three out of four investigated performance parameters (Fig. 5 b-d) - relating to tasks of static target search and

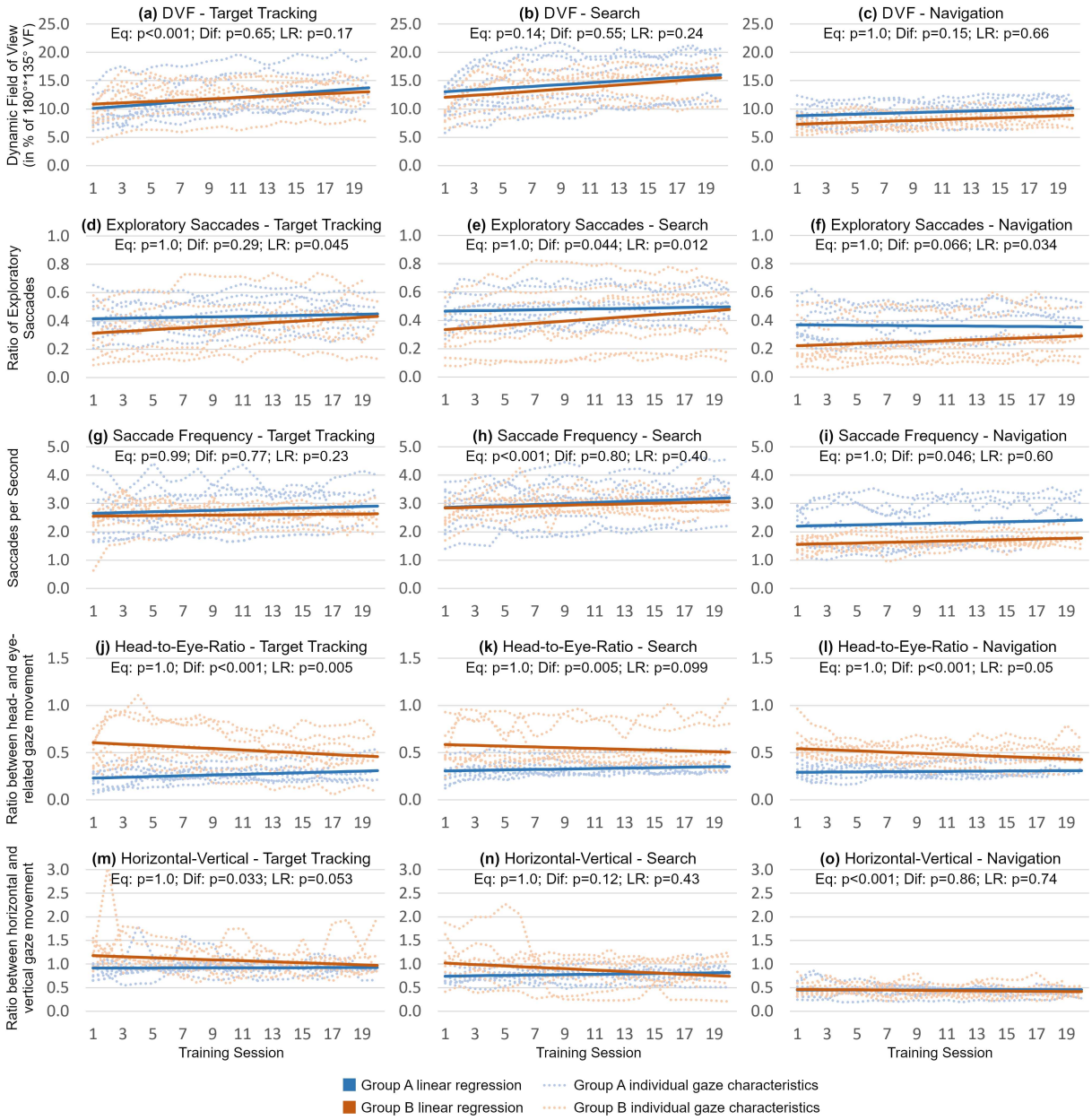

Fig. 6: Results of the gaze characteristic parameters in the three different visual tasks, showing individual results of participants and average regression for Group A and B. Each plot includes the resulting p-values of the statistical models conducted: Eq describes the equivalence between groups found with TOST, Dif describes the effect between groups found with a LMM, and LR describes the interaction effect between the Training Session and Group parameter, meaning differences in the learning rate between groups. Head-to-Eye-Ratio describes the amount of head movement (in visual angles) divided by the amount of eye movement contributing to saccades. Horizontal-to-Vertical describes the amount of gaze movement on the elevation axis divided by the amount of gaze movement on the azimuth axis.

