

# **Effectiveness of a Gamified Mobile Application in Enhancing Treatment Adherence for Children with Amblyopia: A Explorative Study**

Bo Liu, Yisheng Fan, Meng Xu, Fangyuan Chang, Yue Shi, Zhao Liu

Submitted to: JMIR mHealth and uHealth  
on: May 07, 2024

**Disclaimer:** © The authors. All rights reserved. This is a privileged document currently under peer-review/community review. Authors have provided JMIR Publications with an exclusive license to publish this preprint on its website for review purposes only. While the final peer-reviewed paper may be licensed under a CC BY license on publication, at this stage authors and publisher expressly prohibit redistribution of this draft paper other than for review purposes.

*Table of Contents*

**Original Manuscript..... 5**  
**Supplementary Files..... 29**  
    Figures ..... 30  
        Figure 1..... 31  
        Figure 2..... 32

# Effectiveness of a Gamified Mobile Application in Enhancing Treatment Adherence for Children with Amblyopia: A Explorative Study

Bo Liu<sup>1\*</sup>; Yisheng Fan<sup>1\*</sup>; Meng Xu<sup>1</sup>; Fangyuan Chang<sup>1</sup>; Yue Shi<sup>1</sup>; Zhao Liu<sup>1</sup>

<sup>1</sup>Shanghai Jiaotong University Shanghai CN

\*these authors contributed equally

## Corresponding Author:

Zhao Liu

Shanghai Jiaotong University

Shanghai Jiao Tong University 800 Dongchuan Rd Minhang District, Shanghai 200240 China

Shanghai

CN

## Abstract

**Background:** Amblyopia is the leading cause of visual impairment in children worldwide. The predominant clinical treatment, occlusion therapy, is marred by poor adherence, often attributed to the physical discomfort and social stigma associated with eye patching. Adjunct digital visual trainings have not consistently sustained patient engagement due to their repetitive nature, thereby compromising their efficacy.

**Objective:** This study aimed to evaluate the effectiveness of a gamified mobile application designed to increase treatment adherence among children with amblyopia by making the therapeutic process more engaging and accessible within home settings.

**Methods:** An exploratory study was conducted, commencing with qualitative interviews and questionnaires to explore the barriers to traditional treatment adherence. This formative research informed the development of a gamified mobile application, which was shaped by cognitive appraisal theory to address identified emotional and psychological needs, potentially impacting adherence. The subsequent quantitative phase utilized a randomized controlled trial involving 34 amblyopic children aged 7-10, recruited from a local primary school. These participants were randomly assigned to either the intervention group, which used a novel gamified mobile application developed by our team, or the control group, which utilized another commercially available mobile application. Both groups engaged with their respective applications in a home environment. The Morisky Medication Adherence Scale (MMAS-8) was adapted to measure treatment adherence.

**Results:** Over the four-week trial, 34 children aged 7-10 with amblyopia were enrolled and randomized into two groups: intervention (n=18) and control (n=16). Children in both the intervention and control groups engaged daily for 20 minutes at home, using mobile applications designed for visual rehabilitation. The intervention group (n=18) achieved a significantly higher mean adherence rate (Mean = 6.56, SD = 1.06) on the Morisky Medication Adherence Scale (MMAS-8) compared to the control group (n=16, Mean = 5.01, SD = 1.22), with a P-value of 0.001. Thematic analysis of the design process revealed that integrating cognitive appraisal theory effectively enhanced emotional engagement and adherence.

**Conclusions:** The integration of cognitive appraisal theory into the design of a gamified mobile application for amblyopia treatment has shown to significantly improve adherence among children. Clinical Trial: ClinicalTrials.gov NCT06372548

(JMIR Preprints 07/05/2024:60309)

DOI: <https://doi.org/10.2196/preprints.60309>

## Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**

Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.

Only make the preprint title and abstract visible.

No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**

Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain visible to the public.

Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <http://www.jmir.org/>, I will be able to make my accepted manuscript PDF available to anyone at any time.



## Original Manuscript

# Effectiveness of a Gamified Mobile Application in Enhancing Treatment Adherence for Children with Amblyopia: A Explorative Study

## Abstract

**Background:** Amblyopia is the leading cause of visual impairment in children worldwide. The predominant clinical treatment, occlusion therapy, is marred by poor adherence, often attributed to the physical discomfort and social stigma associated with eye patching. Adjunct digital visual trainings have not consistently sustained patient engagement due to their repetitive nature, thereby compromising their efficacy.

**Objective:** This study aimed to evaluate the effectiveness of a gamified mobile application designed to increase treatment adherence among children with amblyopia by making the therapeutic process more engaging and accessible within home settings.

**Methods:** An exploratory study was conducted, commencing with qualitative interviews and questionnaires to explore the barriers to traditional treatment adherence. This formative research informed the development of a gamified mobile application, which was shaped by cognitive appraisal theory to address identified emotional and psychological needs, potentially impacting adherence. The subsequent quantitative phase utilized a randomized controlled trial involving 34 amblyopic children aged 7-10, recruited from a local primary school. These participants were randomly assigned to either the intervention group, which used a novel gamified mobile application developed by our team, or the control group, which utilized another commercially available mobile application. Both groups engaged with their respective applications in a home environment. The Morisky Medication Adherence Scale (MMAS-8) was adapted to measure treatment adherence.

**Results:** Over the four-week trial, 34 children aged 7-10 with amblyopia were enrolled and randomized into two groups: intervention (n=18) and control (n=16). Children in both the intervention and control groups engaged daily for 20 minutes at home, using mobile applications designed for visual rehabilitation. The intervention group (n=18) achieved a significantly higher mean adherence rate (Mean = 6.56, SD = 1.06) on the Morisky Medication Adherence Scale (MMAS-8) compared to the control group (n=16, Mean = 5.01, SD = 1.22), with a P-value of 0.001. Thematic analysis of the design process revealed that integrating cognitive appraisal theory effectively enhanced emotional engagement and adherence.

**Conclusions:** The integration of cognitive appraisal theory into the design of a gamified mobile application for amblyopia treatment has shown to significantly improve adherence among children.

**Trial Registration:** ClinicalTrials.gov NCT06372548

**Keywords:** Amblyopia; Pediatric Eye Care; Gamified Therapy; Mobile Health Applications; Treatment Adherence; Visual Rehabilitation; Randomized Controlled Trial; Child Healthcare Innovation; Serious Game; Emotional Cognition

## Introduction

Amblyopia, the most prevalent cause of visual impairment in children, affects a significant number of young individuals worldwide.[1-4]. It is commonly associated with the reduction of visual acuity, ability of recognizing to position and speed and accuracy of processing visual information[5-8]. Considering the severe impacts of amblyopia on the wellbeings of children and adolescents, prioritizing early intervention and therapy becomes necessary[9-11]. At present, the main intervention for amblyopia involves occluding the healthy eye[1, 5, 12], thereby encouraging patients to use the amblyopic eye [13]. However, children exhibit a compliance rate of less than 50% with occlusion therapy[14,

15], attributed to psychological stress stemming from patching, discomfort and difficulty in delivering the therapy, and insufficient parental knowledge[16-18]. As a consequence, regular treatment becomes challenging to obtain[19, 20]. Against the backdrop, digital therapy, combined with visual tasks, has emerged as a promising method[1, 21, 22]. These visual tasks, often in the form of digital videos or games, encompass a range of activities aimed at improving visual function, including vernier acuity, contrast detection, letter recognition, and spatial frequency discrimination [23-27]. They engage children in demanding activities that specifically target training the amblyopic eye, which contributes to the treatment of amblyopia[28-30]. The combination of digital technology and visual tasks offers a dynamic and engaging approach to amblyopia treatment[1, 9, 21, 22, 31, 32]. Therefore, the innovative form of therapy can serve as valuable supplements to conventional treatment methods.

However, these therapies do not achieve the expected positive impacts due to inappropriate content and format selection of digital solutions [1, 7, 25, 26, 32-39]. Specifically, the effectiveness of digital therapy could be hindered by its monotony and repetitiveness[1], meanwhile insufficient sustained engagement may compromise the effectiveness of digital therapy for amblyopia. Several studies have employed a standard set of mini-games, including Tetris, Gold Miner, and Ping Pong, as visual teaching tools[27]. Yet, these games may not be suitable for frequent, long-term training, particularly for groups of children with limited self-control. Even with DigRush, considered the most "engaging" game in clinical research, only 56% of participants completed more than 75% of the required gameplay[34]. In addition, Many rehabilitation products for treating amblyopia require patients, particularly children, to attend frequent sessions at specific locations and use designated devices for extended periods. However, in practice, individuals may reduce the frequency and duration of these sessions to accommodate children's comfort levels. This adjustment, while well-intentioned, can hinder the establishment of effective long-term healing routines. [21, 33]. Besides, some devices that are designed for adults, like VR equipment, may not be suitable for children, potentially resulting in adverse effects[24].

