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Designing and Evaluating a Virtual Reality Game to Assist Clinicians Working With Amblyopia

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DESIGNING AND EVALUATING A VIRTUAL REALITY GAME TO ASSIST CLINICIANS WORKING WITH AMBLYOPIA

A thesis submitted in partial satisfaction of the requirements for the degree of

MASTER OF SCIENCE

in

COMPUTATIONAL MEDIA

by

Rohan Jhangiani

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Abstract

Designing and Evaluating a Virtual Reality Game to Assist Clinicians Working with Amblyopia

by

Rohan Jhangiani

Amblyopia is one of the most common and treatable neurological eye conditions worldwide, affecting 1-5% of the population. This condition has been traditionally treated through occlusion therapy (patching the stronger eye) to help strengthen the visual pathways from the weaker eye to the brain. This treatment is vital in preventing potential vision loss and other visual problems that can arise if this condition is left untreated. It is usually most effective if the treatment is administered during childhood. However, due to the nature of occlusion therapy, which can be repetitive and uncomfortable since it requires wearing an eye patch for extended periods, it suffers from low compliance rates. This thesis covers developing and testing a Virtual Reality (VR) game designed in close collaboration with an ophthalmology clinic to make visual exercises that make this traditionally cumbersome therapy more enjoyable. Researchers met with a team of clinicians weekly to develop and iterate on this game, ensuring that we consider clinician feedback when making game design decisions. We conducted our research evaluating this game in two parts—the first aimed to test the game's efficacy against a placebo in a clinical setting. In contrast, the second part aimed to introduce scent as feedback to the game, conduct interviews with clinicians to gleam insights about

their experience using the game, and survey participants who played the game. Through this work, we aim to examine how serious games might help make health therapeutics more enjoyable and engaging through technology, such as VR, along with understanding the role multimodal feedback can play in these severe games for health. This research aims to contribute to the field of serious games for healthcare, specifically for visual acuity-related conditions, and provide insights into the process of co-designing games with healthcare professionals. These studies showed promising results for the game's use and some surprising findings about how adding multimodal feedback, such as scent, can augment the experience.

I dedicate this thesis to my late aunt Amita Jhangiani and my family for their undying love and commitment to my education and for allowing me to pursue my dreams. I am forever grateful to them for everything they've provided me materially, emotionally, and spiritually.

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Chapter 1

Towards a Gaze-Based Immersive Virtual Reality Game for Improving Visual Acuity with Amblyopia

1.1 Summary

Amblyopia is the most common neurological eye disorder worldwide, decreasing vision in approximately 1-5% of the global population. To reduce this loss of visual acuity, occlusion therapy is often beneficial for people with Amblyopia, yet this conventional rehabilitation method often suffers from low compliance and adherence rates due to its repetitive nature. Immersive Virtual Reality (iVR) applied to occlusion therapy games has a unique potential to engage players and stimulate their visual acuity. Advances in modern untethered Head-Mounted Display (HMD) systems that increase the accessibility of iVR open up new opportunities for more significant serious games in-

terventions with Amblyopia. To this end, this paper investigates Project Star Catcher, a novel serious iVR HMD exergame refactored as a short 3-minute gaze-based color-matching intervention, and examined the game's effects on the vision of adults with Amblyopia. We present a pilot study [N=51 adults with Amblyopia] that measures changes in LogMAR visual acuity between the serious game (moving a drone to catch shooting stars) vs placebo (moving a drone in an empty starry sky) and younger adults (under 39 years old) vs older adults (39+ years old) from a mean age split comparison between users. Our results suggest that 3-minutes of serious iVR gameplay with experiences such as Project Star Catcher can significantly improve near distance visual acuity by over a mean of 6.2 letters when compared to placebo. We also found that older adults improve their near-distance visual acuity seven times greater than younger adults from gameplay. This paper concludes with discussion and considerations on utilizing iVR HMD serious games for visual acuity and Amblyopia.

1.2 Introduction

Amblyopia or lazy eye affects 1- 5% of the world population and is the leading cause of decreased vision among children [1, 11, 28, 30, 48]. Amblyopia is thought to occur because of an imbalance in visual stimulation between the left and right sides of the visual pathway. Because of this imbalance in visual stimulation, the brain prefers to use only the "stronger" eye when processing visual information. Vision in the "lazy" eye weakens over time, resulting in permanent blurry vision if not treated early in childhood. Untreated Amblyopia may lead to mild to moderate visual disturbances in adulthood. These amblyopic adults may have difficulty with stereopsis and fine motor skills as a result of reduced visual acuity [60]. Depending on the severity of Amblyopia, people may be excluded from career choices because they may not meet minimum visual standards and are excluded from jobs like law enforcement, aviation, military, or commercial driving thresholds for fear of safety and lack of depth perception [67].

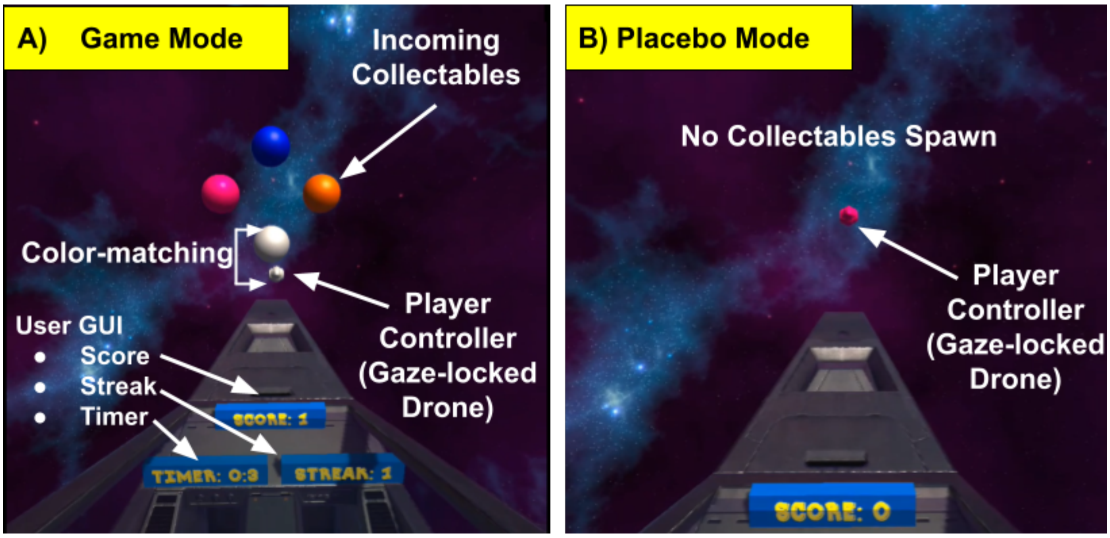

Figure 1.1: Project Star Catcher, a serious iVR exergame refactored for visual acuity through gaze-based color matching, is explored in this study through 51 adults with Amblyopia. A demo video of the game is available at `https://youtu.be/aLIjYMY6V0Q`

Additionally, people with untreated Amblyopia have double the risk of bilateral blindness at around 18% compared to 10% in non-amblyopes leaving some unable to work at all [67]. Lastly, severe Amblyopia can leave the individual with only one eye with usable vision; any changes in vision in the remaining healthy eye can leave an individual visually disabled in a sighted world. Vision loss in the healthy eye can leave an individual visually disabled and unable to work.

Conventional Amblyopia therapy often includes occlusion therapy of the "good" eye, eyeglass correction, and atropine eye drops [11]. However, the level of compliance with patching in children is challenging, noted to be approximately 50% or less. It has been taught that greater than 100-200 hours of occlusive therapy over several years is needed to improve one line versus two lines of visual acuity on the LogMAR eye chart, respectively. The adherence rate drops over time with these children, and research has shown that inconsistent patching significantly reduces improvements in visual acuity [41]. Up to one-third of children who use patching fails to reach their full potential in reading visual acuity and reading ability [9, 31]. Noncompliance is a severe issue with severe consequences that severely affect a person's quality of life. Because neuroplasticity is enhanced during the critical period of adolescence, Amblyopia is much more resistant to treatment in adults, making early intervention essential for everyday life.