navigation - show significant equivalence between RP patients (Group A) and participants with simulated tunnel vision (Group B). For the fourth parameter (Fig. 5 a) - related to the task of moving target tracking -, equivalence between the two data sets can neither be assumed nor rejected based on statistical results. Previous literature found that without the use of simulated VFDs, the task performance of visually healthy participants and patients with peripheral VFD significantly differs within a VR setting (Gopalakrishnan et al., 2020), which further supports the effetiveness of the method presented in this work.

Differences between the two groups' results arise when evaluating specific characteristics of the gaze behavior of participants (Fig. 6). Namely, we have investigated (i) the Dynamic Visual Field (DVF), which describes the amount and efficiency of gaze movements for observing the visual surroundings; (ii) the ratio of exploratory saccades compared to the total number of saccades within a trial; (iii) the frequency of saccades; (iv) the ratio between head movements and eye movements that contribute to overall gaze; (v) the ratio between vertical and horizontal direction of gaze

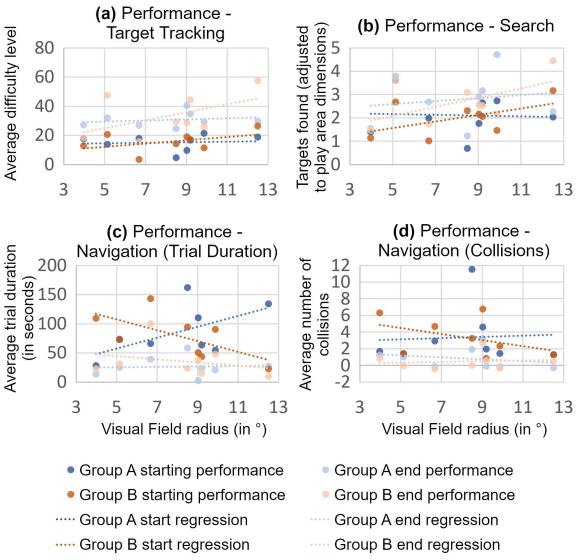

Fig. 7: Relationship between the different task performances and the average radius of the - real or simulated - VFs. The displayed results show the approximate performance at the start and end of the study, respectively.

movements. Here, only few results are found significantly equivalent between groups, and there are no parameters that are consistently equivalent throughout all three tasks. Given the large number of individual analyses conducted regarding the different gaze characteristics, it is possible that the findings are influenced by the Multiple Comparisons Problem (Sullivan and Feinn, 2021). Thus, it is more feasible to focus only on those parameters where notable features occur in multiple related conditions. The first of these is the ratio of exploratory saccades (Fig. 6 d-f), which is found to be significantly higher in Group A in the search task, with visual trends in the target tracking task and navigation task supporting this.

Next, it can be observed that in all three tasks, Group B displayed a significantly higher ratio of head movements to eye movements compared to Group A (Fig. 6 j-l). This behavior is likely related to the technical implementation of the tunnel vision simulation. As was stated in section 2.4.1, Stein et al. (Stein et al., 2021) found the end-to-end latency of VR devices applying the tobii eye tracking system to be around 79ms. Albert et al. (Albert et al., 2017) report that for foveated rendering - a technique similarly dependent on low eye-tracking latency - the range of latency at which participants start reporting a noticeable delay is between 50-70ms. It can thus be assumed that the simulation of tunnel vision applied in this work had an at least subconsciously noticeable delay. Notably, one participant from Group B did mention perceiving a slight delay in eye tracking, but stated that it was not perceived as obstructive. While no exact information about the latency between head-related movement and the displayed visual content - also called Motion-to-Photon (M2P) latency - is given for the Pico Neo 2 Eye, these measurements exist for similar commercial VR devices (Laiho and Nikula, 2020) and were found to range between 0 and 5ms. Assuming the Pico Neo 2 Eye's M2P latency is comparable to these values, it would be substantially lower than the eye-tracking latency. This difference could explain the significantly higher ratio of head movements observed in Group B, as lower latency incentivizes higher reliance on the respective type of tracking. The risk of eye-tracking latency influencing the results was known before experimental trials commenced. However,

