Clinical eHealth 3 (2020) 82-88

Contents lists available at ScienceDirect

Clinical eHealth

journal homepage: ww.keaipublishing.com/CEH

# The design choices for the development of an Augmented Reality game for people with visuospatial neglect



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#### ARTICLE INFO

Article history: Received 9 July 2019 Revised 4 October 2020 Available online 17 November 2020

Keywords: Stroke Visuospatial neglect Visual scanning training Augmented reality Game Design research HoloLens<sup>™</sup>

#### ABSTRACT

*Introduction:* Visuospatial neglect (VSN) is common after stroke and can seriously hamper everyday life. One of the most commonly used and highly recommended rehabilitation methods is Visual Scanning Training (VST) which requires a lot of repetition which makes the treatment intensive and less appealing for the patient. The use of eHealth in healthcare can increase options regarding improved treatment in the areas of patient satisfaction, treatment efficacy and effectiveness. One solution to motivational issues might be Augmented Reality (AR), which offers new opportunities for increasing natural interactions with the environment during treatment of VSN.

*Aim:* The development of an AR-based scanning training program that will improve visuospatial search strategies in individuals affected by VSN.

*Method:* We used a Design Research approach, which is characterized by the iterative and incremental use of prototypes as research instruments together with a strong human-centered focus. Several design thinking methods were used to explore which design elements the AR game should comply with. Seven patients with visuospatial neglect, eight occupational therapists, a game design professional and seven other healthcare professionals participated in this research by means of co-creation based on their own perspectives.

*Results:* Fundamental design choices for an AR game for VSN patients included the factors extrinsic motivation, nostalgia, metaphors, direct feedback, independent movement, object contrast, search elements and competition. Designing for extrinsic motivation was considered the most important design choice, because due to less self-awareness the target group often does not fully understand and accept the consequences of VSN.

*Conclusion:* This study produced a prototype AR game for people with VSN after stroke. The AR game and method used illustrate the promising role of AR tools in geriatric rehabilitation, specifically those aimed at increasing the independence of patients with VSN after stroke.

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#### 1. Introduction

Every year about 15 million people worldwide are affected by stroke,<sup>1</sup> and one of the cognitive consequences of a stroke can be visuospatial neglect (VSN).<sup>2</sup> VSN is an attention disorder that man-

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ifests in a number of ways, including decreased visual perception and awareness of the affected side during self-care, losing one's way, being unable to find objects, and poor perception of people located on the affected side.<sup>3</sup> VSN affects 30–50% of patients immediately following stroke<sup>3,4</sup> and is often accompanied by a reduced awareness of impairment, which negatively impacts the duration and effectiveness of patient recovery.<sup>5,6</sup>

One of the most commonly used and highly recommended rehabilitation methods found in Dutch and international stroke guidelines on VSN is Visual Scanning Training (VST), which is typically delivered by an occupational therapist.<sup>7,2</sup> In this approach a

https://doi.org/10.1016/j.ceh.2020.11.003

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Abbreviations: VSN, Visuospatial neglect; VST, Visual Scanning Training; AR, Augmented Reality; VR, Virtual Reality; CBS, Catherine Bergego Scale.

patient is encouraged to direct eye and head movements toward the neglected side in order to encourage scanning of the whole environment during daily activities.<sup>8</sup> This requires a lot of repetition which makes the treatment intensive and less appealing for the patient.<sup>9,10</sup>

The use of eHealth in modern healthcare offers new possibilities to improve treatment in the areas of patient satisfaction, treatment efficacy and effectiveness.<sup>11</sup> For example, a feasibility study showed that the use of exergaming improved the adherence of people with VSN in the post-acute phase of their rehabilitation process and it also seemed promising in the assessment and quantifying of VSN symptoms.<sup>12</sup> Adherence of the patients was measured by a training diary after each training session and showed a high indication of adherence and also the individual cognitive and spatial exploration skills improved after the training. Another study showed that video games make rehabilitation more enjoyable and achieve higher therapeutic compliance.<sup>13</sup> Computer games in general are known for voluntary participation, longer playing times, and higher probability of therapeutic compliance.<sup>14</sup> Virtual Reality (VR) is also receiving attention and studies have shown that people with neglect who learn to cross the street using VR perform better when crossing streets in real life.<sup>15</sup>

Compared to VR, Augmented Reality (AR) also be a promising tool to provide satisfaction but is not widely investigated.<sup>16</sup> The benefits of AR are a more natural interaction with the environment by projecting images into a real-world setting to lower the barrier to greater home-based use. This can be important when attempting to regain activities of daily living in patients during stroke rehabilitation.<sup>17</sup> Therefore, in this study we investigate how AR could be used as visual scanning-based therapy for patients with VSN, leading to increased more appealing and independence in their rehabilitation process.

