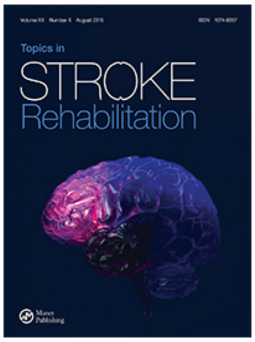


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ARTICLE

# Cognitive training in an everyday-like virtual reality enhances visual-spatial memory capacities in stroke survivors with visual field defects

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**ABSTRACT**

**Objectives**: Visual field defects due to hemi- or quadrantanopia after stroke represent an under-recognized neurological symptom with inefficient instruments for neurorehabilitation to date. We here examined the effects of training in a virtual reality (VR) supermarket on cognitive functions, depressive symptoms, and subjective cognitive complaints in patients with hemianopia/quadrantanopia and healthy controls.

**Methods**: During a 14-day rehabilitation program, 20 patients and 20 healthy controls accomplished a real-life-like shopping task in a VR supermarket. A comparison between pre- and post-training standard neuropsychological measures, depressive symptoms, and subjective memory complaints allowed us to assess a putative transfer of rehabilitation effects from the training tasks to specific cognitive functions.

**Results**: The results indicate that VR training may improve performance not only in the trained task but also in specific neuropsychological functions. After the training, both patients and controls showed improved performances in visual scanning, mental rotation, visuoconstruction, and cognitive flexibility. Moreover, depressive symptoms were attenuated in both groups. In the patient group compared to the control group, the training particularly resulted in improved visual memory retrieval and reduced memory complaints.

**Conclusions**: The results of the current study suggest that VR training can improve particularly visual-spatial skills in patients with hemianopia or quadrantanopia. Our study thus introduces an interesting novel treatment approach to improve cognitive functions relevant to daily life in stroke patients with visual field defects.

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**KEYWORDS**
Stroke; rehabilitation; hemianopia; neuropsychology; cognition

## 1. Introduction

Visual field defects due to hemianopia are typical neurological symptoms following stroke. They are caused by a lesion in the visual pathway resulting in impaired vision or blindness in half of the visual field, most commonly on the left or right side of the vertical midline. In less than 10 percent of stroke patients, only one quadrant of the visual field is affected (quadrantanopia), dependent on the specific location and extent of the respective brain lesion.[1,2] Due to these visual field defects, stroke patients with hemianopia and quadrantanopia also exhibit pronounced deficits in cognitive tasks that require intact visual or spatial processing such as visual scanning or visual memory. A prominent example could be a stroke patient with right-sided hemianopia who shows poor performances in a visual scanning paradigm because target parameters in the right visual field cannot be detected. Unfortunately, spontaneous recovery from hemianopia can be expected in less than 50 percent of patients within the first 3–6 months post-stroke.[3] In many patients, the symptoms persist and severely impede daily life activities associated with visual or spatial functions (e.g. [4,5,6,7]), such as reading, orientating, driving, shopping, cooking, or even walking (due to an increased risk to fall). Overall, vision problems after stroke appear to severely reduce the quality of life[8] as being reflected by depressive symptoms.[9]

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Supplemental data for this article can be accessed publisher's website

While acute stroke treatment is highly efficient and widely established[10], recovery enhancement in the subacute phase of a stroke and subsequent improval of neurological symptoms represents an important unmet need in the overall therapeutic management of these patients.[11] Complex neurological symptoms as hemianopia are not only difficult to diagnose but treatment is often suboptimal including a lack of innovative methods and concepts. In fact, evidence from randomized controlled trials (RCT) regarding the therapy of hemianopia and related visual-spatial dysfunctions is scarce and therapeutic opportunities are therefore limited. The application of peripheral prism glasses was shown to help avoiding obstacles when walking (compared to sham glasses), resulting in an improved mobility of the patients.[12] Besides this purely symptomatic treatment approach, visual scanning or eye-training paradigms have been developed over the last years. A recent RCT showed improved vision-related quality of life in patients treated with a daily visual scanning training of 30 min for 6 weeks compared to untreated controls and patients treated with prism glasses.[13] In another recent RCT, a horizontal scanning training paradigm improved the detection of peripheral stimuli and avoidance of obstacles when moving around.[14] Again, no evidence was found for an improvement in visual functions, reading, or searching for targets on a display.