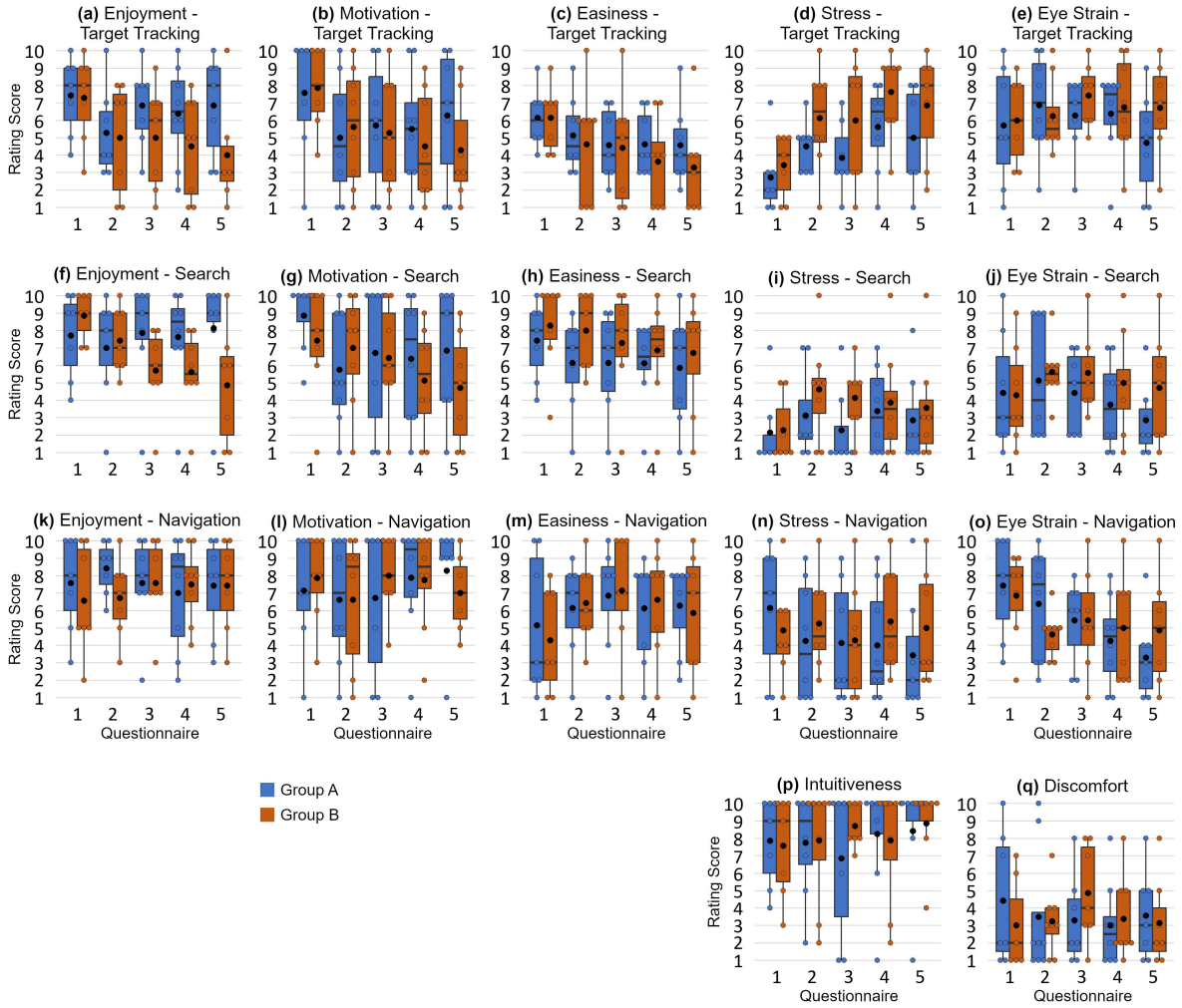

Fig. 8: Rating results for different aspects of the visual training. Questionnaires 1-5 were filled after 1, 5, 10, 15 and 20 training sessions. A rating of 10 equals 'very high', a rating of 1 equals 'very low'.

at the time, the Pico Neo 2 Eye was the only commercially available stand-alone VR device that provided built-in eye-tracking. Alternatives with lower end-to-end latencies, such as the Fove-0 (45ms) or Varjo VR-1 (57ms) (Stein et al., 2021), would require complex setup, including connection to external processing and tracking devices, making them not feasible for use in unsupervised at-home training.

Lastly, it is noticeable that for most gaze characteristics in which both groups show significantly different results - which mostly includes the parameters of exploratory saccade ratio (Fig. 6 d-f) and head movements to eye movements (Fig. 6 j-l) -, the results of the two groups show significant trends to converge over the course of the study. This suggests that even significant differences in those gaze characteristics may be minimized through extended adaption to the simulated visual field defects. It remains to be tested whether this effect is transferable between tasks, meaning whether sighted participants could be 'trained' to adapt gaze characteristics of patients in one task and then display similar performance and gaze characteristics in different tasks.

Regarding the influence of VF size on performance, as shown in Fig. 7, visual trends seem to suggest that the performance of Group B is generally more negatively affected by smaller VFs. Given the lack of statistical significance of these

trends, however, no validated statements can be made regarding these effects.

In the questionnaires, it is overall noticeable that the ratings in both groups show strong variations between individual participants, oftentimes covering almost the entire range from lowest to highest possible score rating. This shows that the perception of the tasks is highly subjective and difficult to predict. On average, it appears as though RP patients report higher enjoyment and lower perceived stress during the visual tasks, especially in the Target Tracking and search tasks. However, given the high variance between answers, it is once again not feasible to derive solid conclusions from the questionnaire results.