The aim of this research was to develop an AR-based scanning training program that will improve visuospatial search strategies in individuals affected by VSN. A Design Research approach was used to develop an AR game and among the contributors, members of the target group were included as the main participants in cocreation.

# 2. Methods

# 2.1. Study design

We applied a Design Research approach using a variety of qualitative design thinking methods. To better understand and improve visual scanning training for patients with VSN, we generated new design elements should be incorporated into the AR game to positively motivate patients to scan the environment by rotating the head or using eye movements to the affected side'. The design thinking model is used to provide a solution-based approach to solving problems.<sup>18,19</sup> This model has five stages and provides an understanding of human needs, as well as a human-centered reframing of the problem and a hands-on approach to prototyping and testing. Two prototypes were tested by patients with VSN using the two design thinking methods 'fly on the wall' and 'think out loud', which are described below.<sup>20</sup> Co-creation was used to evaluate the prototypes from different perspectives, but patient feedback was regarded as the most important input.<sup>11</sup> Following input from all participants, design choices were made and further developed within the AR game.

## 2.2. Elements of VST

We used elements derived from VST as the underlying working theory with which to develop the AR game, as this is the most com-

mon and widely used training method to help stimulate the patient to systematically visually explore their environment during the activities of daily life.<sup>2,21,22</sup> Our AR game merely provides the means to especially the encouraging of paying active and conscious attention while keeping motivation up during repeated and systematic training under more demanding conditions.<sup>23,10,22</sup> Encouragement is usually guaranteed by operant condition, such as reinforcement. With our AR tool this is met by both the therapist who will give verbal feedback as well as during play as finding the objects will result in earning the reward. Additionally, repetition and systematic scanning are very important features of VST and those are made easier as the progression of the game ensures focus and motivation.<sup>10</sup> Last, gradual reduction of various stimulation methods and cues is provided, as feedback cues will diminish when patients incorporate efficient scanning strategies throughout training.

## 2.3. Technology

The AR game was developed using the AR glass 'HoloLens<sup>™</sup>. The HoloLens<sup>™</sup> was designed by Microsoft and provides the opportunity to mix the real world with the virtual world when wearing the device.<sup>24</sup> In this study we used the first generation HoloLens<sup>™</sup> and developed the AR game using the software Unity 5.6.2. Unity 5.6.2. is compatible with different hardware devices as it runs on the iOS, Android and Windows platforms. We used the Windows Mobile 10 operating system to develop the prototypes, together with the software code language C#. The HoloLens<sup>™</sup> was connected to the computer using a local dedicated router, both to achieve the best connection between the devices and for privacy reasons. As the AR game is easy to use, the occupational therapist helps the patient put on the HoloLens<sup>™</sup> device and starts the AR game, and there is no need for a developer or technical expert to be present to help launch and play the game.

#### 2.4. Participants

This study was performed in three skilled nursing facilities provide Geriatric Rehabilitation in the Netherlands.<sup>25</sup> The included patients were: (1) assessed for VSN based on the Catherine Bergego Scale (CBS) or had already been assessed in hospital using traditional neuropsychological tests for VSN;<sup>26</sup> (2) had entered a Geriatric Rehabilitation program at one of the skilled nursing facilities between January 1st 2017 and May 1st 2018; (3) primarily diagnosed with stroke. The exclusion criteria were: (1) severe aphasia leaving patients unable to make verbal statements; (2) visual impairments such as hemianopia or pre-existing visual problems before the stroke; (3) bedridden patients. Participants were informed about the study and gave written informed consent that also covered video and audio recordings.<sup>27</sup> During the study eight occupational therapists and seven other healthcare professionals (including physical therapists, doctors and nurses) were asked for feedback on the two prototypes, four occupational therapists were involved in peer examination during the course of the research, and one game design professional was involved throughout the study. Together these participants formed a co-creative process with the purpose of finding a match between the values of each participant, the technology and the surrounding infrastructure.<sup>11</sup>