Taken together, there is a lack of therapeutical options for patients with hemianopia or quadrantanopia, so that new innovative approaches are urgently needed. One promising approach is training in a virtual environment, since more reality-like training activities involve complex interactions between higher-level cognitive operations. In fact, positive effects of virtual reality (VR) training for stroke survivors were consistently reported by previous research (e.g. [15,16]) For stroke patients with hemianopia or quadrantanopia, however, it remains unclear whether VR training may improve cognitive skills, which is at least partly dependent on the demands of the training tasks and the technical features of the VR device.

### 1.1. Objectives

In a 14 days rehabilitation program, we, therefore, used a 3D VR device that allowed spatial orientation in a 360 degrees virtual supermarket. The idea behind choosing a supermarket task was the possibility to simulate a real-life-like everyday scenario involving different cognitive functions. In fact, shopping skills are regarded as a key indicator of everyday cognitive performance and were related to various cognitive sub-functions in different patient groups.[17–19] During the training sessions, participants had to look in all directions to be able to find and buy products from a previously presented shopping list. The task poses high challenges on orientation and navigation skills, which again involve multiple visual-spatial sub-functions such as visual scanning, visual-spatial memory, and visual-spatial attention. Repeated training of navigation and orientation in a 3D virtual supermarket may thus improve specific visual-spatial functions as well. In the current study, we examined the possible benefits of VR training for stroke survivors with visual field defects due to hemi- or quadrantanopia. Thereby, we did not focus on visual field recovery but on the positive effects of VR training on cognitive functioning. Importantly, a comparison between pre- and post-training neuropsychological measures allowed us to assess a transfer of rehabilitation effects from the training tasks to basic cognitive skills. Another aim of the study was the examination of training-related changes in patient-reported outcome measures such as self-reported memory complaints and depressive symptom severity. Specifically, we hypothesized that training in our VR paradigm may improve cognitive functions associated with navigation and orientation (i.e. visual scanning and visual memory) in stroke patients with hemi- or quadrantanopia. Moreover, we assumed that VR training could lead to a reduction of memory complaints and depressive symptoms in these patients as well.

## 2. Methods

### 2.1. Participants

The current study included 20 stroke patients with hemi- or quadrantanopia and 20 healthy controls, matched with respect to age and education. Patients were recruited in the Neurology Department and the Ambulatory Rehabilitation

Department of the Bethel Hospitals in Bielefeld, Germany. Inclusion criteria were: diagnosis of hemianopia or quadrantanopia after stroke, age ≥18 years, post-stroke IQ ≥85, good knowledge of the German language, stroke incidence within the last 6 months, and infarction in the territories of the medial (posterior parts) and posterior cerebral arteries as being indicated by MRI. All patients were independently evaluated by neurologist and neuropsychologist. Every assessment included clinical examination and line bisection testing to disclose spatial neglect. If necessary, line cancellation testing was used. In addition, all patients were tested for motor and sensory neglect. The visual field was primarily examined using the perimetry test to establish the diagnosis of hemianopia- or quadrantanopia. If necessary an ophthalmological examination using an automated perimetry test (Goldman) was performed. Infarction was restricted to medial (posterior parts) and posterior territories since only lesions in these parts of the brain usually result in hemi- and quadrantanopia. Exclusion criteria were neglect, claustrophobia, aphasia or other language disabilities, and severe psychiatric or other medical comorbidities. Eighteen of the 20 patients were diagnosed with hemianopia; two patients were diagnosed with quadrantanopia. Stroke was ischemic in 18 patients, hemorrhagic in one case, and combined ischemic and hemorrhagic in another one. In nine patients, stroke was right-sided, and left-sided in 11 patients. Fourteen patients had posterior lesions, five patients had combined medial and posterior lesions and one patient additionally had older frontal and basal lesions. None of the patients had motor impairments. Control participants were recruited via a local advertisement in public buildings and received an allowance of 50 € for study participation. Demographic data of patients and controls are summarized in Table 1. All participants gave written informed consent. The study was in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Münster University and the State Medical Board, Germany (2010-523-f-M). The reporting of this study conforms to the STROBE guidelines (www.strobe-statement.org) and the STROBE checklist can be found in the supplemental material.