Different previous studies have shown that the applied approaches to simulate visual field impairments have the desired effects on visually healthy participants in that they reduce their performance in visual tasks (Jones et al., 2020, Krösl et al., 2019, Väyrynen et al., 2016). However, to the best of our knowledge, no previous study has quantitatively assessed performance differences and differences in gaze behavior between real patients and participants with simulated visual field impairments. This makes a comparison between results of different studies difficult and not feasible.

While the results of this work can be relevant for future vision impairment studies and accessibility test setups utilizing VR, some limitations of the findings have to be considered. For one, the experimental setup was designed to assess the influence of visual field defect only. Other aspects of visual impairments, such as limited visual acuity or contrast sensitivity, glare sensitivity, or night blindness, were not considered. The experimental environment was designed to minimize any influence by ensuring that all patients were able to effortlessly detect and recognize any visual target or element within their VF. Furthermore, all measured results of this study were exclusively gathered within a virtual environment, with participants maintaining a stationary seated position. Consequently, it is important to note that these results hold no direct relevance for the practical application of simulations in real-world scenarios. This limitation might initially appear redundant, given that the utilization of a VR headset is essential for the accurate simulation of gaze-contingent visual field defects. However, technology such as mixed reality, while not yet widely popular and commercially available, could change this in the near future. Mixed Reality headsets function similar to VR headsets in that they display a scene to the user through head-mounted displays. However, Mixed Reality devices have the ability to capture the real world through front-facing cameras, projecting the images to the device's displays to allow the user an almost-natural view of the surrounding area. However, as this image of the real world is digitally projected to the screens, the displayed scene can be freely modified using additional virtual contents that are overlayed with the real-world capture. Such virtual content could be a visual field defect mask, which essentially allows to apply the simulation used in this work to real-world tasks. The evaluation of this technology, its feasibility for real-world vision impairment simulation, and the comparison of its results with those of real patients offer interesting questions for future research.