Additionally, while advanced treatments like VR devices and binocular therapy prioritize children's emotions, the emotional well-being of amblyopic children remains understudied. This oversight has led to the paradoxical situation where new treatment modalities may succeed, but neglect the comprehensive needs of the pediatric population. Research into the development of visual training games for children with amblyopia, considering the psychology and emotions of the children, has yet to be explored. This gap has led to ineffective gamified interventions for compliance improvement.

This study introduces a self-developed gamified treatment approach, leveraging mobile devices to facilitate ongoing vision rehabilitation for children with amblyopia in a home setting. This method emphasizes sustainable treatment adherence, meeting the user-friendly therapeutic solutions in health computing. Drawing on the occlusion therapy solution and cognitive appraisal theory, we conducted investigations and randomized controlled trials to ensure usability, acceptability, and compliance of the solution. Our research contributes to the existing knowledge on gamified therapy for young patients with amblyopia, proposing a novel intervention strategy for designers, medical professionals, and affected children. The incorporation of this gamified product into standard vision rehabilitation practices suggests a therapy modality with

improved compliance rates, offering a more engaging and enjoyable therapeutic experience. This approach has the potential to enhance the quality of life and social interactions of children with amblyopia, providing a comprehensive solution to the challenges of treating this condition.

## Methods

### Research design

In this study, we conducted a 3-stage research approach aimed at developing and evaluating a gamified solution to assist children with amblyopia in establishing rehabilitation routines.

Stage 1 focused on gathering qualitative and quantitative data through in-depth interviews with key stakeholders, as well as administering questionnaires to amblyopic children. The objective was to understand treatment protocols, challenges, specific needs, and their impact on treatment adherence. Insights from this stage informed the development of the gamified solution.

Stage 2 involved developing targeted design programs using cognitive appraisal theory as a framework. Semi-structured interviews were conducted with ophthalmologists and game designers to explore the integration of cognitive appraisal theory into game design for amblyopia therapy. Data analysis involved deductive thematic analysis, identifying themes related to game design and treatment adherence.

In Stage 3, we implemented the gamified solution developed in Stage 2 and conducted a randomized controlled trial to evaluate its effectiveness in enhancing treatment compliance. The trial involved recruitment of amblyopic children, random allocation to intervention and control groups, and administration of the gamified intervention over a four-week period. Interviews and questionnaires were used to assess adherence, psychological state, and user experience.

### Methods at Stage1

#### Overview

In-depth interviews were conducted with key stakeholders, including physicians, patients, and their families. The interviews encompass a number of topics, including the treatment protocols, challenges encountered, specific needs, and their impact on adherence to treatment. Besides, questionnaires were administered to examine the general characteristics, tendencies, behavior patterns, and issues related to treatment compliance among amblyopic children. These questionnaires were designed to systematically collect quantitative data from a broader sample. Insights gleaned from face-to-face interviews guided the development of the questionnaire, ensuring comprehensive coverage of relevant topics and concerns. Furthermore, qualitative data from interviews were validated through the identification of trends and patterns in survey responses.

### Data collection

**Individual Interview:** A total of eight in-depth interviews were conducted with physicians



from the EYE&ENT HOSPITAL OF FUDAN. This is to explore current approaches to treating amblyopic children, adherence to medical guidelines during training, and the practical applications of visual training games in the healing process. Furthermore, a total of 22 family members from 8 families were interviewed to enhance the implementation of our serious game in home settings. These interviews focused on assessing the amblyopic children's behavioral performance during their visual rehabilitation training, identifying potential enablers and obstacles related to training games for amblyopia rehabilitation therapy. The interviews also revolved around reasons for children to engage with the game, strategies for parental involvement at home, and effective utilization by guardians. One investigator moderated the interviews while another recorded the interviews.

**Survey Questionnaire:** A total of 80 paper questionnaires were distributed to children at Shenzhen Children's Hospital, with 56 valid responses received. The questionnaire focused on factors that influence children's readiness or reluctance to engage in training, reasons for poor compliance with wearing the eye patch mask, and preferences regarding typical hobbies and pastimes.

### **Data analysis**

The qualitative information gathered from in-depth interviews and questionnaire was analyzed using inductive thematic analysis[40]. This involved three steps: first, we transcribed all interview and questionnaire data into text and examined. Second, we classified the data. Preliminary codes were assigned to segments representing the needs, experiences, obstacles, and factors affecting treatment adherence of parents and children with amblyopia. Last, after classifying and integrating the preliminary codes, the themes that have been found are examined in more detail and improved. Member checking is used to triangulate the final list of themes.

## **Methods at Stage2**

### **Overview**

Based on the findings from the Stage 1, we developed a series of targeted design programs using cognitive appraisal theory as a framework. The primary design objective is to enhance treatment compliance while ensuring the therapeutic effectiveness for children with amblyopia. To achieve this, we conducted semi-structured interviews with both ophthalmologists and game designers. These interviews aimed to delve into the integration of cognitive appraisal theory into the design of games tailored for amblyopia therapy. Deductive thematic analysis was utilized for data analysis, which allowed us to identify and extract themes relevant to game design and treatment adherence from the gathered information.

### **Data collection**

**Expert Interview:** Six experts, comprising three ophthalmologists and three game designers, were engaged in semi-structured interviews. Prior to the interviews, the experts were given ten minutes to review data and information from the initial stage of our research, focusing on the desires and preferences of children and parents throughout the amblyopia treatment process. The aim was to solicit their insights on employing cognitive appraisal theory to guide game designers in creating amblyopia therapy applications. Leveraging their expertise and practical experience, the experts provided valuable input on key considerations in game development, particularly in engaging and sustaining children's interest in therapy. Furthermore, the interviews explored how the dimensions of cognitive appraisal theory—relevance, valence, likelihood, agency, and coping potential—could be leveraged to enhance treatment adherence. They discussed

how these theoretical aspects could be effectively applied in game design to improve overall treatment compliance.

### **Data analysis**

Deductive Thematic Analysis was employed [40], which identified three themes: "design of rehabilitation training games," "optimization of masking therapy," and "design of rehabilitation training games." As shown in Table 2, these themes, along with the five dimensions of cognitive assessment theory, were integrated into a matrix. Subsequently, this matrix was systematically applied to the transcripts of expert interviews, allowing for the pinpointing and annotation of data segments associated with these theoretical aspects. By closely examining and contrasting the coded data, key themes related to game design and improving treatment adherence for children were identified. Lastly, explanations and descriptions of these themes were provided, demonstrating how cognitive appraisal theories can be used to create games that treat amblyopia, and how these theories' guiding principles and strategies can address treatment-related issues faced by children with amblyopia. The final list of themes was triangulated through member checking.

### **Methods at Stage 3**

#### **Overview**

Building upon the findings from the previous stage, we created a 2D graphic game for iPad using Unity. Emphasizing the game's influence on emotions, we focused on enhancing children's interest and engagement (relevance), boosting their confidence and sense of accomplishment (valence), creating opportunities for success (likelihood), reinforcing their sense of control and belonging (agency), and improving coping skills and resilience through gameplay challenges (coping potential). This approach contributed to a therapeutic play environment that is more likely to positively impact children's emotions and behaviors.

We then implemented the game and conducted a randomized controlled trial to evaluate its effectiveness in enhancing treatment compliance. To measure the game's effectiveness in enhancing adherence using cognitive appraisal theory, interviews were conducted with parents and children from both intervention and control groups to evaluate the theory's five mood-related dimensions. Additionally, a user research questionnaire was administered to compare our product's user experience with that of competitors, assessing factors such as ease of use and acceptability.

#### **Research design**

This parallel two-arm randomized controlled trial was conducted in accordance with CONORT-EHEALTH (Consolidated Standards for Electronic and Mobile Health Applications and Online Telemedicine Reporting Trials)[41] □ It underwent clinical trial enrollment (NCT06372548) □

#### **Recruitment and participants**

We recruited amblyopic children from a local Experimental Primary School, adhering to specific inclusion criteria, which were as follows:

##### **(1) Inclusion Criteria**

Diagnosis of amblyopia (including refractive amblyopia, strabismic amblyopia and mixed).