### 2.2. Study design

The study protocol comprised a VR training program in a virtual supermarket[20] as well as neuropsychological and clinical assessments before and after the training program.

### 2.3. VR training program

The training program (Figure 1) required the participants to learn a shopping list (learning task) and to subsequently buy the respective products of this shopping list in a VR supermarket environment (supermarket task). In the learning task, participants had to memorize and recall an auditorily presented shopping list with 20 products. In the supermarket task, participants were asked to enter the VR supermarket and to buy as many products of this shopping list as possible. The shopping list was the same in all sessions. There was no time restriction for each VR session, but participants were instructed to accomplish the task as fast as possible.

The supermarket task poses high challenges on multiple cognitive sub-processes such as navigation and orientation, visual memory, visual scanning/search, planning, cognitive flexibility, and spatial attention. For example, participants had to look in all directions to be able to find specific items of the shopping list being distributed in the supermarket. Consequently, performance parameters in the VR supermarket included the number of correctly bought products, the shopping time (in seconds) and the covered distance (in meters). Moreover, the verbal recall performance in the learning task was recorded.

Overall, the training program included six sessions involving both learning and supermarket

**Table 1.** Study sample characteristics and demographics.

| | Controls | Stroke patients | P Value |
|---|---|---|---|
| N | 20 | 20 | |
| Sex (female/male) | 16/4 | 6/14 | .004 |
| Mean age (SD) in years | 56.9 (22.2) | 59.3 (16.0) | .723 |
| Minimum/maximum age in years | 26–94 | 34–82 | |
| Mean years of education (SD) | 15.1 (3.6) | 13.0 (2.5) | .079 |
| Minimum/maximum educational years | 10–21 | 8–19 | |

(SD standard deviation).

tasks (sessions 1–6). In two additional sessions, the supermarket task was accomplished with presenting a distractor list before (session 7) and without presenting a list before (session 8) to get information about the stability of learning effects (not part of the current work).

The whole training program was accomplished within 14 days. There was a maximum time interval of 48 h between sessions 1–6 and a maximum interval of 24 h between sessions 6–8.

#### 2.3.1. Virtual environment

The VR supermarket was designed as a real, medium-sized supermarket (25 m × 25 m). Overall, more than 50,000 different products were available involving different types, brands, and quantities. All products were designed similar to original labels. Real supermarket sounds were presented as low background noise during the VR shopping.

#### 2.3.2. VR device

The VR supermarket task was presented on a 360°-VR device, the OctaVis that is technically described in detail elsewhere.[21] In the OctaVis, the subject is placed on a swivel chair fixed in the center of a ring of eight LCD-touch-screen monitors (Figure 2). By rotating the chair, the subject determines the direction of movement in the VR. Additionally, a "throttle joystick" (Metallux, Korb, Germany, www.metallux.de) installed on the chair's arm-rest is used to move in the VR (i.e. moving forward, backward, and sideward). Typically, the dominant hand was used in the control group as well as in the stroke patients. Selecting products is realized by tapping the respective item on the touch-screen. All visible products in the supermarket could be selected and each selected product disappeared from the screens. Residual items of the same product remained visible to the participants, since each product is available in multiple units. Selecting a product was confirmed by an electronic sound of cash register. Before the VR training, participants were familiarized with the VR device and obtained practice trials until the technical handling was understood.

### 2.4. Neuropsychological assessment

Neuropsychological assessment included standard neuropsychological tests covering different cognitive domains (i.e. memory, attention, executive functions, visual-spatial functions) including domains known to be associated with the cognitive demands of the VR task (e.g. navigation and orientation). All participants were assessed before and after the VR training (using parallel test forms, if available).

To assess visuoconstruction and planning as well as intermediate (3 min) and long-term (30 min) visual-spatial memory, we applied the Rey-Osterrieth Complex-Figure (ROCF,[22]) and the Taylor Complex Figure Test (TCFT.[23]) These tests involve the direct copy of a complex two-dimensional figure and its unexpected retrieval from memory after a given delay.