Telehealth services have seen explosive growth since the COVID-19 pandemic began, resulting in expanded access to healthcare services, reduced strain on healthcare facilities, and reduced disease exposure for workers and patients [13, 18, 37]. The application of eye care services via telehealth has the potential to provide the same high level of treatment as an in-person eye doctor [2]. Telehealth expansion has resulted in increased access to healthcare, improved treatment for chronic conditions, and transfer of care from hospitals to home [14]. As a result, an acceleration of digital health interventions have also been on the rise, even with smartphone applications for Amblyopia [63]. Virtual reality (VR) is an emerging frontier in providing a new digital health medium for a variety of telehealth areas, including medical therapy, neuropsychology, physical rehabilitation, and more [15,20,54]. Virtual environments (VE) are computer-generated 3D worlds that allow for full immersion of human sensorimotor channels into the VE [5]. The immersion of virtual reality coupled with the high level of control that researchers have over these virtual environments makes VR a highly effective and flexible tool with great potential for treating several different medical conditions without meeting with medical professionals. Combined with serious games, these VR applications can yield a plethora of data from the player's interaction in the VE which can be integrated to predict user outcomes from a variety of physical to affective measures [19,23,51,52] Consequently, the ability to control stimuli with incredible precision and detail and measure precise responses provides an advantageous opportunity when treating conditions such as Amblyopia in VR. A review on the potential applications of VR for children with Amblyopia by Coco Martin et al. discusses the methodological framework for developing serious games for Amblyopia [12]. The four most important points are repetition, sensory feedback, individual motivation, and customization.

1.3 Related Works

Many studies have explored digital interventions for visual acuity in the past. For example, Hurd et al. [33] demonstrated an increase in the visual acuity of adult participants after 45 minutes of monocular blurring in the strong eye coupled with an accessible VR game meant to strengthen the amblyopic eye. The authors examined 9 participants in VR, physically blurred the stronger eye with a Bangerter foil, and had participants play two different games. After three sessions in VR, participants' average long-distance acuity and average depth perception were higher than before they played the game. The study demonstrates VR as a viable alternative to traditional occlusion therapy. Hurd et al. [32] research calls for the implementation of physical activity in future works, which we have decided to implement via head movement and gaze-based scoring mechanics.

To share another example of work in this domain, research by Eastgate et al. [16] used a modified virtual reality technology to treat children. They used an Interactive Binocular Treatment (I-BiT) system to treat seven patients who had not been responsive to traditional occlusion therapy or had not experienced therapy for their Amblyopia. The I-BiT system paired a binocular display, joypad, and a control screen for clinicians to adapt the game for participants as they played. The authors treated patients for an average of 4.4 hours by streaming video clips and having them play interactive games on the binocular display for 1 - 2 sessions a week for 20 minutes each session. Instead of occlusion therapy, however, stimuli to the amblyopic eye were provided to central vision. In contrast, stimuli to the normal eye were provided in peripheral vision. The results were overall improvement in LogMAR visual acuity of 13 letters. Researchers noted improvement after just an hour of therapy exposure. In a 22 month follow up, 2 participants' vision remained stable, 2 participants' vision increased after atropine use, and 1 participant's visual acuity decreased but not to pre-exposure levels. Similar to Hurd's results with adults, this work suggests that VR interventions can positively respond to patients with Amblyopia by increasing their visual acuity after minimal exposure to therapy and even after a 22-month follow-up. In reflecting on these studies, our game prototype explores adaptation. As players progress through the game, it automatically adjusts the difficulty level to match the player's ability (based on a score-streak of collectible objects). We also utilize an Oculus Quest 2 iVR HMD. The recently released system is much more portable and affordable than the I-Bit system used in this past study. Moreover, Eastgate stressed that children needed constant motivation to play the game. We have considered this by implementing a scoring system that provides positive feedback and making the HUD in a way that isn't a distraction from the game, keeping in mind that children with ADHD may have a higher incidence of Amblyopia [59]. Novelties in our design here include increased portability of the system, more participants, a placebo, a more immersive experience, participants of a diverse age group, increased accessibility, and the implementation of physical movement. We use LogMAR tests as well to check the efficacy of our system.

In a different usage, Rabovsky et al. [53] conducted a study where 20 patients were exposed to binocular treatment in VR. The author's protocol examined 11 participants received eight weeks of treatment and 9 participants that received four weeks of sham treatment followed by four weeks of the same binocular treatment. Sessions lasted a total of 1 hour a day each day. An iPhone 6 loaded with therapeutic software and the Zeiss VR One Plus were used to deliver visual input to each eye individually. Treatment consisted of streaming TV shows, movies, and cartoons to each eye. Contrast reduction, monocular flickering, alternate binocular flickering, and central visual pathway stimulation were all used in the therapeutic software to stimulate the amblyopic eye. Researchers found no statistically significant improvement in the amblyopic eye's visual acuity. Still, they saw a minute improvement in participants' mean log stereo acuity. The study demonstrated that the effectiveness of binocular treatment might not be as strong as dichoptic treatment. The dichoptic treatment utilizes continuous blurring of the stronger eye as demonstrated by Hurd et al. [33] while binocular treatment stimulates both eyes using different methods. Our research design uses video game training inspired by the improving visual acuity in Hurd's experiment compared to Rabovsky's use of binocular treatment. The Oculus Quest 2 utilized in our study also offers a much more immersive experience than the iPhone and Zeiss system used here. This research design also did not implement much attentional capture as used by the previous studies, which made the process much more interactive for children. Again, we plan on gamifying the therapeutic intervention to ensure participants focus their attentional resources on the stimuli and are constantly engaged.

Commercial systems like Wow Vision Therapy are being used to treat Amblyopia. Still, their system does not have a placebo arm [61]. Our research design uses both placebo and control along with untethered HMDs. Previous works that used HMDs [69] noted improvements for patients who had Amblyopia but called for the inclusion of a placebo or control group in future studies. Our study design includes a placebo where participants stand in the spaceship for two minutes and do nothing to counterbalance the play condition. They also need constant oversight from medical professionals, decreasing accessibility.

Past works have focused on gamifying treatment for Amblyopia, but we are also emphasizing accessibility features of the game. When constructing the VE, participants' mobility and ability to attend to stimuli were also considered. Participants who have attention deficit disorder and Amblyopia were considered when making design choices for the VE. Distractions were minimized by keeping the design of the spaceship simple with only essential information provided by the HUD, less distracting colors were used, and different difficulties were available to allow more accessibility for patients. To our knowledge, no other studies or games have made such consideration or have emphasized making their system as accessible as possible. Another consideration we made was the limited neck mobility of older adults who often have mobility issues. Due to the nature of our team and its focus on accessibility, we were able to adjust the game as we constructed it.

1.4 Research Goals and Contribution

Our goal is to create a virtual reality game that will engage users (of all ages) with Amblyopia or lazy eye, to improve the vision of their amblyopic eye. It is now thought that Amblyopia can be treated in adults as well as in children [3, 27, 36]. A critical focus of this study is accessibility, easy comprehension, and ease of use. For adult patients with decreased vision from long-term Amblyopia, the games were created with their needs (e.g., poor mobility of their neck muscles, poor hand mobility, and reduced "hand-eye coordination" eye reflexes).