The child has no significant IQ deficits and has no difficulty communicating with others.

## (2) Exclusion criteria

Severe amblyopia.

Suffering from other psychological or physical disorders.

Parents did not agree to sign the informed consent form or the child was not willing to participate in this experiment.

### ***Blinding, allocation concealment, and randomization***

After completing the baseline assessment, participants were randomly allocated into two groups: the intervention group, which utilized the amblyopia training app we designed and developed, and the control group, which utilized the DuoBao Vision Training System, a visual function training therapy software developed by Vision Medical Software. Both interventions employed a gamified training format. Participants remained unaware of both the research group and study hypotheses, as well as any re-randomization or the conduct of two related trials, to prevent bias in exercise adherence behavior. Group allocation was unknown to the statistician. Following allocation, participants in both groups received an email containing links to download the respective apps. Throughout the investigation, participants had the option to contact researchers via phone or email for any issues related to the app or the study. During the investigation, participants could contact the researchers by phone or email for any issues related to the app or the study.

### ***Experiment on Intervention***

For a total of four weeks, the experimental group conducted the intervention trial for twenty minutes each day. The trial included activities such as narrative background on the opening page, wearing eye patches as instructed, visual stimulation, and fine eye training, with brief intervals between different modes. Prior to the initial trial, participants were briefed on the study's aims, tasks, and time frame, and received instructions on applying the experimental intervention. The training was carried out by children and their parents, with 20 minutes of training completed each day and a follow-up assessment after 30 days. With the assistance of their parents, the participants completed the MMAS-8 adherence scale at the conclusion of the session.

**Subject interviews:** Following the experiment, participants were interviewed via Zoom for 20–40 minutes to understand their psychological state following the experiment, focusing on aspects such as relevance, consistency, likelihood, agency, and coping potential. Two researchers transcribed the interview after the full conversation was captured on tape. With the same duration and design as the experimental group, the control group employed a rival product for the experimental intervention. After the interviews, each child received 20 RMB.

**Interviews with stakeholders:** Interviews were held with one or two of the participants' parents. The primary emphasis was on the parents' opinions and sentiments toward the Amblyopia Rehabilitation Training Game, which served as the experiment's intervention object.

**Questionnaire distribution:** The participants in both the experimental and control groups were asked to finish the questionnaire with their parents due to the time required for completion. The evaluation of product design usability concentrated on the experiences of parents and subjects with the experimental intervention.

### ***Instruments and measures***

#### **8-Item Morisky Medication Adherence Scale (MMAS-8):**

The 8-Item Morisky Medication Adherence Scale (MMAS-8) was used to assess patients' adherence through eight questions, including seven yes-or-no questions and one Likert scale question[42]. It classifies adherence levels as high, moderate, and low based, adapted here to support amblyopia recovery in children.

#### **User Experience Questionnaire (UEQ):**

UEQ was administered post-experiment to swiftly and accurately measure user experience [43]. Covering 26 items across six domains, UEQ evaluated the impact of the amblyopia rehabilitation training product on both children and their parents. Due to its language complexity, the questionnaire was completed with parental assistance.

### ***Statistical analysis***

We utilized t-tests in SPSS 26.0 software to compare baseline characteristics between individuals who provided and those who did not provide the primary outcome. Before and after the experiment, between-group and within-group data were analyzed using either the t-test or Mann-Whitney U test. A significance level (alpha) of 0.05 was set for all statistical analyses, with differences considered statistically significant when the p-value was less than 0.05.

### ***Ethical consideration***

This study was approved by the institutional ethical committee (H20230365I).The children, their teachers or parents were asked to give their informed consent to participate in the experiment. The informed consent forms were signed by the parents.

## **Results**

### **Result 1**

As shown in Table 1, two themes derived from the in-depth interviews conducted with stakeholders, focusing on their wishes and preferences regarding the design of rehabilitation training games for amblyopic children. Under the theme of "Wishes," stakeholders expressed the importance of games consistently capturing children's attention through continuous story narratives, the need for games to enhance the appeal of eye patches, and the necessity for games to incorporate a reward mechanism. Under the theme of "Preferences," stakeholders identified children's interests, such as collecting objects with bright colors, engaging in arts and crafts activities, and enjoying cartoons with rich storylines.

Table 1.Results of stakeholder interviews

Themes	Sub Themes	codes
<b>Wishes</b>		

	Games need to consistently capture children's attention	Children need continuous story narratives
		Children need varied forms for game play
		Children need simple, easy-to-understand training methods
	Games need to enhance the appeal of eye patches	Eye patches can lead to physical discomfort for children
		Eye patches can lead to social stigmatization
		Children's visual abilities can be limited by eye patches
	Game needs to have a reward mechanism	Children need timely positive feedback
		Children need diverse positive feedback
		Children need consistent positive feedback
Preferences		
	Children's interest preferences	Children like to collect objects with bright, rich colors
		Children enjoy arts and crafts activities such as painting, puzzles, and building blocks.
		Children enjoy watching cartoons with rich storylines
		Children enjoy role-playing games
		Children enjoy images of animals such as cats, birds, lions, etc.

Three sub-themes were identified related to the theme of “wishes”. First, both children and parents brought up the topic that games need to consistently capture children's attention. They showed concerns on the storyline, play forms, and training methods of the games. In particular, compared to color or size selection games, most children thought that games with storylines were more interesting, and they were thus more likely to continue exploring. Children also expressed dissatisfaction with single-player games (Tetris, Find the Difference) and a desire for the addition of more interactive features like role-playing. Parents also noted that basic and easy-to-understand training methods should be employed because children tend to become confused by instructions that are too complex. Second, most parents felt that eye patches needed to be made more appealing. The majority of children reported discomfort with wearing eye patches, a sentiment echoed by their parents, who cited this discomfort as a key reason for their children's reluctance to wear them consistently. Several parents also noted that their children experienced social embarrassment and humiliation among their peers due to wearing eye patches. Additionally, some children mentioned that wearing eye patches interfered with their daily activities and perception of objects, further contributing to their resistance to eye patching. Third, parents expressed a desire to incentivize their children for completing training tasks. They observed that offering immediate rewards for task completion led to more positive behavior and increased excitement among their children. For instance, one parent noted that, “promising a specific reward, such as a favorite meal, upon task completion was more motivating than vague promises about future rewards”. However, parents also noted that offering the same specific rewards too often could lead to boredom. Additionally, some children expressed enthusiasm for the concept of achieving a “high score” in a game as a form of reward.

Under the "preferences" theme, children spontaneously revealed their color preferences during interviews, often favoring eye-catching and vibrant colors like pink, orange, and blue. They expressed enjoyment in collecting colorful items such as cartoon stickers, stationery, and notebooks. Besides, we discovered that children engaged in hands-on manual activities like puzzles, constructing blocks, and sketching, which parents believed fostered their creative, critical thinking, and motor skills. Furthermore, nearly all children expressed a fondness for comics and cartoons with intricate plots, often imagining themselves as characters within the stories.

On the basis of the findings at this stage, three recommendations were identified to guide game design for children with amblyopia. Firstly, to sustain long-term therapeutic motivation, providing quick and varied positive feedback is essential. Secondly, game design should accommodate children's diverse demands and preferences. Lastly, integrating rich worldviews and narratives from mediums like comics and animation, along with incorporating tiny animals such as lions, birds, and cats, can enhance immersion and foster empathy and creativity in children.

## Result 2

The study identified five evaluation latitudes and three design themes: occlusion therapy optimization ideas, rehabilitation training game design ideas, and rehabilitation training game design solutions (Table 2).