Based on our findings, expanding a group of patients living with visual field defects with a larger cohort of visually healthy participants with simulated visual field defect seems largely feasible if the following conditions are met: (i) The study or accessibility test for which the cohort is recruited can provide meaningful results if realized within a virtual environment; (ii) The study or test mainly focuses on quantitative rather than qualitative results; (iii) The primary emphasis of the study or test is on evaluating task performance rather than specific gaze behavior; (iv) The study or test is primarily concerned with the average results of a group, rather than effects that depend on characteristics of the individual participant; (v) Ideally, the visually healthy participants have the possibility to adapt to the simulation for several hours before taking part in the actual assessment.

5 Conclusion

We evaluated whether the simulation of tunnel vision in visually healthy subjects within a virtual reality setup can accurately mirror performance and gaze behavior of actual patients living with the condition. Findings suggest that the group with simulated tunnel vision succeeds in accurately representing the task performance of the patient group. Gaze characteristics are largely not found to be significantly equivalent and sometimes even significantly differ between groups. However,

over the course of 10 hours of visual task execution, several gaze characteristics between the two groups begin to converge, implying that the extent to which the simulation can represent the actual visual impairment increases with expanded use of the simulation.

6 Supplementary files

- **File S1** List of raw data for all recorded trials.
- **Video S1** Video showcase of the three visual tasks, both with and without simulated tunnel vision.

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Competing interests

This work was done in an Industry-on-Campus cooperation between the University of Tübingen and Carl Zeiss Vision International GmbH. Three of the authors, Nora Castner, Iliya Ivanov, and Siegfried Wahl, are employees of Carl Zeiss Vision International GmbH. Their affiliation with Carl Zeiss Vision International GmbH had no influence in the study. There are no competing interests related to employment, consultancy, patents, products in development, or marketed products.

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Author contributions

Conceptualization: Alexander Neugebauer, Iliya Ivanov, Siegfried Wahl; Methodology: Alexander Neugebauer; Medical guidance and supervision: Katarina Stingl; Formal analysis and investigation: Alexander Neugebauer, Nora Castner, Björn Severitt; Writing - original draft preparation: Alexander Neugebauer; Writing - review and editing: All Authors; Funding acquisition: Iliya Ivanov; Supervision: Siegfried Wahl.