Our specific aims of the study are as follows:

- Aim 1: Using a 3-minute game, can we see visual acuity improvement in the Amblyopic eye?
- Aim 2: Is there a placebo effect: does wearing the virtual reality goggles without the game intervention improve vision?
- Aim 3: Is the game feasible for adults to utilize in an eye MD office with limited time and resources?

To the best of our knowledge, this article prevents one of the first studies to utilize iVR serious gaming for one-eye treatment of Amblyopia rather than dichoptic training – leading to gameplay sessions of just 3-minutes towards improving visual acuity.

1.5 System Design

Amblyopia treatments are often most effective when the patient is younger; traditional forms of Amblyopia therapy are not very engaging or designed for adherence. With this in mind, we created a system that allows for training your visual acuity in VR. We made the Project Star Catcher: Visual Acuity Refactor (PSCR), a novel VR game iteration. PSCR was developed using Unity 2020.3.3f1 in conjunction with an Oculus Quest to create it for use on different immersive virtual reality devices and HMDs. This game is an extension of previous works done by Elor et al [17, 21, 22, 24]. In previous

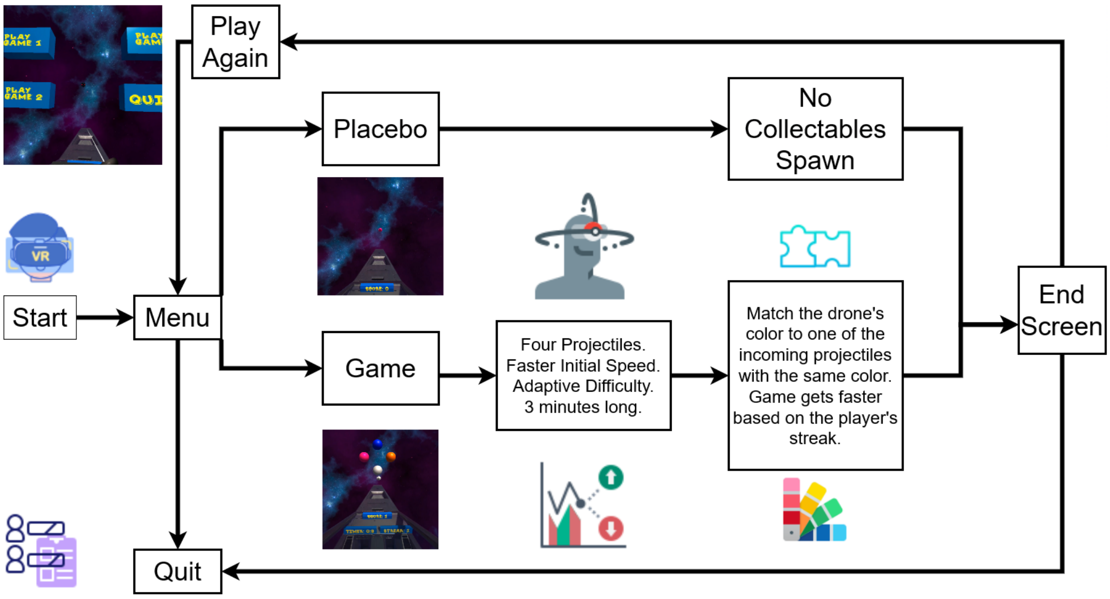

Figure 1.2: Game Loop Flowchart

iterations of Project Star Catcher, the main focus was aiding the physical rehabilitation of people who have suffered a stroke. The gameplay involved catching stars in a VR game environment using a controller to help upper limb rehabilitation. At the same time, the current iteration focuses on using head movements to train the user's visual acuity. The Unity Game Engine was chosen for this project as it allows for easy development of cross-platform games that are usable on various operating systems like Windows, Mac, Linux, Android, and iOS. Unity allows for creating 3D games that can be seamlessly integrated with iVR headsets. The game was designed with accessibility in mind. The entire game is playable by using head movement. The player controls a drone object that is rigged to the Unity XR Rig and moves based on the device's movements. The drone is set at a distance of about 20 meters from the player. The drone allows the user to control the UI and play the game. The gameplay itself is relatively simple, and the player has four spherical objects coming towards them from a distance of about 100 meters away; the objects are color-coded, with different colors chosen to ensure there is a sufficient amount of contrast between the colors, making them easy to distinguish, the player then needs to match the color of the drone to the objects.

Keeping in mind that the game was designed for accessibility and improving a visual impairment, we took steps to make it easier for the player to navigate it. The game announces when it is being started; the player also gets audio feedback that indicates if they matched the color correctly and a different sound if they matched it incorrectly. The game features large UI elements that are easily visible. We ensured that UI text and their backgrounds contrasted each other to ensure they were readable. The objects also spawn at a varying rate and increase their speed to keep up with the player's performance, making its difficulty dynamic and adaptive to the player's performance. The speed initially set at 2000 and is multiplied by 1.01 every time an object is spawned and then adjusted using a difficulty rate determined by taking the player's streak, multiplying it by 40, and then adding it to the speed. This speeds up the projectiles incrementally as the game goes on and takes the player's proficiency into account by using their streak to adjust the speed along with this slow incremental change. If the player selects the wrong ball, the streak is reset to 0, which slows down the balls.

This allows the game to remain challenging and engaging while also making sure it's playable at any skill level. The game features two modes, the normal game mode, and a placebo. The standard game mode is about three minutes long. We made gameplay sessions three minutes long to ensure the game remained engaging. The placebo has the player sit in the spaceship for one minute while a timer indicates how much time has passed. The game ends when the duration of the game mode is completed and either returns the player to the main menu or allows them to quit the game. The game is playable off the Oculus Quest. It allows the player to play the game wholly untethered, making it easy to move around while playing the game. The game runs as a standalone application for the Oculus Quest and thus eliminates the need for an expensive desktop rig, as is the case with many VR devices; this makes the game highly accessible.

1.6 User Study

An Oculus Quest 2 Headset, ASIN of Oculus Quest: B099VMT8VZ (Meta, Menlo Park CA), was used to test the volunteers. Project Star Catcher was successfully deployed to this headset via the Oculus App Lab. The headset was given to a local Ophthalmology clinic in San Jose, California. Informed consent was obtained under IRB guidelines from UC Santa Cruz. The Oculus headset was calibrated, and a stationary boundary was established. This headset was used in one specified room with the same standard lighting. Visual Acuity for the participants was tested with LogMAR (Precision Vision, Inc., Woodstock IL) distance [25]. One eye was tested each time. For the placebo, similar visual acuity testing was performed. Results were recorded in a Google Sheets spreadsheet with no patient identifying information due to HIPAA regulations

