

# **Spatial neglect therapy with the augmented reality app “Negami” for active exploration training – A randomized controlled trial on 20 stroke patients with spatial neglect**

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## **Short Running Head**

Spatial neglect therapy with the AR-based app “Negami”

## Abstract

**Objective:** To investigate the efficacy of the augmented reality (AR) app “Negami” as an active exploration training for the treatment of spatial neglect. Improvements of the ipsilesional attention and orientation bias (and resulting contralesional neglect) will be examined in stroke patients with spatial neglect and compared to a control group.

**Design:** Randomized controlled trial with an experimental *Negami* group, consisting of patients with spatial neglect, and a group of neglect patients receiving standard neglect therapy.

**Setting:** Three rehabilitation hospitals.

**Participants:** Twenty right hemispheric stroke patients with spatial neglect.

**Intervention:** Over a period of two weeks, both groups received five training sessions per week (à 25 minutes). Neglect behavior was assessed weekly over a five-week period, with the *Negami* therapy group receiving a second follow-up assessment at one-to-two-month intervals after completion of training.

**Main outcome measures:** Letter Cancellation, Bells Test, Copying Task, Line Bisection Task, and a self-developed ‘Exploration Test’.

**Results:** Both groups improved significantly. While the *Negami* therapy group improved in four of five neglect tests used, the standard therapy group improved in only one of these tests. We observed significantly better improvement in the *Negami* group already after the first week of training. This difference was also significant after the end of the training as well as one week after the end of training and remained stable one to two months after the end of treatment.

**Conclusion:** *Negami* can be used as an effective alternative or addition to current standard neglect therapy, and may even be superior to it.

**Trial Registration** at “OSF Preregistration”, Registration DOI:

<https://doi.org/10.17605/OSF.IO/H6XN5> and at WHO approved public trial registry “German Clinical Trials Register”, DRKS-ID: DRKS00031446

**Keywords**

Spatial neglect; gamification; augmented reality; visual exploration training; rehabilitation; stroke

## 1. Objective

Spatial neglect is the dominant cognitive disorder following right hemispheric brain damage in humans<sup>1,2</sup>. Typically, it is evoked by strokes in the right middle cerebral artery region that damage the perisylvian network, consisting of the superior/middle temporal, parietal, and ventrolateral frontal cortex. Such patients act as though the left side of space has vanished. The patient's eyes and head are sustainedly oriented to the side of the brain lesion, which is typically the right side<sup>3-5</sup>. The patient's visual and tactile exploration activity is shifted to the right side; information located on the left side is disregarded. Thus, many approaches to treating spatial neglect focus on performing exercises and tasks that stimulate patients to actively orient toward the side that is being neglected, such as, e.g., visual searching and picture description tasks, or reading and copying tasks<sup>6-10</sup>. The described therapeutic approach is known as "visual exploration training" or "visual scanning training" and aims to increase exploration movements and compensating search techniques, which shall improve neglect behavior in everyday scenarios.

The visual exploration training seems to be particularly effective when the active eye and head movement is combined with an active rotation of the trunk in the same direction<sup>11</sup>. Wiart et al. (1997) found significant improvements in neglect symptoms with both acute and chronic neglect who received this combined exploration therapy compared to controls. Their finding was in line with studies that had observed that proprioceptive stimulation by trunk rotation or the vibration of posterior neck muscles reduce spatial neglect and thus may have an additional effect on the efficacy of neglect treatment<sup>12-14</sup>. The augmented reality (AR)-based app *Negami* represents an attractive new tool that builds on these findings<sup>15</sup>. It is based on the principle that patients are playfully motivated to orient themselves to their neglected side of the real room by (a) following and (b) searching for a virtual element (an origami bird), actively exploring space by turning their eyes, head, and trunk. *Negami* uses the principle of AR in which the visual, real world is augmented by a virtual figure via a video camera of an electronic device such as a tablet.