Appendix A Visual fields

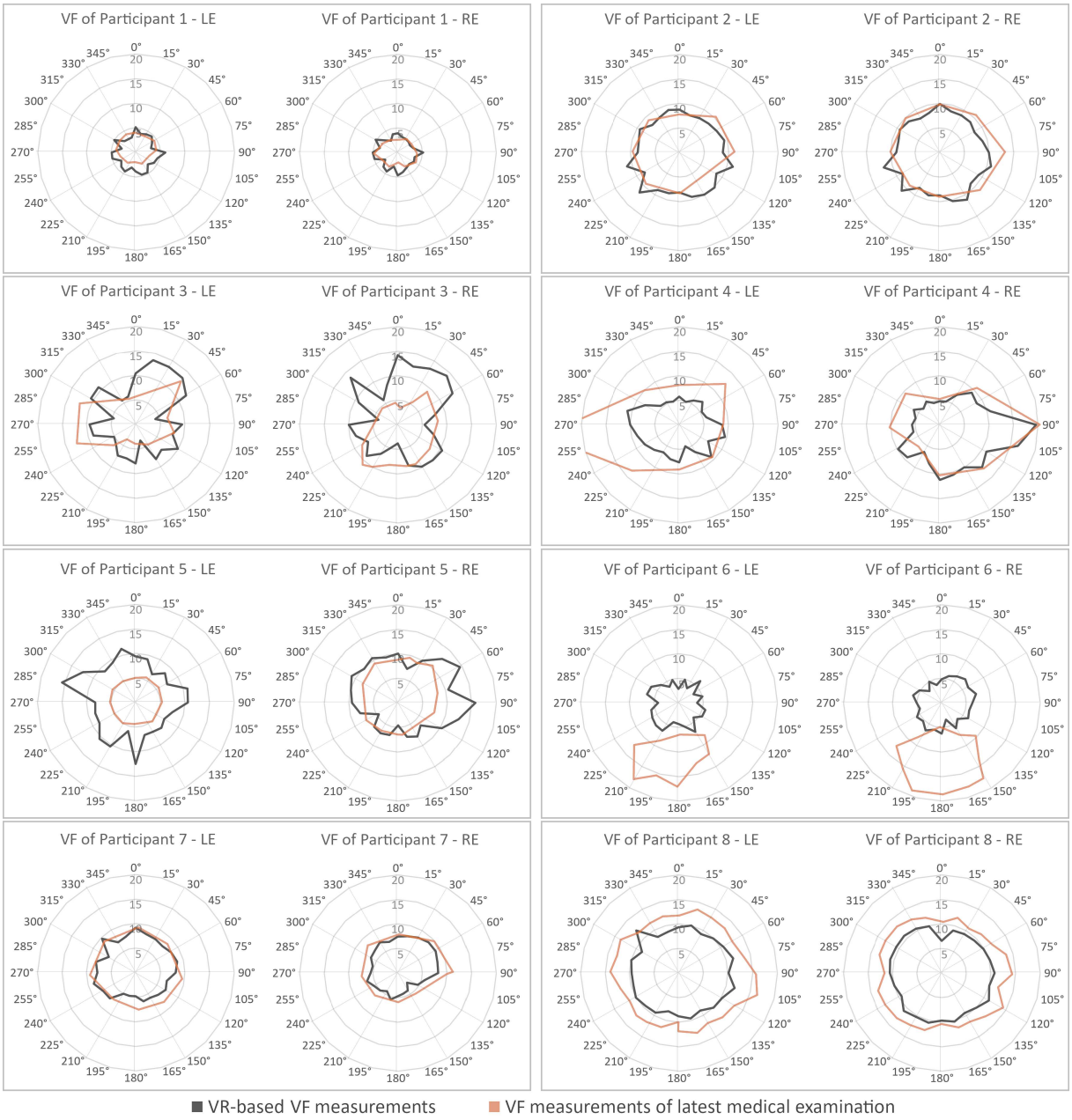

Fig. 9: Comparison of the VFs of patients from their most recent medical exam and the VFs directly measured within the Virtual Reality setup.

Fig. 9 displays the visual fields of the eight RP patients of group A, as reported in (Neugebauer et al., 2023).

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Supplementary information

1 Description of software components of the GazeQuest

This chapter describes the individual software components found in Fig. 3.1 and Fig. 3.2.

1.1 Existing frameworks

This section includes all of the GazeQuest's components that come from external sources.

- **Unity3D game engine (version 2021.3LTS)** This is the core platform used to develop the GazeQuest framework. The Unity3D game engine features an environment for object-oriented programming, handling interactions between different scripts and other components of a scene, such as static objects or player-controlled actors. The Unity3D game engine handles graphics computations and rendering required for the display of three-dimensional scenes and environments. It also provides tools to integrate the developed application in different hardware platforms, such as VR devices and their controllers, and it detects haptic input events on these devices. Lastly, a scene editor provides a toolkit for the creation and modification of three-dimensional scenes and customized user interfaces.

- **Pico XR SDK (version 1.2.4)** This software development kit (SDK) processes the spatial data received by the tracking systems of the Pico Neo 2 Eye VR headset and controllers, providing tools to access this spatial data – position and rotation – within the Unity3D game engine.

- **Tobii XR SDK (version 3.0.1)** This SDK interprets video footage from infrared eye-tracking cameras embedded in the Pico Neo 2 Eye headset. By continuously detecting the wearer's pupils, it assesses the current gaze vector. The SDK makes this gaze vector accessible from within the Unity3D game engine.

1.2 Project-specific components

This section includes all software components integrated in the GazeQuest framework - shown in Fig. 3.1 - that were developed as part of this work.