Table 2. Results of expert interviews

Assessment Dimensions with Definitions		Occlusion Therapy Optimization Ideas	Rehabilitation Training Game Design Ideas	Rehabilitation Training Game Design Solutions
<b>Relevance</b>				
	The degree to which a situation is important to the individual's current goals	1. Combine the eye stickers with the background of the game 2. Give special meaning to the eye stickers in the game. 3. Designing visual elements that meet children's preferences	1. Set play goals that match children's interests 2. Incorporate educational elements and understandable therapeutic goals	Play as a doctor-in-training; treat sick critters; make friends with critters through treatment
<b>Valence</b>				
	The degree to which the situation is positive or negative or consistent with the goal	1. See eye patches as the key to the game 2. Use stories to show the positive impact of wearing eye patches. 3. Progress in the game is directly related to the use of eye patches.	1. use elements that meet children's psychological expectations 2. provide positive feedback and guidance during play	Requires daily completion of therapeutic tasks for animal patients (i.e., visual training tasks); combines forms of visual training with therapeutic behaviors in play, e.g., packages fine discrimination

				tasks as "finding the virus"; Child-friendly cartoon visual style and elements.
<b>Likelihood</b>				
	Certainty of the current situation and future expectations	1. Showing the direct game effects of eye patch wear 2. Progress of the treatment corresponds to the use of eye patches 3. Game difficulty is compatible with eye patch use	1. Adaptation of game difficulty 2. Clear goal setting and feedback	Set the game's different maps to gradually increase in difficulty; add logos (corresponding eye sticker patterns) to the maps after a successful breakthrough; add an icon collection and achievement system
<b>Agency</b>				
	Referring to self, others, or non-personal situations	1. Make children feel that they play a key role in play through eye patches 2. Enhance children's sense of impact on the world of play	1. Emphasize the leading role of children in the game 2. Emphasize role-playing	Add interaction with animal companions, after successful treatment you can turn on the friend flag with the critter, check the status or visit in the friend list at any time
<b>Coping potential</b>				
	Steps that can be used to cope	1. Teach the correct use of eye patches through guided animation. 2. Incorporates eye patch wearing into the game experience. 3. Provides positive feedback to enhance control and success.	1. The game can adjust the difficulty 2. Emphasizes progress rather than success	Three achievement levels for each map, with children deciding whether to progress to higher levels based on interest and proficiency

For the optimization concept of occlusion therapy, there are three main design points to consider. Firstly, the eye patch should be used as a tool to enter the game world. Game designers suggest incorporating the eye patch as a crucial element within the game, imbuing it with special significance, such as a gift from animal friends. This will integrate the act of wearing the eye patch with the context and goal of the game. This approach aims to improve children's psychological acceptance of wearing eye patches by incorporating them into the game experience and adding to the sense of purpose of the game. Secondly, the eye patches were combined with role-play to provide positive feedback related to wearing them in the game, which could enhance children's acceptance of eye patches and their initiative to wear them. For instance, by identifying distinct eye patch patterns, we were able to unlock various game maps and tasks.

Additionally, doctors suggested that wearing eye patches could have a positive therapeutic effect when incorporated into playful storytelling. Finally, the designers proposed adding a tutorial animation on how to wear the eye patches before starting the game. This associates with our interviews with parents, as many illustrating that their children tend to use the eye patches incorrectly.

For the design of rehabilitation training games, design ideas and solutions were suggested by doctors and designers based on the five dimensions of cognitive appraisal theory, as summarized in Table 2. Drawing on the inputs from both doctors and designers, we have chosen interactive storytelling as the primary game format. Firstly, a backstory of an animal doctor was created for the game. Players assume the role of an intern doctor and are required to complete daily treatment tasks, which included visual training tasks, for animal patients. After completing each level in the game, players can turn on the friend sign with the critter and check its status at any time. Secondly, game maps with three levels of difficulty were created. Children can choose one map themselves based on their interest and proficiency, and reduce the difficulty level when they feel overwhelmed. Additionally, an incentive mechanism has been set up in the game, including the collection of illustrations and achievement content. Finally, the game's design features a cartoon style that is popular among children.

### Result 3

#### *Gamified Treatment Application*

The gamified mobile application "Find You! Cure My Animal Friends" developed for this study is designed to enhance treatment adherence in children with amblyopia by integrating cognitive appraisal theory. It provides a series of visually stimulating activities that are specifically crafted to improve visual acuity and encourage regular use, as shown in figure 1. The main game interface and level interface is shown in Figure 2.

Figure 1. Visual stimulation training and Fine eye training

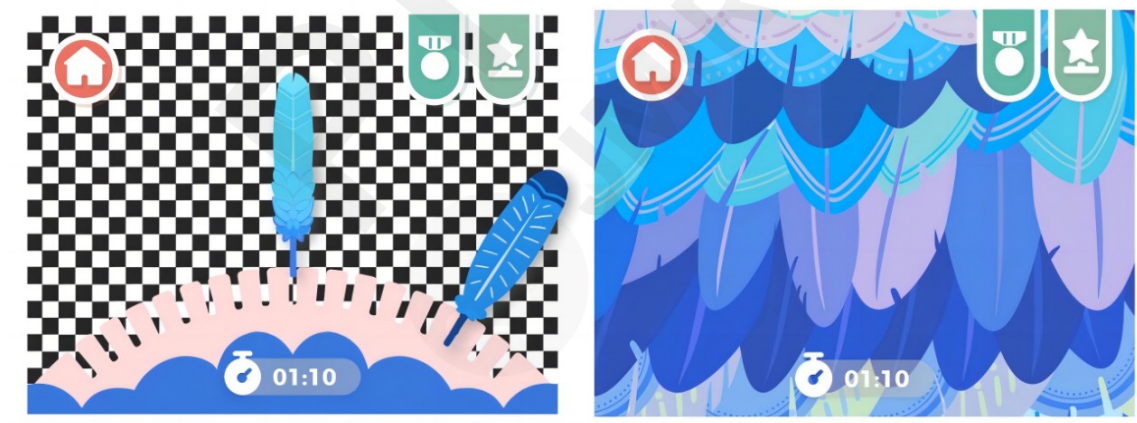
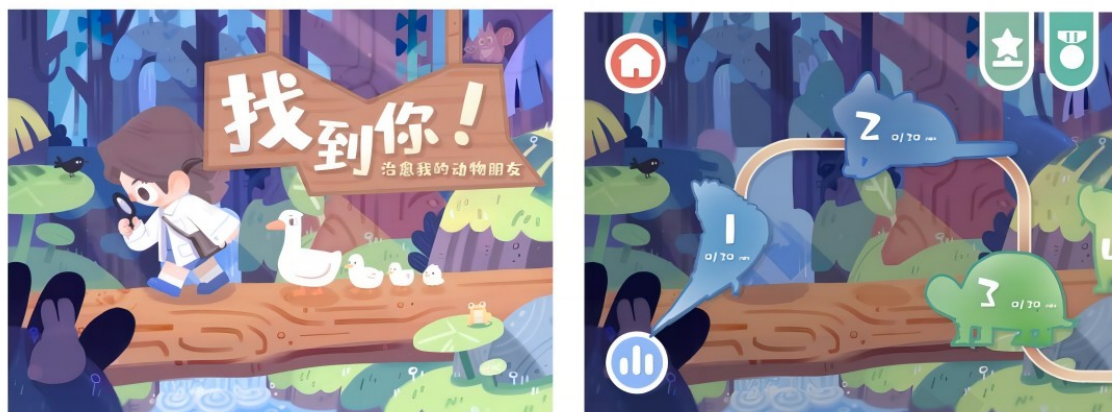


Figure 2. Main game interface and level interface





## User Statistics

A total of 34 participants aged 7 to 10 years were recruited. Of these participants, 24 (70.59%) were boys and 10 (29.41%) were girls. The average age of the participants was 9.29 years. There were 9 students in the third grade, 13 in the fourth grade, and 12 in the fifth grade. There were no significant differences in age or gender between the two groups. Participant characteristics are shown in Table 3.

Table 3. Participant characteristics

		Experimental group		Control group	
		□	%	□	%
<b>age</b>					
	10 years old	6	33.33	6	37.5
	9 years old	7	38.88	6	37.5
	8 years old	4	22.22	3	18.75
	7 years old	1	5.55	1	6.25
<b>Sex</b>					
	Male	13	72.22	11	68.75
	Female	5	27.77	5	31.25
	Total	18	100	16	100

Before conducting the data analysis, we tested the normality of the 8-item Morisky Medication Adherence Scale questionnaire scores using the Shapiro-Wilk test. The results are presented in Table 4.

Table 4. Results of normality test

	Experimental group	Control group
<b>Test statistic (W)</b>		
	0.946	0.963
<b>p-value</b>		

	0.371	0.708
--	-------	-------

## Adherence

After conducting an independent samples t-test, a significant difference was found in the adherence scores on the MMAS-8 scale between the experimental group that used the amblyopia training game ( $M = 6.56$ ,  $SD = 1.06$ ) and the control group that used another commercially available game ( $M = 5.01$ ,  $SD = 1.22$ ) ( $t$ -statistic (35) = 3.896,  $p = 0.0005$ ), as shown in Table 5. The results indicated that the experimental group had significantly higher adherence scores than the control group.