Figure 1.3: User wearing an Oculus Quest 2

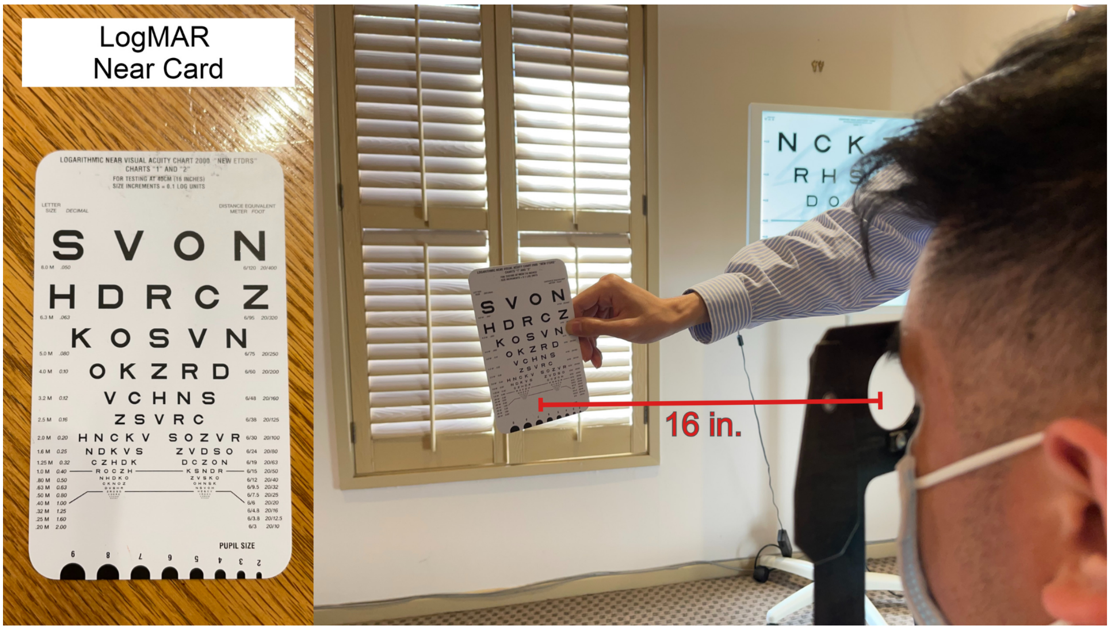

Figure 1.4: LogMAR Near Vision Test

and IRB protocol. The records were secured with multi-factor authentication.

1.6.1 Participants

Volunteers for the study are recruited through and tested at a local Ophthalmology clinic located in San Jose, California, between January to March of 2022 with the following:

- **Inclusion Criteria-** Adults with Amblyopia, participants between ages between 18-80 years old, English speakers, able to comprehend informed consent.

- **Exclusion Criteria-** Inability to operate the Oculus Headset due to neck surgeries, neck injuries, and other head movement limitations.

1.6.2 Protocol

Participants begin by reviewing and signing an informed consent document. Afterward, participants are brought into the clinician's office for user testing. One clinician is always present to record the LogMar visual acuity, then administer the testing protocol with the Oculus Quest iVR HMD system. The protocol is as follows:

1. Pre-Visual Acuity LogMAR: Visual acuity is measured through a LogMAR chart (shown in Figure 1.5 on the Amblyopic eye for both distance and near vision.

2. VR Intervention: The clinician verbally introduces the Oculus Quest iVR HMD to each participant. After answering any questions, the right eye is tested if the patient wishes that eye to be tested. The left eye is physically patched with two pads of 2-inch x 2-inch sterile gauze and taped from the nasal area of the eyebrow to zygoma. Then, the HMD is placed on the head of the participant, as shown in Figure 1.3 for either the gameplay or placebo Project Star Catcher modes:

    - Game 1 - Gameplay: The user enters a virtual cockpit of a virtual spaceship with a starry cosmic background. A virtual drone is placed at the center of the user's gaze and moves with slight head rotation. Projectile collectibles are spawned with different colors, varying from 2-4 collectibles depending on the user's scorestreak. The drone changes color to indicate to the user which collectible they must collide with – a successful collection is complete when the drone collides with a sphere of the matching color, leading to an increase in score-streak. The VR session automatically ends after 3 minutes.

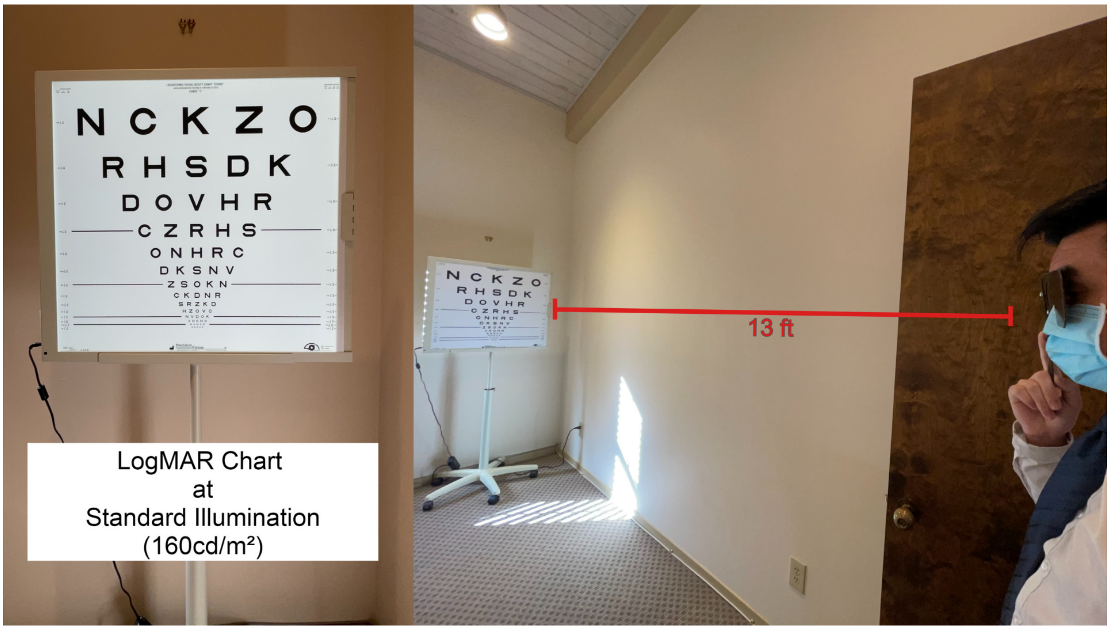

Figure 1.5: Distance Vision Test

- Game 2 - Placebo: The user enters a cockpit of a virtual spaceship with a starry cosmic background. There are no collectibles spawned. The VR session automatically ends after 3 minutes. If the participant wants to test the other eye, we would repeat the above procedure.

3. Post-Visual Acuity LogMAR: Visual acuity is measured through a LogMAR chart on the affected eye with Amblyopia for both distance and near vision, as shown in Figure 1.4.

On average, user testing sessions took a total of 9 minutes from the instructions to the end of the game and the removal of the headset.

1.7 Results

A total of 51 participants volunteered for the study and successfully completed the user testing protocol – providing ample data to explore the effects of Project Star Catcher on visual acuity. We found that visual acuity on the LogMAR chart increased by an average of 6.2 letters for 19/30 improved users. For each of the dependent measures (e.g., LogMAR distance and near visual acuity pre, post, and change), we performed a one-way repeated measures ANOVA with the display condition as the independent variable (2 levels: game vs. placebo and game players from older adults of 39+ vs. younger adults of 39- based on an age mean split). Statistic tests and measure descriptives were analyzed through IBM SPSS Statistics v27. We report upon the results that were found to be statistically significant ($p < .05$), with total measures shown in Table 1.1. Interestingly, no significant differences were found from LogMAR distance comparisons for either level.

1.7.1 Game vs. Placebo Effects on Visual Acuity

To understand the influence of the iVR game on visual acuity, clinicians collected LogMAR before and after the VR headset was placed on the user. Participants were split into the gameplay (catching color-coded projectiles with gaze for 3 minutes [N=29]) and placebo (passively viewing the starry sky with no projectiles [N=21]). Mean ages between the groups were as follows: Game (M=39.52 years/old, SE=3.706), Placebo (M=43.89, SE=4.653), and Total (M=41.17, SE=2.886). Those who played the game were found to result in significantly more LogMAR near visual acuity change (Post-Pre, p=0.040, F=4.470, partial η^2 = 0.089) when compared to those who received the placebo (passively viewing cosmic environment with HMD), with full differences shown in Table 1.1. We did not see any significant differences in LogMAR visual distance.