- **Controller input manager** This script handles all controller selection related functions of the GazeQuest framework. It utilizes the spatial information provided by the Pico XR SDK to test via so-called RayCast function whether the controller is pointed at an interactable scene element, such as a user interface button or a selectable target. This information is used to highlight interface elements when the controller selection ray rests on them. If a haptic input – meaning a press of one of the controller's keys – is detected by the Unity3D input system while the controller is pointed at an interactable element, the element will be triggered.

- **Coordinate transformation** This script accesses the gaze vector provided by the Tobii XR SDK and the headset rotation provided by the Pico XR SDK. Both parameters are transformed from Cartesian coordinates into radial coordinates, allowing to determine azimuth and elevation angles of both head-related and eye-related gaze direction. This gaze direction data is required in all further gaze-related calculations.

- **Gaze-contingent visual field defect simulation** This script realizes gaze-contingent simulation of VFDs within the three visual task scenes. The remaining VF shape can be set as a uniform circle with a specified radius or customized using a texture derived from patients' perimetry measurements. Areas outside the specified remaining VF are obscured by a black masking layer to simulate visual loss. Utilizing eye-related azimuth and elevation gaze angles provided by the coordinate transformation script, the masking layer adjusts with the user's gaze, allowing the remaining VF to move accordingly. The script's functionality can be toggled on and off and is active only during experiments with visually healthy participants.

- **Saccade detection** In this script, saccades are detected based on an algorithm by Nyström et al. [174], utilizing combined movements of eye-related and head-related gaze. More details on the process can be found in chapter 3.2.1 of the thesis and in the methods sections of Publications B and C.

- **Gaze pattern similarity calculation** This script calculates the similarity between participants' actual gaze movements and an 'ideal' systematic scanning pattern based on sequences of multiple saccades, as is described in chapter 3.2.1 of the thesis. To find the best match between the actual gaze pattern and the suggested

systematic scanning pattern, a MultiMatch algorithm [180] is applied. A more detailed description of the functionality of this algorithm is found in Appendix S1 of Publication B. To achieve run-time performance of the MultiMatch function, the script utilizes a binary search tree [181].

- **Dynamic visual field calculation** This script calculates the dynamic visual field based either on eye-related gaze movements, head-related gaze movements, or gaze movements of both head and eyes combined. A detailed description of the computation and calculation is described in Appendix S1 C of Publication B.

- **Visual tasks** The visual task scenes are the part of the GazeQuest that users directly interact with. Each visual task scene incorporates several scripts and scene components, visualized in Fig. 3.2 and described later in this supplementary information section.

- **Task selection menu and Main menu interface manager** The Task selection menu acts as the main menu of the GazeQuest, loading upon startup of the application. It includes interface buttons that navigate to the three visual tasks, as well as a button to close the application. Furthermore, the menu provides information on the number of completed sessions and trials. The functionality of this menu is handled by the Main menu interface manager, which receives information on the current progress of completed trials and sessions by the Progress manager.

- **Progress manager and progress storage file** This script handles serialization and storage of all parameters that persist across trials and training sessions, such as the current difficulty level of each visual task and the number of trials completed. Data is converted to a string format and written to the Progress storage JSON file. During application startup, the Progress manager reads the stored data from the file, restoring the application to its prior state at the time of exit.

- **Gaze data files** These files store all gaze-related data captured during each individual visual task trial in CSV format, facilitating the access for post-experimental analysis and evaluation.

- **Task result data files** Similar to the Gaze data files, the Task result data files store the results of each visual task trial, as well as the respective difficulty level of this trial.

1.3 Visual tasks

This section describes the software components integrated in the three visual task scenes, visualized in Fig. 3.2. Detailed descriptions of the visual tasks themselves are found in the methods sections of Publication B and C, and rationale for the design of the tasks is found in chapter 3.1.3 of the thesis.

Target tracking scene

- **Game State Manager** The game state manager of each visual task scene acts as the basis of the scene's 'game logic'. It handles interactions between other scripts and components in the scene. It also tracks the current phase of the trial, such as initialization, task execution phase, and trial completion. Lastly, it calls required functions for each phase and activates/deactivates components as needed.