# 2.5. Procedure

The researcher who collected all qualitative data had considerable experience with the target group and with VST. The Boeije roadmap, which was used in the analysis of verbal and nonverbal data, is a systematic and thorough approach to the analysis of qualitative data.<sup>28</sup> The data were open coded by the first author and by an independent occupational therapist and subsequently discussed in order to increase internal validity. The data were then coded axially by comparing the codes to determine similarities and differences. In case of consensus, the codes were used for analysis. To complete the analysis, selective coding was applied to provide further structure in the plurality of separate main and sub codes. Selective coding provides the researcher with insight into the data collected and the story it tells in the light of the problem. In addition to the transcripts and video recordings, literature searches were also analyzed using ATLAS.ti, so that all data could be brought together in a single overview.<sup>29</sup> Following data analysis, the most common data were selected and integrated into the prototypes using the guided story telling method, together with the game design professional. Fig. 1 schematically illustrates which groups of participants took part in this study and which design thinking method was used.

#### 2.5.1. Observation and interviews

In this study two observational methods were used to test the two prototypes together with patients with VSN. The first was the 'fly on the wall' method which was used in the case of four patients with VSN in order to evaluate the first protoype.<sup>18</sup> As a component of Design Research, several methods were used to obtain relevance data. As implied by the name, the fly on the wall method is an observational tool whereby the researcher remains as unobtrusive as possible, observing and collecting relevant data without interacting with the patient.<sup>18</sup> The second method was the 'think out loud' approach whereby four patients with VSN were asked to communicate all thoughts and experiences aloud while using the second prototype.<sup>18</sup> One patient was included in the testing of both prototypes to order to allow us to see and hear how a patient reacts to the different prototypes. In both observational methods the patients were filmed from a distance using a video camera and images were simultaneously recorded from the Holo-Lens<sup>™</sup> to compare the two recordings and assess behavior during prototype testing. For every design element the verbal and nonverbal reactions of the patients were analyzed. In this way, the motivation, ease of use and VST approach during the observations were mapped and coded according to corresponding pre-defined themes



Fig. 1. Participants and corresponding design thinking methods.

in Atlas.ti.<sup>29</sup> Following both observations, the researcher completed semi-structured interviews to evaluate the prototypes with the patients. The questions were based on personal data, personal preferences, and the needs and experiences related to use of the prototype based on the included design elements. To simplify the answering patients were first asked closed-ended questions, followed by open-ended questions based on the answer given. The observations and interviews were used as input for the design of the following prototype and priority was given to the outcomes that emerged in the case of more than one patient. All interviews were later recorded and transcribed.<sup>27</sup>

#### 2.5.2. Guided story telling

Supported by the design professional, the prototypes were critically examined by means of guided storytelling. Here, the design elements within the game were discussed using the story of a patient in the target group.<sup>18</sup> This process led to a set of design choices which were then tested with the patients and substantiated with scientific literature or vice versa.

## 2.5.3. Questionnaire

After using the first prototype, a self-developed semi-structured questionnaire was completed by eight occupational therapists and seven other healthcare professionals including physical therapists, doctors and nurses. Prior to testing the prototype, the participants were asked to imagine themselves from the perspective of a 70-year-old patient with VSN.<sup>18</sup> The questions focused on their experience with patients with VSN and how the motivation, independence and compensation elements in the game can be processed.

# 2.5.4. Literature

Due to the iterative process, no keywords were identified prior to the literature review. For every design choice, corresponding literature was retrieved in order to provide additional support.

#### 2.5.5. Peer examination

In order to increase reliability, the outcomes were tested by four occupational therapists through peer examinations at the end of the study.<sup>30</sup> All design choices were critically assessed for relevance from the perspective of both the patient and the occupational therapist.

# 3. Results

The results of this study are a series of design choices that together constitute a HoloLens<sup>™</sup>-based AR game, developed for people with VSN after stroke. The final form of the AR game is a virtual museum in which the patient is located and where he or she must search for virtual paintings projected 'on to a wall', as shown in Fig. 2. During the game the patient is stimulated to scan the environment and feedback is given as soon as a painting is overlooked. After looking at the painting, the patient is rewarded with a video linked to the painting. The paintings illustrate nostalgic themes from the Netherlands such as crafts, national holidays and older vehicles, and as such the game provides extrinsic encouragement to scan the environment while moving around. Further game specifications are described in the design choices below.

# 3.1. Design choice 1: Extrinsic motivation

The most important outcome of the interviews conducted with seven patients with VSN was the method of motivating recovery from VSN. The interviews showed that these patients are not intrinsically motivated to work towards recovery because less self-awareness impedes their acceptance of their limitations. One M.D.J. Bakker, N. Boonstra, T.C.W. Nijboer et al.