Attentional functions as alertness and visual scanning were assessed by subtests of the computer-based Test of Attentional Performance (TAP.[24]) In the alertness subtest, participants had

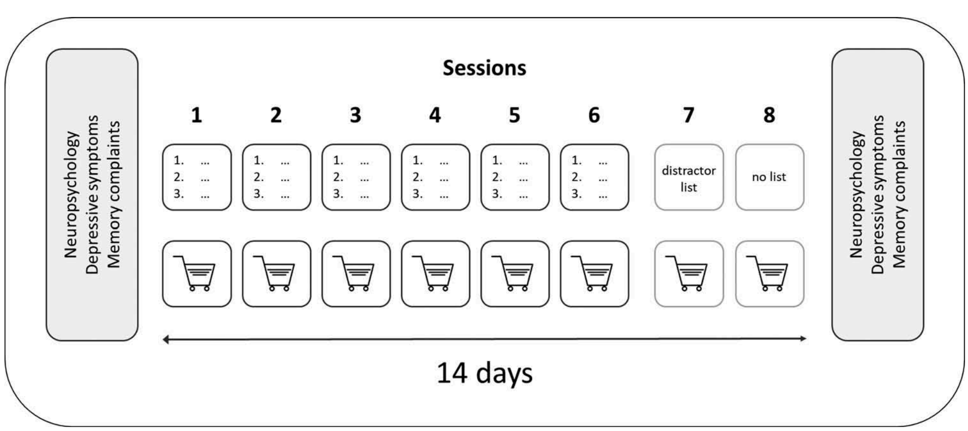


**Figure 1.** Training program.

Figure 2. The OctaVis VR training device in experimental (left) and baseline (right) mode.

to press a button as quickly as possible in reaction to a cross on the monitor. In the visual scanning subtest, it has to be decided as fast as possible by button press whether a certain target stimulus was part of a symbol matrix (critical trials) or not (non-critical trials).

To assess verbal short term and working memory, the Digit Span task [forward and backward] of the Wechsler Memory Scale-Revised (WMS-R[25]) was used, which requires the participant to repeat increasing sequences of digits in forward and reverse order, until two consecutive sequences of the same length are incorrect.

For the assessment of nonverbal short term and working memory, we applied the Corsi block-tapping test[26] measuring the maximum length of a sequence of spatial target locations that can be reproduced correctly on a board with nine different locations in total.

Executive functions as phonematic verbal fluency (K-/M-words) and cognitive flexibility (G/R-words and H/T-words, respectively) were assessed with the Regensburg Word Fluency Test (RWT.[27]) In these tests, participants are required to generate as many words as possible in 1 min beginning with predefined or changing initial letters.

The Bergen Right-Left Discrimination Test (BRLD) was applied to measure visual-spatial abilities covering low (BRLD-A[28]) and high demands (BRLD-B[29]) on mental rotation and left-right discrimination skills. The BRLD-A consists of sequences of stickmen of which either the front or the back side is shown and which differ in varying arm positions. Within 90 s, participants have to mark the left (or the right) hand of each stickman with a pencil. The same procedure applies to the BRLD-B. However, the BRLD-B requires more mental rotation skills, because the stickmen are additionally displayed from upside-down here.

For all tests, except for attentional sub-functions (TAP), a higher score reflected better performance. In the TAP subtests, higher scores reflected poorer performance since reaction times were collected for further analyses.

### 2.5. Clinical measures

In addition, subjective memory complaints (Memory Assessment Clinics Questionnaire, MAC-Q[30]) and the severity of depressive symptoms (Beck Depression Inventory, BDI-II[31]) were assessed. The MAC-Q involves six questions related to memory function in daily activities (e.g. “Recalling where you have put objects in your home or office”). The BDI-II includes 21 items covering various depression symptoms, such as sadness, hopelessness, self-blame, restlessness, or suicidality. In the MAC-Q, higher scores reflect more severe memory complaints. In the

BDI-II, higher scores reflect more severe depressive symptoms.

### 2.6. Statistical analysis

Data were analyzed using SPSS Statistics, version 20.0. The general significance level was set to $\alpha = .05$ and two-tailed.