Table 5. Results of independent samples t-Test

Group	Simple size (N)	Mean (M)	Standard deviation (SD)	Standard error (SEM)	95% confidence interval (CI)	T statistic	P value
<b>Experimental group</b>							
	18	6.56	1.06	0.25	[6.03, 7.08]	3.8964	0.001
<b>Control group</b>							
	16	5.01	1.22	0.31	[4.36, 5.66]		

Significant behavioral differences were found when comparing patient adherence to an amblyopia training game (experimental group) with other games on the market (control group). It revealed that 61.11% of patients in the experimental group showed high adherence, compared to only 18.75% in the control group who achieved the same level. Additionally, the experimental group demonstrated a significantly lower percentage of patients with low adherence (38.89%) compared to the control group (81.25%), as shown in Table 6.

Table 6. Scores for the MMAS-8 scale

	Experimental group	Control group
<b>High adherence</b>		
	61.11%	18.75%
<b>Low adherence</b>		
	38.89%	81.25%

No significant differences were observed between the experimental and control groups for questions about forgetting to take medication (Q1, 22.22% vs. 31.25%,  $T=0.58$ ,  $P=0.57$ ), adjusting medication without informing the doctor (Q3, 11.11% vs. 12.50%,  $T=0.12$ ,  $P=0.90$ ), and whether they took their

medication the previous day (Q5, 11.11% vs. 50.00%,  $T=2.59$ ,  $P=0.02^*$ ). Significant differences emerged in other questions, notably 'Have you missed any doses in the past two weeks?' (Q2, 11.11% vs. 56.25%,  $T=3.03$ ,  $P=0.00^*$ ), indicating a higher compliance in the experimental group. Similarly, for 'Did you find it challenging to adhere to the treatment program?' (Q7, 11.11% vs. 50.00%,  $T=2.59$ ,  $P=0.02^*$ ), the experimental group showed significantly better adherence. The percentage of subjects who scored 0 in each question revealed higher scores in the control group for Q2, Q5, and Q7, aligning with the significant differences observed in our statistical analyses. The Table 7 displays the MMAS-8 scale scores for each question.

Table 7. MMAS-8 scale scores for each question

Q	Experimental group (%)	Control group (%)	T statistic	P value
1. Do you ever forget to take your medication?	22.22	31.25	0.58	0.57
2. Have you missed any doses in the past two weeks?	11.11	56.25	3.03	0.00*
3. Do you adjust your medication without consulting your doctor when your symptoms worsen or new symptoms arise during treatment?	11.11	12.50	0.12	0.90
4. Do you sometimes forget to bring your medication with you when traveling or away from home for extended periods?	22.22	25.00	0.18	0.85
5. Did you take your medication yesterday?	11.11	50.00	2.59	0.02*
6. Have you ever stopped taking your medication before completing the prescribed course, even if your symptoms improved or disappeared?	22.22	25.00	0.18	0.85
7. Did you find it	11.11	50.00	2.59	0.02*

challenging to adhere to the treatment program?				
8.How frequently do you forget to take your medication?	5.56	12.50	1.43	0.16

### User Experience Questionnaire (UEQ)

The results showed that our product outperformed the competition in all dimensions except validity. Specifically, our product scored significantly higher than the competitors in attractiveness, understandability, convenience, and satisfaction. The competing product has a slight advantage in the controllability.

According to the results, among the six dimensions assessed, 'Attractiveness', 'Novelty', and 'Facilitation' received the highest scores, while 'Efficiency' received the lowest rating. The specific results of the UEQ are displayed in Table 8.

Table 8. User experience questionnaire scores

Scale	Experimental group					Control group				
	Mean	SD	N	Confidence	Confidence interval	Mean	SD	N	Confidence	Confidence interval
<b>Attractiveness</b>										
	2.14	0.59	18	0.27	1.87-2.41	0.39	0.41	16	0.20	0.18-0.59
<b>Understandability</b>										
	1.88	0.78	18	0.36	1.51-2.24	0.19	0.57	16	0.28	-0.09-0.47
<b>Efficiency</b>										
	1.08	0.49	18	0.22	0.86-1.31	1.20	0.26	16	0.13	1.07-1.33
<b>Reliability</b>										
	1.35	0.62	18	0.29	1.06-1.63	1.30	0.23	16	0.11	1.19-1.41
<b>Facilitation</b>										
	1.92	0.45	18	0.21	1.71-2.13	1.14	0.26	16	0.13	1.01-1.27
<b>Novelty</b>										

	2.1 3	0.3 8	1 8	0.17	1.95- 2.30	1.09	0.3 2	1 6	0.16	1.03- 1.35
--	----------	----------	--------	------	---------------	------	----------	--------	------	---------------

### Personal Interviews

As shown in Table 10, three general themes were identified, including attitudes toward the treatment of amblyopic children, experiences with the treatment of amblyopic children, and attitudes toward wearing eye patches. Table 9 identifies a total of five dimensions of cognitive appraisal theory, including goal relevance, congruence, likelihood, agency, and coping potential.

Table 9. Criteria for dividing dimensions of cognitive evaluation theory

Relevance	The anticipation of achieving a more valuable goal or outcome can result in a heightened emotional response. This is closely linked to the experience of interest[44, 45], which is a typical reaction to situations that are subjectively significant and elicit high levels of attentional activity. This, in turn, increases the likelihood of responding effectively to events and evokes strong positive emotions, such as enjoyment[46].
Valence	Individuals are more likely to experience positive emotions, such as happiness or gratitude, when they perceive an experience as related to a positive goal and moving them closer to that desired goal[46].
Likelihood	The likelihood dimension assesses the probability of a situation leading to a specific outcome, identifying associated emotions such as hope, fear, or anxiety.[46, 47].
Agency	Consider the influence of the user, others, or the environment/objects on the outcome of the situation, as well as factors related to controllability, in the evaluation of the agent[48].
Coping potential	Coping potential is the perceived ability to manage or change a situation and is categorized into three main groups: benign-positive, neutral, and stressful[47].

Table 10. Results of individual interviews

Themes	Experimental group		Control group	
	Codes	dimension	Codes	dimension
Rehab training treatment experience				
	Children like the background of the story in the game	Relevance ↑	Children find the mini-games a little boring	Relevance ↓
	Children enjoy	Relevance ↑ Agency ↑	Children find	Valence ↓

	playing the role of a doctor		the game graphics unattractive	
	Children enjoy interacting with animal friends in the game	Relevance↑ Agency↑	Children like getting high scores in games	Relevance↑ Likelihood↑
	children like the illustrations in the game to collect/unlock the list of friends.	Relevance↑ Valence↑ Likelihood↑		
<b>Attitude towards rehabilitation training</b>				
	Children like to play the game repeatedly to achieve high levels of achievement.	Relevance↑ Coping potential↑ Likelihood↑	Children report resistance the first time they use the game	Relevance↓ Valence↓
	Children perceive the game as difficult, but are more likely to want to complete the challenge.	Coping potential↑ Likelihood↑	Children say they are reluctant to repeat the training after experiencing all the mini-games	Relevance↓
	Children were still motivated to play the game at the end of the 30-day experiment.	Relevance↑ Agency↑	Children play the same game 2-3 times to get a high score	Relevance↑ Likelihood↑ Coping potential↑
<b>Attitude towards wearing eye patches</b>				
	children are generally motivated to wear eye patches.	Relevance↑ Agency↑	Children are often resistant to the eye patch and require parental	Valence↓ Coping potential↓

			intervention.	
	Children like eye patches with special patterns and keep them carefully.	Relevance↑ Valence↑		
Note: "↑" indicates an increase or improvement, while "↓" signifies a decrease or reduction.				

The study found that children in the experimental group had a positive reaction to the gamified rehabilitation training. This positive response may be attributed to the game design being consistent with cognitive appraisal theory,. Children particularly enjoyed storytelling, role-playing, interacting with in-game animal characters, and collecting icons. These elements increased their perceptions of goal relevance and congruence, as well as their assessments of the likelihood of successfully completing the game. Furthermore, enabling the children to actively engage in the game and interact with the surroundings enhanced their sense of control and ability to cope, which could account for the experimental group's greater participation in the game and adherence to rehabilitation training. The experiences and attitudes of the children in the control group differed significantly, as they mostly expressed disinterest in the game content or found the images unattractive. However, even in the control group, children were willing to play the game repeatedly to achieve a high score, indicating that perceptions of likelihood and coping potential can still be improved with appropriate incentives. Furthermore, the experimental group's children exhibited a higher level of positive acceptance towards the specially patterned eye patches, which provides additional evidence that increasing goal relevance and consistency can enhance treatment adherence. Conversely, the control group's children were less receptive to eye patches and needed parental intervention.