1.7.2 Older Adults (39+) vs. Younger Adults (39-) Gameplay Effects on Visual Acuity

Excluding the placebo group, we investigated the effects of the game to understand differences in age groups as visual acuity declines with aging. Through performing a mean split, participants were separated into age groups of 39+ (39 years or older [N=11]) and 39- (38 years or younger [N=19]) based on the total mean of ages from the participants. Mean ages between the groups were as follows: Older Adults in the 39+ group (M=64.82 years/old, SE=2.169), Younger Adults in the 39- group (M=24.89, SE=0.976), Total (M=39.53, SE=3.706). Older adults (those who were 39 years or older) were found to result in significantly more LogMAR near visual acuity change (Post-Pre, p=0.039, F=4.617, partial η^2 = 0.015) when compared to younger adults (those 38 and under), as highlighted in Table 1.1. Once again, we did not see any significant differences in LogMAR visual distance.

1.8 Discussion

Aims 1 & 2. Our results show that after a single three minute session of the VR game vs. placebo yielded significant improvements near vision visual acuity. This

Grouping	Measure	Game$^{\lambda}$	Placebo$^{\lambda}$	Total$^{\lambda}$
Distance Vision[a]	LogMAR (Post-Pre)	**-4.90 (2.026)**	-2.14 (1.154)	-4.228 (1.407)
Near Vision[b]	**LogMAR (Post-Pre)***	**6.55 (2.568)**	-1.46 (1.904)	3.94 (1.915)
Grouping	**Measure**	**Younger Adults 39-$^{\lambda}$**	**Older Adults 39+$^{\lambda}$**	**Total$^{\lambda}$**
Distance Vision[a]	LogMAR (Post-Pre)	**-5.84 (1.991)**	-3.23 (3.997)	-4.90 (1.906)
Near Vision[b]	**LogMAR (Post-Pre)***	2.53 (1.495)	**12.54 (5.622)**	6.20 (2.383)

Table 1.1: Comparisons between visual acuity gameplay results between Game vs. Placebo and Older Adults (39+ years) vs. Younger Adults (38 years or younger) as well as Total (combined results). *Note:* $^{\lambda}$ Mean (SE); * $p < 0.05$ (significant difference by via one-way ANOVA); Greater improvement between groups in **bold**. Scales are reported by 20/N: [a] Negative N indicates logMAR visual acuity improvements for distance vision, [b] Positive N indicates logMAR visual acuity improvements for near vision.

is promising for a number of reasons: the lack of a significant placebo effect means that the system allows for the player to train their eyesight and could thus be modified to improve its efficacy for various measures relating to visual acuity. Moreover, the near visual acuity improvement in the older aged participants in our study, may have been correlated to their lower visual acuity pre-test due to age, and thus they had more potential to improve. The majority of the younger participants, in our study, had 20/20 to 20/25 visual acuity thus leaving only a few letters of possible improvement. In the future, we hope to get larger sample sizes of different age groups and visual acuity. For children, there is greater potential for improvement because of brain plasticity and the often low compliance rates of occulusion therapy that may be address through VR game engagement. Additionally, the PSCR game has collectables spawning from a relatively near focal point triggering accommodation and near vision. This may explain why near vision is affected more than distance vision in the results. It is promising to see that immersive technology can be an avenue for treating multiple conditions in patients, while our system was tested primarily on adults (ages 18 and over), the intention behind creating a game is to also make treating Amblyopia fun for children. Recent research has shown improvement in vision with adult Amblyopia with dichoptic training and video games [3, 27, 36].

Aim 3. The system design recommendations we used to ensure that the game is made accessible and easy to play worked as intended since most players seemed quite pleased with the game and did not have complaints. The use of large UI elements with contrasting colors made it easy for players to read the text on screen and keep track of their score, streak and the amount of time they were in the game. Using head movements to control the game allowed for increased accessibility, players were able to play the entire game without the use of controllers making the game accessible and easy to play for people with all levels of motor control as described in the inclusion criteria. Clinicians also expressed that the Oculus Quest iVR HMD and the controllers were compact and easy to use. The actual equipment does not take up much space. The time from beginning of the test to the removal of the headset, is 9 minutes. It has much to offer to the patient who has Amblyopia. The actual three minute VR Game is painless, faster than occlusion therapy. While this study looks at the immediate visual results, in the future, we hope to study repeated testing and follow up at 3 months and 6 months. This test has been used on patients aged 65 and older. They were able to perform the tests. There were no complaints among the patients about the heaviness of the headset.

1.8.1 Recommendations for Game Design

While we did not perform dichoptic training with our VR game, we intentionally tested one eye at a time and physically patched the other eye. We felt that this would take the place of occlusion therapy which obstructs the good eye. This monocular way of using VR strengthens each eye or the eye that is amblyopic. Lastly, focusing on one eye at a time would make the test more time efficient. Most other studies have focused on dichoptic training for the past 20 years for adults and children using lengthy games of at least one hour per session [39, 64, 65]. Future serious iVR games for visual acuity may want to incorporate these shortened modules to test for similar efficacy. With new knowledge about brain plasticity and retinal ganglion plasticity, our study has embodied those theories in the creation of this VR game module.

In the future, games such as PSCR may benefit from running follow up studies in evaluating dichoptic protocol versus single eye protocol. For the dichoptic training, we can present one eye with the placebo, non moving spaceship without spawning collectables. Also for dichoptic training, we can digitally blur the image. The use of games to treat Amblyopia seems promising when the game is designed correctly. There are certain recommendations to ensure that games designed for patients with conditions that affect their visual acuity. The games should use large and legible texts with simple fonts to ensure readability, have bright colors that contrast against each other, ensure that the game is easy to play and can be played in a short amount of time to ensure player engagement and have some sort of auditory cues to help guide the player.

1.8.2 Limitations and Future Work

Due to the COVID-19 pandemic, our ability to effectively develop this system in an iterative manner was severely limited, we had difficulties deploying the system and conducting user testing since we would find different bugs and have to fix them over the course of a week making it hard to conduct user tests frequently and make the necessary changes to our system. Despite that, we have managed to iterate this game and create a build that is effective at improving one's eyesight. We are also limited by the capabilities of the Oculus Quest, with newer HMD's that support eye tracking, we could create a system that is significantly more effective at training and improving a patient's eyesight. Given this pilot study we plan to iterate on this system and create more accessibility options in future updates, we would like to add eye tracking as a means to play the game since it would be interesting to see the different levels of efficacy between different means of gameplay.

Future research can expand upon this work by comparing the efficacy of different gameplay methods, like eye tracking, head movement and controllers against each other and compare the efficacy. We hope to continue testing PSVR against a placebo to gather more data and gain more insight into the effectiveness of our system, so that we can make improvements to it in future versions. Gameplay could also be improved upon by adding a sense of novelty through different gameplay mechanics such as adding non linear paths, different kinds of projectiles, adding power ups, and creating different game modes. If this system proves to be an effective means to improve visual acuity, the development of a campaign mode of sorts to improve long term adherence would be something that should be considered.

1.9 Conclusion

To our knowledge, this is the first untethered iVR HMD serious game for visual acuity that was found to improve visual acuity in less than 3 minutes per eye in a patient setting. Our findings suggest that gaze-based iVR games have potential towards stimulating the visual pathways for vision improvement in adults with Amblyopia. We designed a unique gameplay experience where participants discriminate between incoming spheres to perform color-matching with gaze movement through vision in their amblyopic eye while their healthy eye is physically blurred. The use of physical movement coupled with visual discrimination task in VR seems to be an effective alternative to traditional occlusion therapy which often has poor compliance rates and requires hundreds of hours to see improvement. This is particularly exciting as participants who experienced vision improvement improved by average of 6.2 letters (19/30 improved) immediately in our control group, while the placebo group saw no improvement. Future work should explore the long-term effects of gaze-based color-matching iVR games for adults with Amploypia.

Furthermore, by incorporating accessibility features in the game, we hope to provide accessible experiences for visual acuity training to many different groups, such as young children and older adults. Our hope is that this system design will inform future designs and developments in Amblyopic treatment and benefit future virtual experiences for visual acuity.