Within- and between-group differences were assessed using Wilcoxon- and Mann-Whitney-U Tests, because of a non-normal distribution in numerous variables (according to a Kolmogorov-Smirnov-Test). To examine the effects of the VR training on standard neuropsychological measures, depressive symptoms, and memory complaints, two-way repeated measures analysis of variance (ANOVA) were performed. Between factor was group (patients versus controls) and within factor was training (pre versus post training). In case of significant interaction effects, Bonferroni-adjusted post-hoc-tests were performed with an $\alpha = .025$ to specify the effects. If not all of the assumptions were met, corresponding non-parametric analyses were run.[32] Appropriate effect size measures were computed ($\eta_p$, $r$, Cohens $d$; effect size interpretation: minimum effect $\eta_p = .04/r = .20/d = .41$; moderate effect $\eta_p = .25/r = .50/d = 1.15$; strong effect $\eta_p = .64/r = .80/d = .2.70$[33])

## 3. Results

All descriptive statistics, detailed results of the within- and between-group analyses as well as the repeated measures ANOVAs can be found in the supplementary material (Tables S1–S3).

### 3.1. VR training performance

Due to the non-normal distribution of training variables, within- and between-group comparisons were examined with Wilcoxon- and Mann-Whitney-U Tests. As outlined in Figure 3(a), stroke patients with hemi- or quadrantanopia showed a significantly lower free verbal recall than healthy controls at the first learning trial ($p = .022$, $r = .36$, Table S1).

Both groups increased their performance across the course of the training (healthy controls:

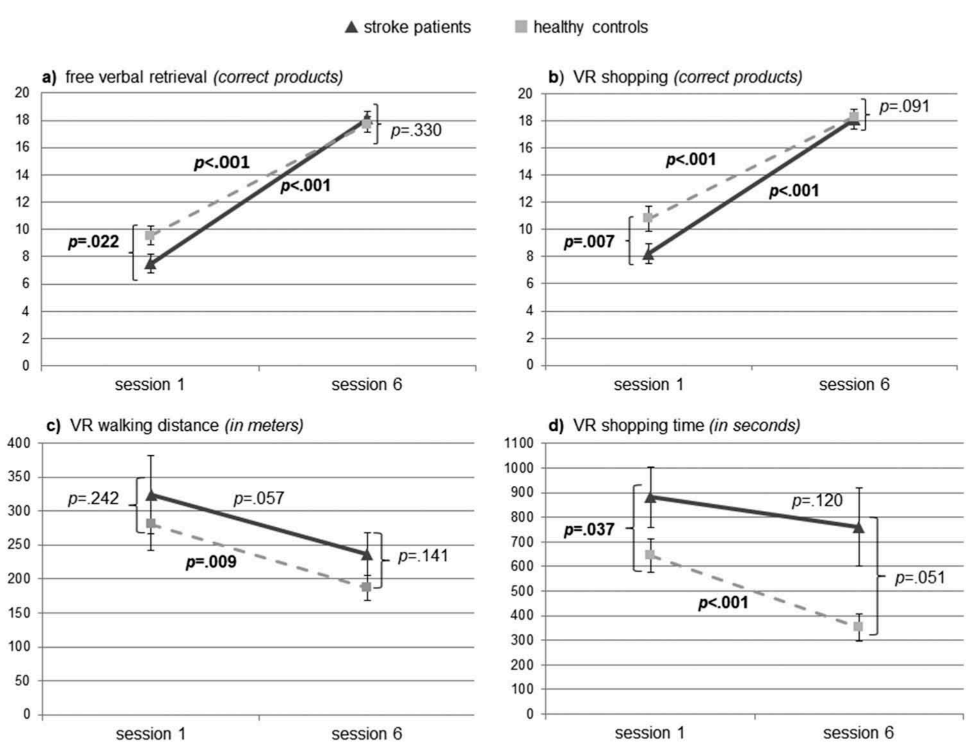


Figure 3. Virtual reality training (VR) performances (first and last learning session) of patients and controls for free verbal retrieval of correct products (a), correctly bought products (b), walking distance (c), and shopping time (d). Means and standard errors of the mean are displayed.

$p < .001$, $r = .62$; patients: $p < .001$, $r = .61$) and showed the same performance level at the last learning trial ($p = .330$, $r = .16$). The same pattern of results (Figure 3(b)) was evident for the amount of correctly purchased products in the VR supermarket (trial 1: $p = .007$, $r = .61$; healthy controls: $p < .001$; $r = .61$; patients: $p < .001$, $r = .62$; trial 6: $p = .091$; $r = .28$).