## Discussion

### Principal Results

This study proposes a novel intervention for improving compliance with amblyopia treatment in children by integrating Cognitive Appraisal Theory's five dimensions of emotional influence. A rehabilitative training game tailored for amblyopic children is developed to optimize occlusion therapy by addressing emotional and psychological needs, aiming to increase treatment efficacy through improved patient compliance.

The results show that children using our amblyopia training game had higher compliance rates compared to those using commercially available games. Analysis of the MMAS-8 scale showed that the experimental group showed significantly higher scores in areas concerning medication forgetting, daily adherence, and perceived difficulty in adhering to the treatment regimen. This indicates a greater adherence to long-term rehabilitation therapy compared to the control group. While the games used by the control group may initially engage children as effectively as our product, the depth and richness of the game content plays a critical role in maintaining compliance over time. Our game's emotional and narrative interactions that not only make the gameplay engaging, but also integrate educational aspects of the treatment into the

storyline, giving our game with a distinct advantage in content depth. The experimental group maintained high compliance over a 30-day treatment period, while the control group's performance declined.

Cognitive appraisal theory and the design appropriate for children with amblyopia may be key factors was successful in engagement in therapy, thereby improving compliance. Both the optimization of occlusion therapy and the design of a rehabilitative training game were guided by the following five dimensions in cognitive appraisal theory [44]: relevance (the extent to which a situation is important to the individual's current goals) [47, 49]. Valence (the degree to which a situation is positive, negative, or goal-aligned) [47, 49, 50]. Likelihood (referring to the certainty of the current situation as well as future expectations) [47, 50]. Agency (related to self, other, or impersonal situations) [47, 50], and Coping Potential (related to the steps available for coping) [47, 51]. The results of the interviews demonstrated the significant advantages of our game in the three dimensions of Relevance, Valence, and Coping potential. These significantly enhanced dimensions correlate with our theory-guided design program.

Within a narrative in which children assume the role of doctors treating animals, we redefined the medical eye patch as a symbol of commitment to their animal friends. This role-playing approach allows children to "heal" animals by applying an eyepatch, making the act of occlusion therapy emotionally meaningful and fostering acceptance through empathy. This process impacts the dimensions of relevance and valence. Children generally expressing pride in assuming the role of doctor and a willingness to wear the eyepatch proactively. Some children also expressed a sentimental value for the eyepatch, viewing it as a "token" of friendship with the animal characters in the game. Notably, many continued to use our product voluntarily after the trial ended, driven by a desire to complete more levels or visit their "animal friends" in the game. By closely integrating training content with the game's narrative and goals, the game not only addressed children's resistance to traditional occlusion therapy, but also increased their sense of immersion and ownership [52]. Even after the four-week trial period, children in the experimental group maintained a positive attitude and emotional state within our rehabilitative training game. This result re-emphasizes the validity of cognitive appraisal theory in the rehabilitation of children with amblyopia.

The results of the UEQ highlighted significant strengths of the game in the dimensions of "attractiveness", "novelty", and "stimulation". These results indicate that the game design successfully captured the interest of the target audience and motivated them to participate. In particular, the game's incentive mechanisms, such as immediate feedback and rewards, proved effective in encouraging continued engagement in the therapy process [53]. In addition, the game's high level of interactivity, coupled with visual designs tailored to user preferences, further enhanced the attractiveness and acceptance of the product [54]. However, despite exemplary performance on most dimensions, the game scored relatively low on the efficiency dimension, suggesting that future design iterations should consider and optimize the game's efficiency.

## Limitations

Despite the innovative design and implementation of this study, there are several limitations: first, the relatively small sample size may limit the generalizability of the results. Second, the study focused mainly on short-term compliance improvement, and the sustainability of long-term effects requires further research. In addition, the game design was primarily aimed at children and did not take into account the direct involvement of parents or guardians, who play an important role in the treatment process for children. Finally, although the design of the game was based on cognitive appraisal theory, the



specific mechanisms regarding the influence of emotions still need to be further elucidated through in-depth studies. The Mmsa scale was used for medication adherence, which needs to be analyzed in terms of reliability and validity, but the use of the game was spontaneously suggested by respondents in our qualitative research, resulting in an increase in adherence.

## Conclusion

The study shows that a rehabilitative training game for children with amblyopia, designed according to the Cognitive Appraisal Theory and its five dimensions of emotional impact, significantly improves treatment adherence. This innovation offers a new intervention tool for the field of amblyopia treatment and provides valuable insights for other therapeutic areas seeking to improve patient adherence. Future research should aim to increase the sample size, explore long-term effects, and consider parental or guardian involvement to improve compliance and facilitate visual rehabilitation of children with amblyopia. Additionally, investigating the specific mechanisms of emotional impact within game design will provide a scientific basis for developing more effective therapeutic interventions.

Our research revisits the traditional yet universally effective treatment of occlusion therapy and integrates it with serious games. Unlike many discussed examples that primarily engage children with simple and repetitive visual stimuli, our approach addresses the problem of diminished engagement due to a lack of compelling game content. We utilized a user-centered design methodology to create visual forms, mechanisms, and content that are tailored to the cognitive preferences and physiological acceptability of children with amblyopia. This approach aims to improve children's acceptance of each treatment step, leading to optimal compliance. Additionally, we incorporated an engaging narrative into the game, allowing children to participate in helping characters while seamlessly integrating visual training. This gameplay is designed to encourage the concurrent use of occlusion therapy outside of the game. Game elements are used in a therapeutic context to create gamified products that guide children in developing rehabilitative training habits. The findings from our research demonstrate the potential of utilizing mobile and tablet technology to optimize amblyopia treatment for children within home and mobile treatment environments. By integrating such technologies, the treatment can be seamlessly incorporated into the daily lives of patients, ensuring greater accessibility and adherence.

## Conflicts of Interest

None declared.

## Uncategorized References

1. Levi DM. Rethinking amblyopia 2020. *Vision Res.* 2020 Nov;176:118-29. PMID: 32866759. doi: 10.1016/j.visres.2020.07.014.
2. Fu Z, Hong H, Su Z, Lou B, Pan CW, Liu H. Global prevalence of amblyopia and disease burden projections through 2040: a systematic review and meta-analysis. *Br J Ophthalmol.* 2020 Aug;104(8):1164-70. PMID: 31704700. doi: 10.1136/bjophthalmol-2019-314759.
3. Hashemi H, Pakzad RM, Yekta A, Bostamzad P, Aghamirsalim M, Sardari SM, et al. Global and regional estimates of prevalence of amblyopia: A systematic review and meta-analysis. *Strabismus.* 2018 Dec;26(4):168-83. PMID: 30059649. doi: 10.1080/09273972.2018.1500618.
4. Ciuffreda KJ, Levi DM, Selenow A. *AMBLYOPIA: BASIC AND CLINICAL ASPECTS*1991. ISBN: 0409951714.
5. Tailor V, Bossi M, Greenwood JA, Dahlmann-Noor A. Childhood amblyopia: current management and new trends. *Br Med Bull.* 2016 Sep;119(1):75-86. PMID: 27543498. doi: 10.1093/bmb/ldw030.