Fig. 2. One of the paintings of the virtual museum.

of the interview questions was, "What is necessary for you to be able to function independently again?" In response the patients' answers only referenced physical functions, while cognitive functions are clearly very important to independent functioning. During the interviews and through observation it became clear that some of the patients were aware of the need for VST but disliked daily feedback encouraging them to pay more attention to their neglected side. These observations further underline the importance of making VST more engaging and the need to develop a game that provides patients with extrinsic motivation. This aspect should also be taken into account during the implementation of the game.

#### 3.2. Design choice 2: Metaphor

In conversation with the game design professional, we discussed the way in which learning is conveyed via the game and the need for the game to be enjoyable in order to enhance the motivational effects on learning. The outcome of these conversations was the choice of using a metaphor. Metaphors can, without being necessarily based on reality, create a learning effect within the user and make a gaming experience more enjoyable.<sup>31</sup> Because patients with VSN are not intrinsically motivated, figurative transfer using metaphors can be especially useful.<sup>31</sup> These issues were discussed during the guided story telling session with the game design professional, which resulted in a suitable metaphor during the development of the first prototype. A museum was chosen because it is a place where people come to learn but at the same time wish to be entertained, a dual function that fits well with the purpose of the game to make aspects of VST both educational and entertaining. Furthermore, research shows that people who are 65 or older constitute the largest group of museum-goers so the metaphor also fits well with normal target group activities.<sup>32</sup> When the patients in the study were asked about their experience of museums, they were positive but were now unable to visit museums due to impaired physical functioning.

#### 3.3. Design choice 3: Nostalgia

In addition to discussing the museum as metaphor with the game design professional, nostalgia emerged as an additional possible theme, which accords with a report by the Dutch Museum association that history is a main theme in 61% of museums.<sup>32</sup> Further investigation of the literature on use of nostalgia showed that it stimulates certain areas of the brain and helps to motivate patients.<sup>33</sup> Nostalgia is regularly used in games because it can inspire feelings of pride and pleasure in older people as they remember objects and events, with the attendant positive effect on the player's mood.<sup>34</sup> In the AR game, nostalgia is elicited using

virtual video footage of past scenes which are displayed on a wall as in a real museum. This design choice was tested in the first and second prototypes by asking the target group to wear the Holo-Lens<sup>™</sup> to search and watch the video's projected sequentially onto the wall. Observations of patient reactions to the prototypes and the outcomes of the interviews all indicated a positive response. The first prototype included three nostalgic videos which were randomly chosen on the theme labor, and in the second prototype additional themes such as vacation and healthcare were added to increase variety. Six of the seven patients smiled watching the videos or were positive about it during the interview afterwards. One patient expressing this as "Nice to just be able to see it again" and one patient recognized his own neighborhood and started talking about good memories of his childhood. Another patient preferred videos about nature above the themes used in the game. The single patient who did not enjoy the nostalgic videos also had difficulty with the game due to major cognitive problems. which may have influenced the outcome.

#### 3.4. Design choice 4: Independent movement

The interviews with the seven patients emphasized that the main goal of geriatric rehabilitation is to recover abilities to perform activities patients undertook before their stroke, and patients specified physical problems following stroke as the limiting factor in these activities (e.g. "As long as I can use my arms and legs again"). In literature geriatric rehabilitation is defined as "optimize functional capacity, promote activity and preserve functional reserve and social participation in older people with disabling impairments."<sup>35</sup> Therefore, the game focused on independent movement (walking or using a wheelchair) as one of the basic functions of activities of daily living, and integrated this into the game by placing the paintings at a distance from each other so that the patient had to physically move from painting to painting while scanning the environment in order to play the game.<sup>36</sup> This element also emerged from the literature as a priority, in the form of a relevant functional task within occupational therapy and to promote independence.<sup>2,8</sup> Four of the seven patients involved in this research used a wheelchair and one patient required a walking aid to move safely. Although not all patients were able to move independently, they were stimulated to practice this aspect in the game by scanning while walking or using a wheelchair.