Chapter 2

Olfaction-Enhanced Virtual Reality Game for Visual Acuity in Adults with Amblyopia

2.1 Summary

Amblyopia (lazy eye) is one of the most common neurological eye conditions in the world, where the brain ignores the vision of the weaker eye. It is usually treated before age 10 with an eye patch to cover the strong eye, forcing the brain to use the weaker eye. The use of serious games in virtual reality (VR) has shown promising results in therapy for adults with amblyopia, which was often considered significantly harder to treat. This paper reports using a VR game developed in collaboration with an Ophthalmologist to improve visual acuity in adults with amblyopia. We hypothesize that adding olfactory stimulus makes the game more effective by increasing presence in

the virtual environment and acting as a reward to help maintain the player's attention and improve their performance on the training task. 105 participants played the game with and without the use of olfactory feedback. We found that while participants' visual acuity didn't increase by a clinically significant margin, the game scores were significantly higher in the smell condition.

2.2 Introduction

Amblyopia is one of the most common neurological conditions in the world, affecting approximately three percent of the world's population [29, 42, 68]. This condition is marked by reduced visual acuity in one eye (called the weaker eye) [7]. The underlying causes are undiscovered anisometropia (unequal refractive error between the two eyes), visual deprivation such as congenital or juvenile cataracts, or strabismus with anisometropia. Treatment can be as simple as a pair of glasses. Treatment may mean occlusion therapy of the stronger eye, ensuring that the "weaker" or amblyopic eye gets visual stimulation. The critical period of visual development occurs in the first decade of life, however recent studies have found that this neuroplasticity might extend into adulthood [62].

It was previously thought that amblyopia could only be treated during childhood, but recent studies suggest that it is treatable in adulthood through interventions that stimulate the weaker eye [7, 62]. We should note, however, that amblyopia treatment in adults is a long-term commitment that can last years. There have been multiple attempts to create games or virtual reality games to aid in the treatment of this condition [4, 6, 32, 34], due to the ability of virtual reality to leverage a person's innate neuroplasticity [38,56,57], which allows for the strengthening of neural pathways to the weaker eye, which can aid in the rehabilitation of a person's visual acuity.

One virtual reality game for adult amblyopia was developed using a user-centered approach with a team of licensed ophthalmology clinicians [35]. The game was tested with 51 patients, and after one session of 3-minute gameplay, the clinicians noticed that the participants experienced a 6.2 letter score improvement in their near vision and no significant improvements in distant vision.

Our study aims to investigate whether enhancing a virtual reality game with olfactory feedback can improve distance vision in adults with amblyopia and make them enjoy the therapy more than traditional ways of treating it. Along the way, we hope to extract design lessons for multimodal virtual reality games for visual rehabilitation and healthcare purposes.

2.3 Related Works

2.3.1 Serious Games for Health and Rehabilitation

The field of serious games is constantly evolving, with games designed to help patients regain their abilities after a traumatic event or improve their medical conditions through interactive training sessions that are made enjoyable through various game mechanics and gameplay. In recent years, the use of serious games, specifically games that employ virtual reality, has become more prominent in different avenues of health and rehabilitation practices. One of the main reasons VR can be so beneficial in these cases is its immersive ability, leading to better ecological validity in these digital interventions [58]. There have been multiple serious games designed for physical therapy by Elor et al. [17, 19, 21–24] that use a variety of tasks in a virtual reality environment for upper limb rehabilitation. Aside from their use in physical therapy, a variety of VR-based serious games for visual acuity [32, 35, 36, 53] have also been developed in recent years and show promising results for amblyopia. This can be attributed to the unique nature of VR, which is a controlled and immersive environment where specific tasks that train visual acuity can be performed.

2.3.2 Olfaction Technology

The use of olfaction in games and other computer applications has become popular recently, with some commercially and publicly available olfactory dispersion technology [40, 44, 45]. There have also been numerous attempts to use olfactory sensations as inputs and outputs, from using smells as a feedback mechanism for notifications to using smells as a part of the game mechanics [8, 44, 66]. Olfaction also seems to play a role in increasing presence in VR [43, 45], a key in making health interventions more palatable. Using olfactory memory training has also improved visual memory [46, 47]. However, another study shows that increased cognitive load might lead to an inability to notice smells for a short period of time [26].

2.3.3 Olfactory Feedback

Olfactory feedback has been shown to have various beneficial cognitive effects in tasks involving information recall, feature identification, and location detection [49]. Olfactory stimuli also positively affect relaxation and the ability to make virtual experiences feel more pleasant in the context of serious games for therapeutic purposes [10,50]. However, olfaction is a highly individualized experience, and the lack of adequate technology to create olfactory experiences has posed challenges for developers seeking to incorporate olfaction in their games [10].

The use of smell in serious games remains relatively unexplored, with some work being done on using smell to aid in treating post-traumatic stress disorder (PTSD) and promoting relaxation in virtual environments [50, 55]. Niedenthal et al. created a graspable olfactory display that allows users to smell objects in their virtual environment. Scents are created from a mixture of four distinct aromas and are stored and released from the controllers. This specific location promotes realistic scent intensities, emulating the sensation of smelling scents from a close location and further stimulating olfactory responses. The virtual environment allows various interactions with odor-releasing objects in various contexts, from educational to therapeutic. A case study of a "wine-cellar" game—in which participants were tasked with identifying different wine fragrances was found to be an intuitive and effective tool for smell training [44].

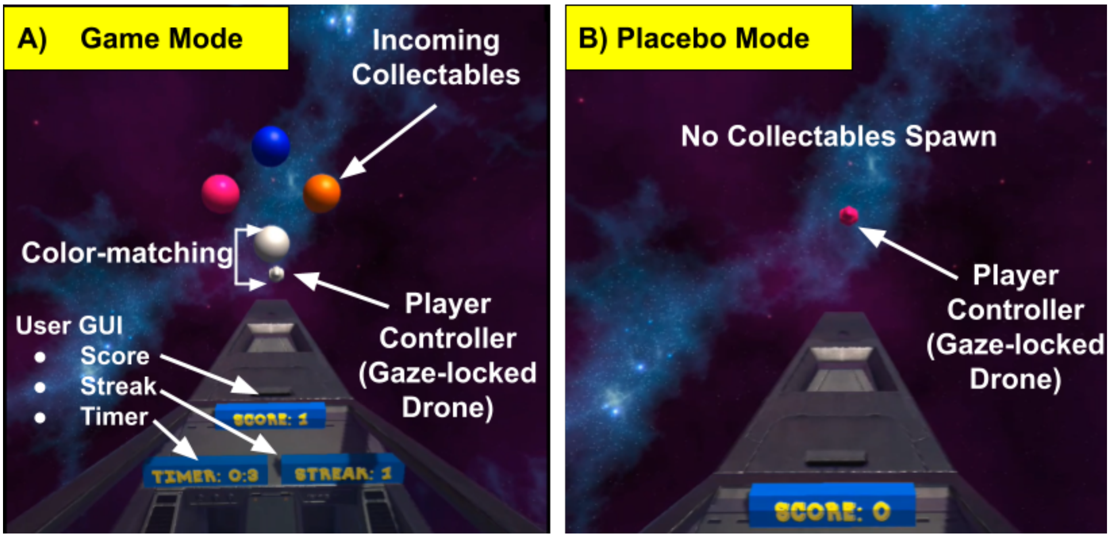

Figure 2.1: Screenshot of the Game, with labels to explain the different components

2.4 System Design

For this study, we designed a VR game using the Unity 3D game engine and played using an Oculus Quest headset, in which the player's head movement controls a drone within a virtual space environment. The space setting features a dark skybox to create a strong contrast between the brightly colored projectiles and the dark environment, promoting enhanced visual focus. Each gameplay session was approximately 3 minutes, with four spherical projectiles of different colors moving towards the player. The player's objective is to match the drone's color to that of the incoming projectile, essentially a visual training task to enhance color discrimination and visual attention skills.