6. Birch EE. Amblyopia and binocular vision. *Prog Retin Eye Res.* 2013 Mar;33:67-84. PMID: 23201436. doi: 10.1016/j.preteyeres.2012.11.001.
7. Gambacorta C, Nahum M, Vedamurthy I, Bayliss J, Jordan J, Bavelier D, et al. An action video game for the treatment of amblyopia in children: A feasibility study. *Vision Res.* 2018 Jul;148:1-14. PMID: 29709618. doi: 10.1016/j.visres.2018.04.005.
8. Syntosi A, Felizzi F, Bouchet C. A Social Media Listening Study to Understand the Unmet Needs and Quality of Life in Adult and Pediatric Amblyopia Patients. *Ophthalmol Ther.* 2022 Dec;11(6):2183-96. PMID: 36175822. doi: 10.1007/s40123-022-00571-2.
9. Holmes JM, Levi DM. Treatment of amblyopia as a function of age. *Vis Neurosci.* 2018 Jan;35:E015. PMID: 29905125. doi: 10.1017/S0952523817000220.
10. Holmes JM, Lazar EL, Melia BM, Astle WF, Dagi LR, Donahue SP, et al. Effect of age on response to amblyopia treatment in children. *Arch Ophthalmol.* 2011 Nov;129(11):1451-7. PMID: 21746970. doi: 10.1001/archophthalmol.2011.179.
11. Fronius M, Cirina L, Ackermann H, Kohnen T, Diehl CM. Efficiency of electronically monitored amblyopia treatment between 5 and 16 years of age: new insight into declining susceptibility of the visual system. *Vision Res.* 2014 Oct;103:11-9. PMID: 25130409. doi: 10.1016/j.visres.2014.07.018.
12. Wong AM. New concepts concerning the neural mechanisms of amblyopia and their clinical implications. *Can J Ophthalmol.* 2012 Oct;47(5):399-409. PMID: 23036539. doi: 10.1016/j.jcjo.2012.05.002.
13. Loudon SE, Simonsz HJ. The history of the treatment of amblyopia. *Strabismus.* 2005 Jun;13(2):93-106. PMID: 16020365. doi: 10.1080/09273970590949818.
14. Wallace MP, Stewart CE, Moseley MJ, Stephens DA, Fielder AR, Monitored Occlusion Treatment Amblyopia Study C, et al. Compliance with occlusion therapy for childhood amblyopia. *Invest Ophthalmol Vis Sci.* 2013 Sep 17;54(9):6158-66. PMID: 23882695. doi: 10.1167/iovs.13-11861.
15. Loudon SE, Polling JR, Simonsz HJ. Electronically measured compliance with occlusion therapy for amblyopia is related to visual acuity increase. *Graefes Arch Clin Exp Ophthalmol.* 2003 Mar;241(3):176-80. PMID: 12644939. doi: 10.1007/s00417-002-0570-z.
16. Loudon SE, Passchier J, Chaker L, de Vos S, Fronius M, Harrad RA, et al. Psychological causes of non-compliance with electronically monitored occlusion therapy for amblyopia. *Br J Ophthalmol.* 2009 Nov;93(11):1499-503. PMID: 19661070. doi: 10.1136/bjo.2008.149815.
17. Searle A, Vedhara K, Norman P, Frost A, Harrad R. Compliance with eye patching in children and its psychosocial effects: A qualitative application of protection motivation theory. *Psychology, Health & Medicine.* 2010 2000/02/01;5(1):43-54. doi: 10.1080/135485000105990.
18. Webber AL, Wood JM, Gole GA, Brown B. Effect of amblyopia on self-esteem in children. *Optom Vis Sci.* 2008 Nov;85(11):1074-81. PMID: 18981922. doi: 10.1097/OPX.0b013e31818b9911.
19. Carlton J, Kaltenthaler E. Health-related quality of life measures (HRQoL) in patients with amblyopia and strabismus: a systematic review. *Br J Ophthalmol.* 2011 Mar;95(3):325-30. PMID: 20693563. doi: 10.1136/bjo.2009.178889.
20. Carlton J, Kaltenthaler E. Amblyopia and quality of life: a systematic review. *Eye (Lond).* 2011 Apr;25(4):403-13. PMID: 21274010. doi: 10.1038/eye.2011.4.
21. Leal Vega L, Pinero DP, Hernandez Rodriguez CJ, Molina Martin A, Morales-Quezada L, Vallelado Alvarez AI, et al. Study protocol for a randomized controlled trial of the NEIVATECH virtual reality system to improve visual function in children with anisometropic amblyopia. *BMC Ophthalmol.* 2022 Jun 7;22(1):253. PMID: 35672688. doi: 10.1186/s12886-022-02466-z.
22. Molina-Martin A, Leal-Vega L, de Fez D, Martinez-Plaza E, Coco-Martin MB, Pinero DP. Amblyopia Treatment through Immersive Virtual Reality: A Preliminary Experience in Anisometropic Children. *Vision (Basel).* 2023 May 19;7(2):42. PMID: 37218960. doi: 10.3390/vision7020042.
23. Astle AT, Webb BS, McGraw PV. Can perceptual learning be used to treat amblyopia beyond the critical period of visual development? *Ophthalmic Physiol Opt.* 2011 Nov;31(6):564-73. PMID: 21981034. doi: 10.1111/j.1475-1313.2011.00873.x.
24. Martin S, Portela JA, Ding J, Ibarrondo O, Levi DM. Evaluation of a Virtual Reality implementation of a binocular imbalance test. *PLoS One.* 2020;15(8):e0238047. PMID: 32822405. doi: 10.1371/journal.pone.0238047.
25. Hess RF, Thompson B. Amblyopia and the binocular approach to its therapy. *Vision Res.* 2015 Sep;114:4-16. PMID: 25906685. doi: 10.1016/j.visres.2015.02.009.
26. Herbison N, Cobb S, Gregson R, Ash I, Eastgate R, Purdy J, et al. Interactive binocular treatment (I-BiT) for amblyopia: results of a pilot study of 3D shutter glasses system. *Eye (Lond).* 2013 Sep;27(9):1077-83. PMID: 23807383. doi: 10.1038/eye.2013.113.