Regarding walking distance in the supermarket (Figure 3(c)), analyses revealed a significant decrease across the learning trials in the healthy controls ($p = .009$, $r = .40$), but only a tendency in the same direction in the patient group ($p = .057$, $r = .33$). There was no significant group differences at the first ($p = .242$, $r = .19$) and the last training trial ($p = .141$, $r = .25$). Contrary to the patient group ($p = .120$, $r = .27$), a significant reduction in shopping time across the learning trials was observed in healthy controls ($p < .001$, $r = .54$). In general, healthy controls required significantly lower shopping times (Figure 3(d)) than the patient group (trial 1: $p = .037$, $r = .30$; trial 6: $p = .051$, $r = .32$).

### 3.2. Neuropsychological performance

For visual memory retrieval after a delay of 30 min, repeated measures ANOVA did not result in the main effects of training ($p = .128$) or group ($p = .587$) (statistical ANOVA parameters are provided in Table S3). However, results revealed a significant training x group interaction ($p = .036$, $\eta_p^2 = .12$), indicating that the VR training program differentially affected pre- and post-training performances of stroke patients with visual field defects and healthy controls. In fact, exploratory post hoc comparisons indicated that the patients group showed significantly improved visual memory retrieval performances after the training ($p = .019$, $d = .60$, Figure 4(a)) and reached a performance level equivalent to that of healthy controls. For immediate visual memory retrieval after a delay of 3 min, results indicated a similar trend (interaction: $p = .059$, $\eta_p^2 = .10$; training: $p = .217$; group: $p = .497$).

For visual scanning (critical trials; TAP), a main effect of group ($p = .029$, $\eta_p^2 = .19$) was evident, but neither a main effect of training ($p = .673$) nor a training x group interaction ($p = .858$). Stroke patients with visual field defects showed slower reaction times in this subtest than healthy controls (Table S2). Results for non-critical trials revealed a marginally significant main effect of group ($p = .051$, $\eta_p^2 = .16$) and a significant main effect of training ($p = .037$, $\eta_p^2 = .18$), indicating that both groups showed better post- than pre-training performance, with higher performance in healthy controls than in the patient group. No training x group interaction was found ($p = .821$).

For cognitive flexibility (RWT), a significant main effect of training was found ($p = .002$, $\eta_p^2 = .23$), indicating that both groups showed better post- than

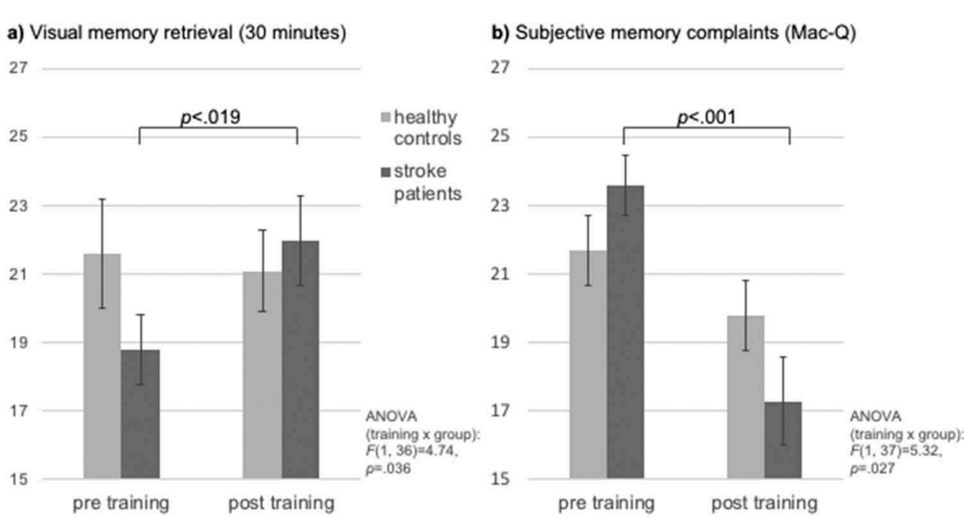


Figure 4. Training x group interactions for nonverbal memory retrieval and subjective memory complaints. Means and standard errors of the mean are displayed.

pre-training performances. There was neither a significant main effect of group ($p$ = .245) nor a significant training x group interaction ($p$ = .590).