- **Target spawning & movement** This script handles the initial creation and placement of the moving targets of the target tracking task. It also manages the movement logic of the targets during the tracking phase. Targets move along the surface of a spherically curved area, ensuring that angular movement speed as well as angular size of the targets remain constant from the user's perspective. This requires transformation of movement and facing direction of the targets from Cartesian coordinates to radial coordinates. Furthermore, to ensure that targets do not occlude each other, the script adjusts the randomized movement of the targets to automatically avoid collisions, gradually turning targets in a different direction when moving close to another target. A similar function is applied to ensure that targets stay within the bounds of the defined search area.

- **Trial interface manager** Each visual task scene features a menu interface that appears in-between trials. These interfaces provide feedback on the task-specific results of the previous trial: The number of errors in the target tracking task, the number of targets found in the visual search task, and the trial duration and number of collisions in the navigation task. Additionally, feedback on gaze behavior is provided to participants in form of the average dynamic visual field and gaze pattern similarity displayed by the participant within the previous trial. The interface also features selections to continue with the next trial, return to the task selection menu, or to declare the previous trial as invalid in case of unexpected external interference during training. All functionalities of the interface

are handled by this script.

- **Task result assessment** These scripts include the success criteria of each respective task and determine the task results in each trial based on these criteria. In case of the target tracking task, for example, the script detects whether a correct or incorrect target is selected during the selection phase, counting the number of incorrect selections and returning this number as task result parameter.
- **Dynamic difficulty adjustment** This script contains the logic behind the automated step-wise difficulty adjustment of the visual tasks, described in chapter 3.1.3 of the thesis. The difficulty adjustment is based on the task results provided by the Task result assessment script.

Visual search scene

- **Trial interface manager** See 'Trial interface manager' under Target tracking scene.
- **Game state manager** See 'Game state manager' under Target tracking scene.
- **Target placement** Similar to the Target spawning & movement script in the target tracking scene, this script handles the initial placement of the static targets of the visual search task, as well as the creation and placement of a new target once an existing target was found and selected. Targets are placed on a radial surface within a defined search area, at a minimum distance of 8° visual angle to each other. Additionally, any targets created during the search phase are positioned outside of the current visual field of the user, incentivizing exploratory gaze movements.
- **Task result assessment** See 'Task result assessment' under Target tracking scene. Here, the task result parameter is the number of targets found during the 20-second search phase.
- **Dynamic difficulty adjustment** See 'Dynamic difficulty adjustment' under Target tracking scene.

Navigation scene

- **Trial interface manager** See 'Trial interface manager' under Target tracking scene.

- **Game state manager** See 'Game state manager' under Target tracking scene.
- **Randomized obstacle course generator** This script handles the creation of the randomized obstacle course layout and the obstacles placed within. The corridor of the obstacle course always consists of six tiles: Two straight corridor tiles, two right corners and two left corners. By placing these tiles in randomized order, 96 different obstacle course layouts can be generated. Within each course layout, 8 obstacles of different types, described in the methods section of Publications A-C, are placed, randomly selected from a set of 16 obstacles. An example layout for the obstacle course is found in Fig. 2 of Publication C.
- **Player movement & collision detection** In this script, the movement of the 'player avatar' – the actor within the scene that represents the user's position in the scene – is handled. Locomotion is controlled via the thumb-stick of the VR controller, accessed through the Unity3D input system. Rotation and facing direction of the player avatar is controlled via the rotation of the VR device, allowing the user to physically turn around and face the direction they are walking in the virtual scene. The script also detects collisions between the player avatar and obstacles or walls. The collision is indicated to the user through a sound cue, and the player avatar is repelled back a short distance, providing some space to adjust the walking path.
- **Task result assessment** See 'Task result capture' under Target tracking scene. Here, the task result parameters are the duration to reach the marked goal area of the obstacle course, as well as the number of collisions within the trial.
- **Dynamic difficulty adjustment** See 'Dynamic difficulty adjustment' under Target tracking scene.