The first design of the game did not contain any olfactory stimuli. The game featured a playable game mode, as seen in Fig. 2.1, where the player controls a drone while in a spaceship. The player could use their head movements to control the drone. Players score points by correctly matching the drone's color to the projectile's color. The game score increases for maintaining a streak of correct color matches, with the reward size increasing as the winning streak gets longer. If the player fails this color-matching task, the score resets to 1 again. This first version of the game was developed to test that the scoring system worked reliably.

2.4.1 Clinician Feedback and Revised Game

This initial game was given to three clinicians to play. Afterward, we interviewed all of them to get their feedback on the game design. We received various feedback, and two of the most common themes that emerged from the interviews were to shorten the gameplay and include additional modalities beyond visual stimuli.

We implemented the feedback in the revised version of the game by shortening the game sessions to about two minutes. We also added smell and sound as a form of multimodal feedback for participants to accommodate varying levels of accessibility and make system feedback clearer for participants. The olfactory display we used was the OVR ION 2, developed by OVR Technologies. The ION 2 is a wearable smell display that fits under the Oculus Quest headset and disperses a smell through a tiny scent diffuser near the participant's nose.

For the olfactory feedback, we picked citrus since it is a simple, pleasant, and easily recognizable smell, along with adding sound effects when the player matches the colors correctly. We did not add any visual features to the game to avoid making it too

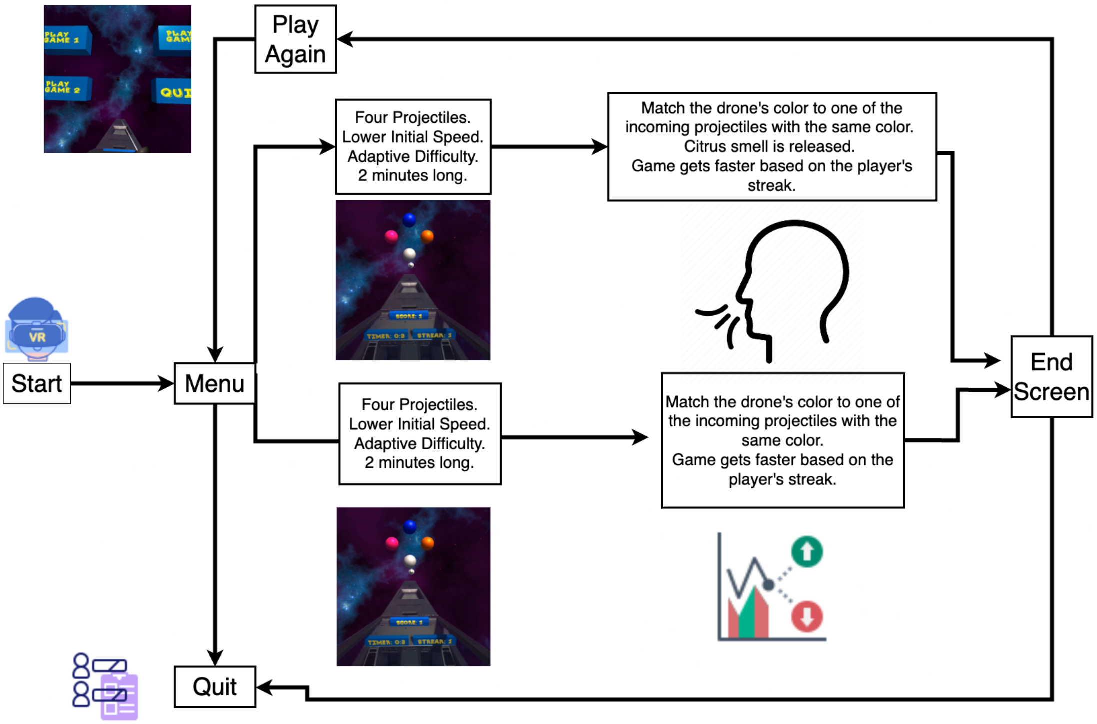

Figure 2.2: Updated Game Loop Flow Chart

cognitively demanding for participants and running the risk of having them experience inattentional smell blindness [26].

2.5 User Study

Participants were recruited to evaluate the game from the office of our collaborating ophthalmologist. Testing was conducted with the Oculus Quest 2 Headset, ASIN of the Oculus Quest: B099VMT8VZ (Meta, Menlo Park CA), and the OVR Technology ION 2 smell mask. A consent form approved by our Institutional Review Board (IRB) was presented to each participant before the study began. To limit confounding factors from affecting our outcome, each trial was run in the same room with minimal to no changes to the room during the user study sessions. Some participants were requested to complete a survey after playing the game to better understand their perspectives.

2.5.1 Participants

Volunteers performed the user studies in San Jose, California, at an Ophthalmology clinic. Those brought to the clinic satisfied the following criteria:

- **Inclusion Criteria**- Adults (18-80 years old) that speak English and comprehend informed consent.
- **Exclusion Criteria**- Adults who cannot operate the Oculus Headset. This could be due to neck surgeries, injury, or limitation of the movement of the head/ neck.

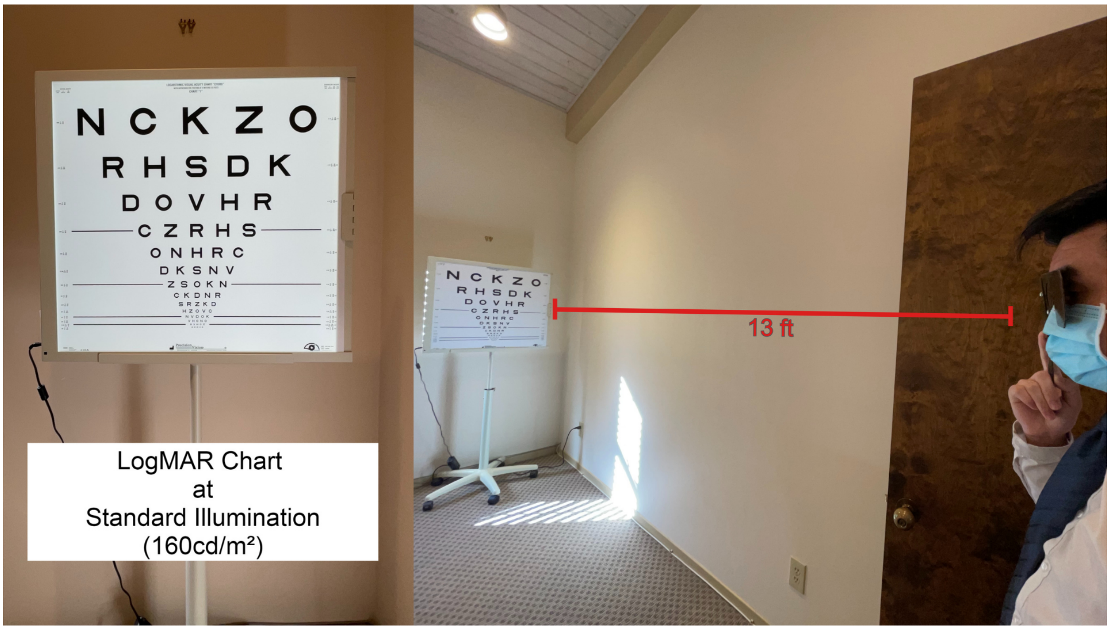

Figure 2.3: Distance Vision being measured using LogMAR

2.5.2 Measures

Participants had their distant vision measured using a LogMAR chart (as seen in Fig. 2.3) by a clinician, along with completing a short survey asking some basic questions about their experience with the game, whether they would recommend the game to others, etc. The LogMAR scores allowed us to measure changes in visual acuity, while the survey helped us gain some subjective insights into our game.