#### 3.5. Design choice 5: Search element

The search element of the game (in order to view all virtual paintings) provides an extra incentive for head rotation, in accordance with the stated goals of VST.<sup>2</sup> This aspect quickly became clear to users, as all patients visually searched their environment for the virtual paintings. The HoloLens<sup>™</sup> has various options for controlling the game, including head movements, hand movements or by verbal communication with the device.<sup>24</sup> The two prototype tests showed that operations based on hand movements are difficult or impossible due to the physical consequences of stroke and this also impedes use of a mobility aid. Of the three HoloLens™ control modes (head movements, hand movements or verbal response) a conscious decision was made to use the head movement function as this encourages the patient to scan the environment by means of head rotation, and thus supports the goals of VST.<sup>2,10</sup> The 'Voice' aspect is incorporated into the game only in the sense that the patient is initially asked via the device for certain verbal confirmations, such as whether the HoloLens<sup>™</sup> fits comfortably. During the first prototype test it became apparent that the positioning of the HoloLens  $\ensuremath{^{\rm TM}}$  on the head was difficult for a few patients. A check to ensure proper fit at the beginning of the game was therefore incorporated into the second prototype. When the

HoloLens<sup>™</sup> is comfortably fitted, participants are asked to say 'start' in order for the game to continue.

#### 3.6. Design choice 6: Object contrast

During our fly on the wall observations when testing the first prototype it became clear that the difference between the real world and the virtual world needed to be readily apparent to participants. If not, holograms go unnoticed and there is a loss of distinction between things that do and do not belong in the game. We noticed that patients perceived paintings, photographs or other real objects on a wall as game objects. Black and white video images on a grey wall or curtain were also not clearly distinguished by patients and thus went unnoticed. In the design process for the second prototype it was therefore decided that a luminous gold frame would be added to the black-and-white images, a setting that also fits well with the museum theme because similar frames are often found in museums. The 'think out loud' observations with the second prototype indicated that patients noticed the paintings more readily.

# 3.7. Design choice 7: Direct feedback

During the fly on the wall observations we also noticed that three of the four patients needed considerable guidance during testing of the first prototype. Although an audio recording in the first prototype explained the intention of the game in advance, this explanation was not sufficient to allow all participants to carry out the instructions. We also observed that after the first painting was found, some patients stopped searching for further paintings. To be able to guide players, more feedback is required within the game, but keeping in mind the cognitive problems of the patients, feedback needs to be given during the performance of the game.<sup>37</sup> Direct feedback also serves to make the patient aware that a painting is being overlooked, so that they can potentially come to understand that this is due to VSN. In the second prototype direct feedback was added in the form of pleasantly-voiced audio feedback, so when a patient passes a painting the game prompts the player with "You forgot one, go back and take a look at that painting". As the audio feedback originates from the same side as the neglected painting, a subtle prompt is generally first provided from the neglected side.<sup>2,9</sup> This concept was tested with four other patients and the feedback was processed and integrated into the game. The game introduction was also changed from audio to video in the second prototype so that the patient can better focus on what is being said. During the introduction an example is shown of the virtual person patients have to look for in the game (see Fig. 3 for how this was incorporated into the game). This alter-



ation was tested in a second round with four patients, and this time patients were better able to perform the game and needed less instruction from the researcher. Both prototype tests made it clear that the amount of instruction and feedback necessary depends on an individual patient's cognitive level, so levels of feedback and instruction should vary to suit an individual patient.

#### 3.8. Design choice 8: Competition

In this study, the aim of occupational therapists and patients was to discover which aspects are important when developing a game aimed at improving visuospatial search strategies in individuals affected by VSN.<sup>38</sup> An important aspect in this process was the necessity of include an element of competition in order to ensure a motivational effect.<sup>38</sup> Competition has also been described in the literature as an important motivator that increases therapy adherence.<sup>39</sup> The patients differed in opinion regarding how the competitive element should specifically manifest in the game. Most of the patients wished to see their own score and progress upon completion of game, while some patients wanted to compare their own score with that of others. The occupational therapist's hope was that the game could to be used as a measurement instrument to assess the degree of independence of a patient with VSN. A first set-up paper prototype was developed in which a distinction was made between left and right-sided scores, so that the side and extent of a patient's perception of the paintings became clear. Upon completion of the game, the patient could see on which side he or she scored higher.

# 4. General discussion

Augmented reality represents a promising addition to traditional treatments for VSN and can potentially increase patient motivation and natural interactions with the environment. Nevertheless, AR has not yet been widely implemented in Geriatric Rehabilitation. The primary aim of this study was to develop an ARbased scanning training program that will improve visuospatial search strategies in individuals affected by VSN. The main findings of this study can be summarized in eight design choices that together form an AR game: extrinsic motivation, metaphor, nostalgia, independent movement, direct feedback, object contrast, search elements and competition.

Design choice 6 covered the difficulty that some patients with VSN had to understand or see the projected images in the AR environment. Although we saw positive results when certain elements were changed, that did not alter the fact that some patients with cognitive problems may experience problems with understanding the contrast of AR against their own environment or other elements of the game. In the further development of AR based scanning training, the impact of cognitive problems on eligibility of playing the game should be addressed.