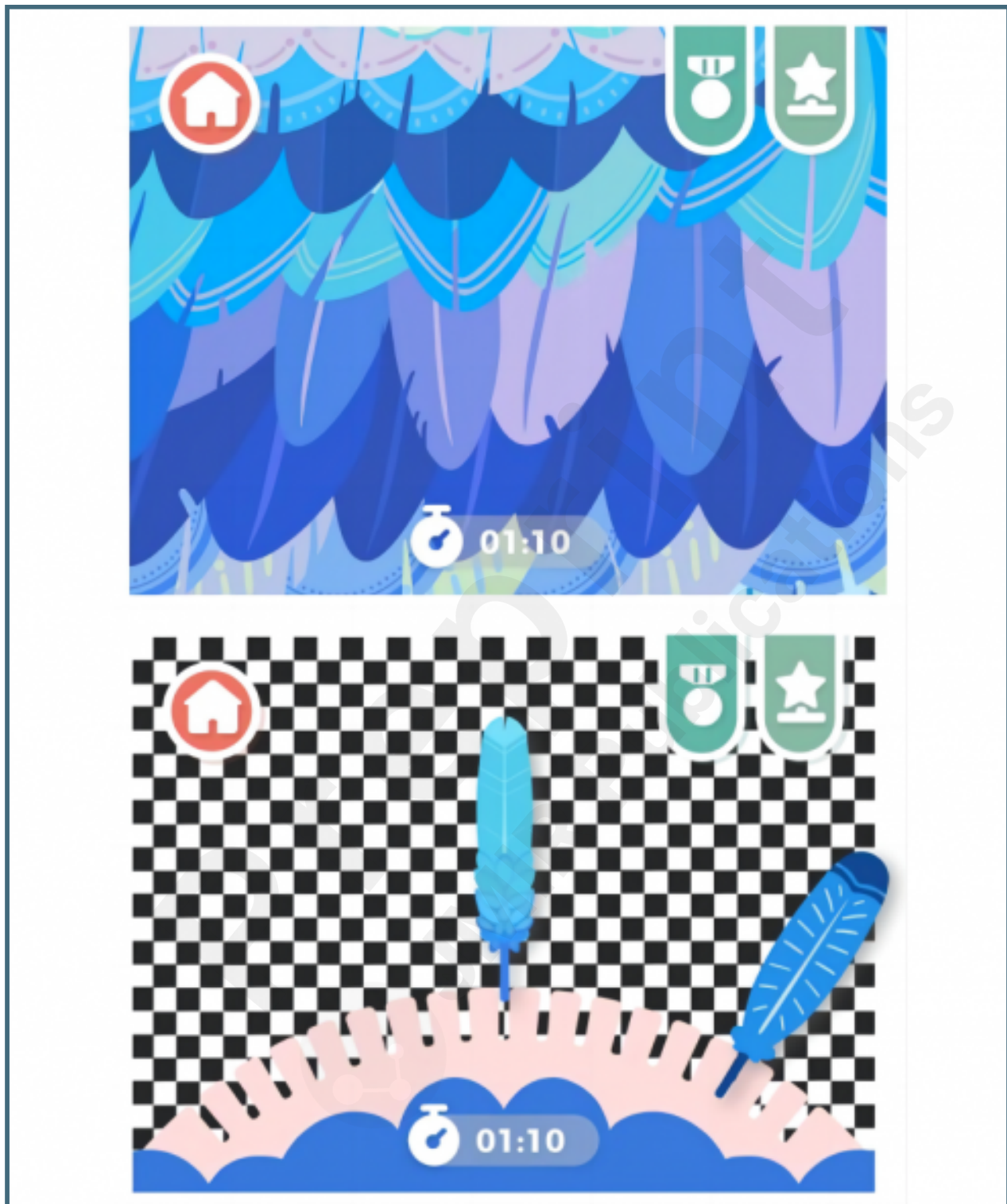
27. Kelly KR, Jost RM, Dao L, Beauchamp CL, Leffler JN, Birch EE. Binocular iPad Game vs Patching for Treatment of Amblyopia in Children: A Randomized Clinical Trial. *JAMA Ophthalmol*. 2016 Dec 1;134(12):1402-8. PMID: 27832248. doi: 10.1001/jamaophthalmol.2016.4224.
28. Polat U, Ma-Naim T, Belkin M, Sagi D. Improving vision in adult amblyopia by perceptual learning. *Proc Natl Acad Sci U S A*. 2004 Apr 27;101(17):6692-7. PMID: 15096608. doi: 10.1073/pnas.0401200101.
29. Zhang JY, Cong LJ, Klein SA, Levi DM, Yu C. Perceptual learning improves adult amblyopic vision through rule-based cognitive compensation. *Invest Ophthalmol Vis Sci*. 2014 Apr 1;55(4):2020-30. PMID: 24550359. doi: 10.1167/iops.13-13739.
30. Doshier B, Lu ZL. Visual Perceptual Learning and Models. *Annu Rev Vis Sci*. 2017 Sep 15;3:343-63. PMID: 28723311. doi: 10.1146/annurev-vision-102016-061249.
31. Noah S, Bayliss J, Vedamurthy I, Nahum M, Levi D, Bavelier D. Comparing dichoptic action video game play to patching in adults with amblyopia. *Journal of Vision*. 2014;14(10):691-. doi: 10.1167/14.10.691.
32. Manh VM, Holmes JM, Lazar EL, Kraker RT, Wallace DK, Kulp MT, et al. A Randomized Trial of a Binocular iPad Game Versus Part-Time Patching in Children Aged 13 to 16 Years With Amblyopia. *Am J Ophthalmol*. 2018 Feb;186:104-15. PMID: 29196184. doi: 10.1016/j.ajo.2017.11.017.
33. Herbison N, MacKeith D, Vivian A, Purdy J, Fakis A, Ash IM, et al. Randomised controlled trial of video clips and interactive games to improve vision in children with amblyopia using the I-BiT system. *Br J Ophthalmol*. 2016 Nov;100(11):1511-6. PMID: 26951772. doi: 10.1136/bjophthalmol-2015-307798.
34. Kelly KR, Jost RM, Dao L, Beauchamp CL, Leffler JN, Birch EE. Binocular iPad Game vs Patching for Treatment of Amblyopia in Children: A Randomized Clinical Trial. *JAMA Ophthalmology*. 2016;134(12):1402-8. doi: 10.1001/jamaophthalmol.2016.4224.
35. Gao TY, Guo CX, Babu RJ, Black JM, Bobier WR, Chakraborty A, et al. Effectiveness of a Binocular Video Game vs Placebo Video Game for Improving Visual Functions in Older Children, Teenagers, and Adults With Amblyopia: A Randomized Clinical Trial. *JAMA Ophthalmol*. 2018 Feb 1;136(2):172-81. PMID: 29302694. doi: 10.1001/jamaophthalmol.2017.6090.
36. Pineles SL, Aakalu VK, Hutchinson AK, Galvin JA, Heidary G, Binenbaum G, et al. Binocular Treatment of Amblyopia: A Report by the American Academy of Ophthalmology. *Ophthalmology*. 2020 Feb;127(2):261-72. PMID: 31619356. doi: 10.1016/j.ophtha.2019.08.024.
37. Birch EE, Li SL, Jost RM, Morale SE, De La Cruz A, Stager D, Jr., et al. Binocular iPad treatment for amblyopia in preschool children. *J AAPOS*. 2015 Feb;19(1):6-11. PMID: 25727578. doi: 10.1016/j.jaapos.2014.09.009.
38. Knox PJ, Simmers AJ, Gray LS, Cleary M. An exploratory study: prolonged periods of binocular stimulation can provide an effective treatment for childhood amblyopia. *Invest Ophthalmol Vis Sci*. 2012 Feb 21;53(2):817-24. PMID: 22169103. doi: 10.1167/iops.11-8219.
39. Vedamurthy I, Nahum M, Bavelier D, Levi DM. Mechanisms of recovery of visual function in adult amblyopia through a tailored action video game. *Sci Rep*. 2015 Feb 26;5(1):8482. PMID: 25719537. doi: 10.1038/srep08482.
40. Fereday J, Muir-Cochrane E. Demonstrating Rigor Using Thematic Analysis: A Hybrid Approach of Inductive and Deductive Coding and Theme Development. *International Journal of Qualitative Methods*. 2016;5(1):80-92. doi: 10.1177/160940690600500107.
41. Eysenbach G, Group C-E. CONSORT-EHEALTH: improving and standardizing evaluation reports of Web-based and mobile health interventions. *J Med Internet Res*. 2011 Dec 31;13(4):e126. PMID: 22209829. doi: 10.2196/jmir.1923.
42. Janezic A, Locatelli I, Kos M. Criterion validity of 8-item Morisky Medication Adherence Scale in patients with asthma. *PLoS One*. 2017;12(11):e0187835. PMID: 29190693. doi: 10.1371/journal.pone.0187835.
43. Rauschenberger M, Schrepp M, Perez-Cota M, Olschner S, Thomaschewski J. Efficient Measurement of the User Experience of Interactive Products. How to use the User Experience Questionnaire (UEQ). Example: Spanish Language Version. *International Journal of Interactive Multimedia and Artificial Intelligence*. 2013;2(1). doi: 10.9781/ijimai.2013.215.
44. Ellsworth PC, Smith CA. Shades of Joy: Patterns of Appraisal Differentiating Pleasant Emotions. *Cognition & Emotion*. 1988 1988/10/01;2(4):301-31. doi: 10.1080/02699938808412702.
45. Perugini M, Bagozzi RP. The role of desires and anticipated emotions in goal-directed behaviours: broadening and deepening the theory of planned behaviour. *Br J Soc Psychol*. 2001 Mar;40(Pt 1):79-98. PMID: 11329835. doi: 10.1348/014466601164704.
46. Ma J, Gao J, Scott N, Ding P. Customer delight from theme park experiences. *Annals of Tourism Research*. 2013 2013/07/01;42:359-81. doi: 10.1016/j.annals.2013.02.018.
47. Lazarus RS. *Emotion And Adaptation*: Oxford University Press; 1991. Available from: <https://doi.org/10.1093/oso/9780195069945.001.0001>.

48. Watson L, Spence MT. Causes and consequences of emotions on consumer behaviour. *European Journal of Marketing*. 2007;41(5/6):487-511. doi: 10.1108/03090560710737570.
49. Appraisal processes in emotion: Theory, methods, research, (2001).
50. Smith CA, Ellsworth PC. Patterns of cognitive appraisal in emotion. *J Pers Soc Psychol*. 1985 Apr;48(4):813-38. PMID: 3886875. doi: 10.1037/0022-3514.48.4.813.
51. Scherer KR. The dynamic architecture of emotion: Evidence for the component process model. *Cognition & Emotion*. 2009 2009/11/01;23(7):1307-51. doi: 10.1080/02699930902928969.
52. Kim M. Does playing a video game really result in improvements in psychological well-being in the era of COVID-19? *Journal of Retailing and Consumer Services*. 2021 2021/07/01/;61:102577. doi: 10.1016/j.jretconser.2021.102577.
53. Mayer I, Bekebrede G, Harteveld C, Warmelink H, Zhou Q, van Ruijven T, et al. The research and evaluation of serious games: Toward a comprehensive methodology. *British Journal of Educational Technology*. 2013;45(3):502-27. doi: 10.1111/bjet.12067.
54. Crutzen R, de Nooijer J, Brouwer W, Oenema A, Brug J, de Vries NK. Strategies to facilitate exposure to internet-delivered health behavior change interventions aimed at adolescents or young adults: a systematic review. *Health Educ Behav*. 2011 Feb;38(1):49-62. PMID: 21189422. doi: 10.1177/1090198110372878.

## Supplementary Files

## Figures

Visual stimulation training and fine eye training.



Main game interface and level interface.