2.5.3 Protocol

Before participating in the study, the participants were given an informed consent document to review and complete. During testing, one clinician remained present to administer the testing protocol with the Oculus Quest and the OVR Technology ION

2. The clinician also recorded the participants' scores on the LogMAR and the game and their survey responses. The survey was administered by asking the patient simple questions, which the clinician recorded using a Google Form we created specifically for this study.

To summarize, the protocol is as follows:

1. Participants review and sign the informed consent document.

2. Pre-Game LogMAR: The clinician tests the participants' distant vision using a LogMAR chart.

3. VR Intervention: The participant chooses which eye to test, and the other is patched with two pads. These pads are 2-inch x 2-inch sterile gauze covering the eye, from the eyebrow to the zygoma. The participant then puts on the Oculus Quest with the OVR ION 2.

4. The patient is then randomly assigned either the smell or the no smell condition by the clinician present and plays the VR game. In both conditions, the participant is placed in a spaceship's cockpit with a starry cosmic background. A virtual drone is placed at the center of the user's gaze and moves with their head movement. Projectiles are spawned with different colors. These projectiles grow increasingly fast depending on the player's streak.

    - **Smell Condition**: The drone changes color to indicate to the user which collectible they must collide with – a successful collection is complete when the drone collides with a sphere of the matching color, leading to an increase in their streak, a reward sound and a short burst of citrus smell. The game automatically ends after 2 minutes.

- **No Smell Condition**: The drone changes color to indicate to the user which collectible they must collide with – a successful collection is complete when the drone collides with a sphere of the matching color, leading to an increase in their streak, and a reward sound. The game automatically ends after 2 minutes.

5. Post-Game LogMAR: The clinician tests the participants' distant vision again using a LogMAR chart.

6. The participant is asked if they would like to complete an optional survey that asks a couple of questions about the game and their experience playing it.

2.6 Results

The data collected from the original study and this second round of testing brought the total number of eyes tested using either of the game conditions to 105. The data was analyzed using IBM SPSS Statistics v27.

2.6.1 Quantitative Outcomes

There are almost equal numbers of participants in the smell condition (N=54) and the no smell condition (N=51). The smell condition had a mean age of 31.98, and the no smell condition was 35.38. Using a Chi-Square analysis (p=0.032), we found significant differences in the number of participants that experienced changes in their LogMAR scores pre and post-test: specifically, in the smell condition, 44 out of 54 participants showed some (Mean=2.30) improvements in their distant visions after playing the game, while in the no smell condition, only 32 out of 51 show some improvements (Mean=2.63 letter improvement).

We ran a Kruskall-Wallis test on the LogMAR scores and final game scores. There is no significant difference in the pre-post LogMAR scores (p=0.990) between the smell (Mean=2.30 letter improvement) and no smell (Mean=2.63 letter improvement). However, there was a significant difference (p=0.001) in the participants' final game scores between the two conditions, smell (Mean=1140) and no smell (Mean=634).

Through the survey data (N=22), we found that all participants said they would recommend the game to others, and most of the participants (21/22) liked the shape of the projectile and the colors used in the game. Most participants reported that the game's length was just right (18/22), with some participants finding the game too long (3/22), and one participant said it was too short. Since the survey was administered by the clinicians, we could not survey all of the participants since the survey was optional.

2.6.2 Qualitative Outcomes

The interviews with the clincians revealed some useful insights, with one of the major complaints being the weight of the headsets themselves, with one of the clinicians reporting that "sometimes the patients will complain and say this, the headset's too heavy". Another key insight from clinicians was that longitudinal data on this system could be beneficial, stating, "We're doing a one-shot deal. We're doing the intervention, and then we're checking the vision afterward. We don't know if we send the patient home with this and we make them do it four times a day or once a day for a week once a day for a month, come back what that would mean". When asked about the system design and the game itself clinicians reported that "I think that there's nothing like it out there so that the novelty can be inviting to some patients you know that it's new it's different it's not the same old thing, and it's not like you just patching the good eye you know then that we've done for decades," "fun concept for the patients" and "I think it drives attention and focus more. It is such an immersive environment using VR"

Clinicians also provided us with some interesting criticisms, stating that "maybe if you could have at least the menu screen controlled by handheld controllers, I think that makes it easier to control, and it saves us time when administering the test" since participants were likely to trigger menu options on accident when moving their head around. Clinicians also brought up the clunky nature of the headset and some issues with the straps used to adjust the headset, saying, "The straps are kind of one of the biggest issues and the weight of the headset."

From the survey data we collected from participants, we found that most patients enjoyed the game, with many reporting that the game was "fun." An interesting and surprising result was two patients reporting their own perceived changes in visual acuity, with one of the patients stating, "It was very enjoyable, and I feel like it slightly improved my vision for the second test." and another stating, "It was really interesting to see the differences in vision."

2.7 Discussion

The improvements in in-game scores with the smell condition might result from the increased presence the participants might experience from the addition of smell or could be linked to smell being used as a form of positive feedback leading to better player performance. The number of participants who saw a change in their visual acuity in the smell condition vs the no smell condition shows that olfactory feedback might be playing a role in acute improvements to visual acuity.

The qualitative findings show that this game still needs some improvements and give insights into the future design of serious games for healthcare.

2.7.1 Implications for Design

One of the key implications for designing with smell might be keeping gameplay simple to avoid cognitive overload while still making the task engaging for participants. Game sessions should be kept short to make it easier for clinicians and patients alike, and gameplay could be more varied to avoid becoming too repetitive over time. A strong contrast between backgrounds and objects that a player interacts with is a key element of designing for people with varying degrees of visual acuity, along with using other feedback modes like smell and audio to create multi-modal and engaging gameplay experiences.

The use of smell as feedback in games is also interesting. Picking easily recognizable smells and using them as feedback or even as a core part of gameplay could be interesting and have implications for various serious games.

2.7.2 Implications for Future Research

The use of smell in games opens up an interesting avenue for future research and is already promising in various areas of serious games. The scent could be feedback for people with limited visual acuity or other sensory processing issues. Future work could be studied using games like this longitudinally to see if these effects are just acute or can lead to sustained differences with participants.

2.7.3 Limitations

One of the biggest limitations is the form factor of current VR headsets, with many of them being too heavy and can prove to be difficult for people with disabilities or medical issues to use safely. Another key limitation of this study is that it only measures acute differences, and we did not measure near-vision changes. We also used a single smell through a smell mask, which limits the nature of our olfactory feedback, along with being unable to ask participants more detailed questions in the interest of their time and the clinician's time.

We tried to address some of these concerns by ensuring that the game is still accessible, doesn't require advanced motor skills, and uses multiple feedback modalities to ensure participants remain immersed in the gameplay loop. We also tried to keep gameplay short and simple to make it easy for clinicians to administer while collecting additional data on the system's usability.

2.8 Conclusion

In this study, we explored a novel virtual reality game using the existing literature on olfaction and its uses in VR to create a system that might benefit those with amblyopia and other conditions that affect visual acuity. Our system used smell as an additional sensory feedback to study its effects on visual acuity and game performance. We found that while participants LogMAR scores increased, it wasn't by a clinically significant margin, there was significant differences in game scores for the scent feedback condition compared to those in the no smell condition, combined with more participants noticing an acute improvement in visual acuity when scent feedback was present. The main goal of this work was to explore the use of smell in VR games for visual acuity along with scent as a novel form of sensory feedback in games. We hope this work can inform future works to create multi-modal games and other technical systems. The use of smell in VR is becoming more feasible every year, with major technical developments making this area of research even more relevant.

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