Analysis of the RCFT/TCFT figure-copy trial yielded a significant main effect of training ($p$ = .014, $\eta_p^2$ = .16), but no main effect of group ($p$ = .759) and no significant training x group interaction ($p$ = .367), indicating that both groups showed enhanced visuo-constructive performances after the training (Table S2).

For mental rotation measured by the BLRD-A subtest, repeated measures ANOVA resulted in a significant main effect of training ($p$ < .001, $\eta_p^2$ = .49), indicating that both groups showed better post- than pre-training performances. There was neither a significant main effect of group ($p$ = .076) nor a training x group interaction ($p$ = .231). The same pattern was observed for the BLRD-B subtest (training: $p$ < .001, $\eta_p^2$ = .53; interaction: $p$ = .329; group: $p$ = .240), demonstrating that both groups showed a significantly improved mental rotation performance after the training.

For all other neuropsychological tests (alertness, digit span, Corsi task, phonematic fluency) statistical analyses did not reveal significant effects (Table S3).

### 3.3 Clinical measures

#### 3.3.1. Memory complaints

For MAC-Q scores (Figure 4(b)), ANOVA results revealed a significant main effect of training ($p$ < .001, $\eta_p^2$ = .36) and a significant training x group interaction ($p$ = .027, $\eta_p^2$ = .13), but no main effect of group ($p$ = .598). Before the training, self-reported memory complaints were marginally higher in the patient group than in healthy controls, with an opposite pattern after the training. (before: $T$(38) = −1.35, $p$ = .185, $d$ = .43; after: $T$(37) = 1.79, $p$ = .082, $d$ = .57). For the patients group, the extent of self-reported memory complaints was significantly reduced after the training ($T$(18) = 4.43, $p$ < .001, $d$ = 1.50). A respective tendency in the same direction was found in healthy controls ($T$(19) = 1.80, $p$ = .088, $d$ = .42, see Figure 4).

#### 3.3.2. Depressive symptoms

For BDI-II scores, repeated measures ANOVA revealed significant main effects of training ($p$ = .002, $\eta_p^2$ = .25) and group ($p$ = .021, $\eta_p^2$ = .15), indicating that both groups showed a lower severity of depressive symptoms after than before training with healthy controls showing less symptoms than stroke patients with hemi- or quadrantanopia. No training x group interaction was found ($p$ = .182).

## 4. Discussion

In the current study, we examined the possible benefits of a repetitive training in a virtual supermarket environment for stroke survivors with visual field defects due to hemi- or quadrantanopia. Thereby, we did not focus on visual field recovery but on positive effects of VR training on cognitive functions, depressive symptom severity, and memory complaints. Overall, the data show that a real-life-like VR training may improve cognitive performance not only in the training task itself but also in specific neuropsychological domains. Our results thus indicate a transfer from the training of daily life activities to basic cognitive skills and additionally suggest positive effects on depressive symptom severity and subjective memory complaints.

Stroke survivors with hemi- or quadrantanopia and matched healthy controls both showed enhanced performances after the training than before the training. These improvements involved different cognitive sub-functions such as visual scanning, mental rotation, visuoconstruction, and cognitive flexibility. Moreover, depressive symptom severity was reduced after the training in both groups. Since the respective analyses did not reveal interactions between training effects and experimental group, the positive effects may refer to stroke patients and healthy individuals in the same way (main effects of training). However, our results additionally revealed that VR training differentially affected the rehabilitation of visual memory skills with a particular benefit for the patient group (training x group interaction). As Figure 4 shows, visual memory performance in the patient group was higher after the VR training than before. Thereby, patients reached a performance level after the training equivalent to that of healthy individuals. This training effect may be due to the specific demands of the VR training program since participants had to memorize the locations of different products within the supermarket. Healthy individuals, by contrast, showed comparable visual memory performances pre- and post-training, probably because a resource ceiling had already been reached. A similar result pattern was observed for subjective memory complaints. Together, the latter results indicate both a subjective and objective improvement of memory skills in stroke survivors with hemi- or quadrantanopia. In sum, our results revealed positive training effects in several cognitive functions for both the patient and the control group with the patient group specifically benefitting with respect to visual-spatial memory.