Another design choice was to focus on independent movement, which among the many activities of daily living mentioned by patients was a particular wish of the patient group. Literature also confirms that the use of participation outcome measures is very important as a geriatric rehabilitation goal.<sup>40</sup>

All design choices were selected in relation to VST, which is the recommended treatment for VSN,<sup>28</sup> and elements of VST were used as a working theory in the development of the AR game. The most important design choices with regard to VST were the use of a search element and the direct feedback in combination with the activity of moving. While the search element gave the patient the incentive to scan the environment in an agreeable manner, direct game feedback and to control the HoloLens<sup>™</sup> by head movements stimulated head rotation. Both fit well with the goals of

VST.<sup>7</sup> The combination of searching while moving aims to stimulate a change in behavior and encourage scanning during activities of daily living. An advantage of AR is that you can practice in a familiar environment, which hopefully makes transfer to the real world easier. Our hope for the game is therefore that patients internalize a scanning behavior that they then apply outside of the context of the HoloLens<sup>TM</sup>. However, further research is needed to determine the therapeutic effect of the AR game beyond the incorporated VST elements.

Design choice 6 covered the difficulty that some patients with VSN had to understand or see the AR environment. Although we saw positive results when certain elements were changed, that did not alter the fact that some patients have major cognitive problems and may experience problems with this or other elements of the game.

The game was developed using Design Research, which pays particular attention to the evaluation of theories and instruments, encouraging the researcher to clearly define both the research problem space and the solution space before confirmatory studies proceed.<sup>21</sup> One of the major benefits of this process is prototype testing in collaboration with end users in order to design a realistic and technically feasible game.

It is a matter of debate whether the results are generalizable to the larger target group (patients with VSN older than 60) because the research group was small and the qualitative data obtained were interpreted by a single researcher (an occupational therapist). However, co-creation involved the distinct perspectives of various healthcare professionals including twelve occupational therapists and a game design professional. This collaboration undoubtedly resulted in a qualitatively better prototype. The variety of the different professions involved in this study increases the likelihood of implementation in practice because the background of the envisaged end users matches that of the co-developers. Furthermore, the results were first coded and then discussed with two occupational therapists, and the final results were peer examined by four occupational therapists in order to create consensus using the Boeije method.<sup>28</sup>

To the best of our knowledge, this is the first study to focus on the development of an AR game for VSN patients in geriatric rehabilitation. The design choices have contributed to increasing our knowledge and experience regarding the development of AR tools for this target group, specifically those patients with VSN after stroke. Recommendations for further development of the AR game prototype include adding an element of competition, further personalization, and grading (on a physical and cognitive level) to improve ease and motivation for use. This should be followed by an effectiveness study to determine whether the game represents a worthwhile addition to visual scanning-based therapy for patients with VSN.

# 5. Conclusion

This study produced a prototype AR game for people with VSN after stroke. The design thinking methods applied here resulted in the following design choices: extrinsic motivation, nostalgia, metaphors, direct feedback, independent movement, contrast of objects, search element and competition.

Study output consists of an AR game in which the patient searches for virtual nostalgic images projected onto a wall as in a museum, and during the game the patient is encouraged to scan the environment while moving around. The AR game and method used illustrate the promising role of AR tools in geriatric rehabilitation, specifically those aimed at increasing the independence of patients with VSN after stroke.

## 6. Authors' contributions

MB is the principle investigator and contributed to all aspects of the research. MB and NB are responsible for the acquisition of the data. MB did the data analysis. MB, NB, TN, MH, WA and NC interpreted the data. NC is responsible for the concept, design, and for revising the manuscript. MB had full access to all data in the study and takes responsibility for integrity of the data and accuracy of the data analysis. MB, MH, NB, TN and WA prepared the manuscript. All authors read and approved the final manuscript.

#### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

# Acknowledgements

I would like to thank Derek Kuipers (Game Design Professional) and Robert Terpstra (student Communication and Multimedia Design) for helping develop the AR game, Ellen Witteveen for mutual feedback during the research period, the lecturers at NHL-Stenden University of Applied Science who furnished me with the knowledge and skills to carry out this Design Research, and Omring (GRZPLUS) to giving me the opportunity to carry out this study. Most importantly, I would like to express my gratitude to the many patients and colleagues who participated in this research for their input and their valuable contributions to the design and testing of the AR game.

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