Noteworthy, the majority of enhanced cognitive functions involved visual-spatial sub-functions. For example, the current paradigm required the participants to look in all directions in order to search and find specific products. Training of visual search might help to adapt the patients' scanning strategies to their restricted visual field, thus targeting an efficient compensation of the visual field loss. Often hemianopia disrupts normal scanning patterns with patients exhibiting disorganized scan paths resulting in high rates of refixation and inaccurate saccades.[34] It has therefore been proposed that the loss of reentrant pathways from higher visual areas to the damaged striate cortex may result in uncertainty about spatial locations across saccades.[35] Since patients with hemianopia often show a series of small saccades with long latencies into their blind field, training is typically targeted to produce systematic horizontal or vertical scanning saccades into the blind field (oculomotor training).[35,36] Such visual search training usually leads to an enlargement of the region in which subjects can successfully locate a target with eye movements (the visual search field) and to a reduction in response times.[37,38] However, saccades and visual field size were not examined in the current work. Hence, these conclusions remain hypothetical.

A second example for the involvement of visual-spatial functions in the VR training task is mental rotation. Mental rotation may be understood as a visual-spatial cognitive operation that requires an internal spatial manipulation of an object. It has been suggested that mental rotation belongs to the group of those visual-spatial abilities, that are highly relevant for everyday routines[29,39,40] and play an important role in occupational practice.[41,42] With respect to approaches to an everyday and occupation-focused rehabilitation of stroke patients with hemianopia or quadrantanopia, the mental rotation might thus be an interesting target.

Apart from visual-spatial sub-functions, patients and controls showed improved cognitive flexibility after the training program. The program required executive operations including a flexible switch between different products and locations in order to realize a fast and efficient way through the supermarket. Consequently, positive training effects on cognitive flexibility are not surprising.

Finally, the current results indicate that the here applied virtual supermarket training paradigm consistently led to enhanced performances in the training task itself. In fact, important daily activities such as buying correct products, speed of shopping time, and the lengths of walking trajectories in the VR supermarket were found to be improved in both patients and controls. For VR shopping of correct products and verbal recall of the shopping list, patients even reached the post-training level of healthy controls.

## 5. Conclusions and limitations

Taken together, our results revealed positive VR training effects on different (mainly visual and spatial) cognitive sub-functions in both stroke patients with hemi- or quadrantanopia and healthy individuals. Moreover, VR training improved depressive symptom severity and subjective memory complaints in both groups. Specifically, as indicated by training x group interactions, stroke survivors with hemi- or quadrantanopia benefitted with respect to visual-spatial memory and subjective memory complaints. Overall, our results thus indicate a successful transfer from the training of daily life activities to basic cognitive skills and additionally suggest positive effects on depressive symptom severity and subjective memory complaints. We, therefore, propose that VR training approaches may be highly efficient in the rehabilitation of visual-spatial dysfunctions.

However, our study involves a couple of limitations. First, we compared the training effects in stroke patients with hemi- or quadrantanopia only to those of healthy individuals. Adding a control group of stroke patients without visual field defects would have certainly increased the validity of the effects, just as a control group of stroke patients with hemi- or quadrantanopia completing a similar training task that is not VR-based. A second shortcoming of the study involves the unequal sex distribution in the two experimental groups. In fact, previous research points toward sex differences in spatial tasks with male subjects generally showing better performances than female subjects.[43,44] If so, however, group differences and training effects in our study are rather underestimated (i.e. more female participants in the control group and more male participants in the patient group). Thirdly, we focused on the positive effects of VR training on cognitive functioning. A quantification of visual field defects could have allowed more valid conclusions about possible training effects on visual field recovery.

Despite these limitations, however, our study represents an interesting novel treatment approach to improve daily-life relevant cognitive functions in stroke patients with hemi- or quadrantanopia. Further studies should focus on repetitive training cycles to assess a potential "dose" of VR training and its timing with relation to stroke onset in order to optimize the regenerative potential of the treatment as well as long-term outcomes.

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