The aim of the present study was to investigate the effectiveness of using the app *Negami* for the treatment of spatial neglect. For this purpose, a randomized, two-arm therapy study should be conducted with an active control group receiving standard treatment of spatial neglect therapy in three different rehabilitation facilities. Our goal was to enrich the established visual exploration trainings by an innovative new offer, encouraging patients in a playful way to actively explore space by turning their eyes, head, and trunk.

## 2. Material and Methods

### 2.1 Participants

Without exception and independent of any clinical, demographic or other variables, every patient who met the diagnostic criteria (see below) was included in the study. Twenty patients with right-sided stroke and spatial neglect participated after the exclusion of one patient who was transferred to another hospital for treating hydrocephalus. Patients were recruited from three different rehabilitation facilities (Schmieder-Klinik, Stuttgart-Gerlingen, Germany [n = 14 patients], Neurological Rehabilitation Center Quellenhof, Sana Kliniken AG, Bad Wildbad, Germany [n = 5 patients], Kreiskliniken Reutlingen, Reutlingen, Germany [n = 2 patients]) and were randomly assigned to either the experimental *Negami* therapy group or the standard neglect therapy group (n=10 each). Simple randomization was performed using a time criterion<sup>16</sup>: the first ten patients admitted to any of the three participating rehabilitation facilities were assigned to the experimental *Negami* therapy group and the next ten patients admitted to any of the three rehabilitation facilities to the standard neglect therapy group. Demographic and clinical details are given in Table 1. Beyond spatial neglect (see below), neurological examination revealed that all patients suffered from contralesional hemiparesis; the ipsilesional extremities were not affected by sensory or motor dysfunction in any patient. Structural imaging was acquired by computed tomography (CT) or magnetic resonance imaging (MRI) as part of the clinical routine procedure carried out for all stroke patients in the acute phase at stroke-onset (see supplementary material). For MRI, we used the FLAIR scans. Lesion maps were normalized into  $1 \times 1 \times 1 \text{ mm}^3$  MNI space using SPM (<https://www.fil.ion.ucl.ac.uk/spm>) and the Clinical Toolbox<sup>17</sup>. Patients with tumors or patients in whom scans revealed no obvious lesions were not included. All participants gave their informed consent to participate in the study, which was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki.

**Table 1.** Demographic and clinical data of all 20 right brain damaged neglect patients.

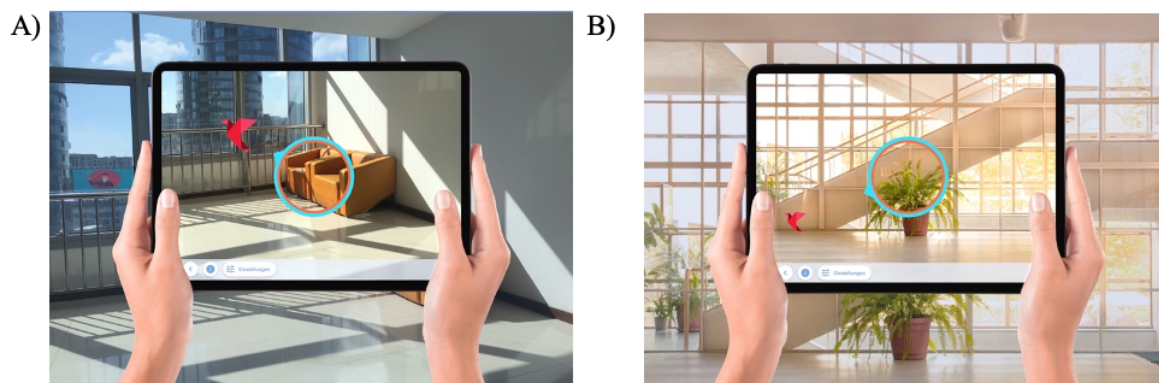
|                                    | <i>Negami</i> therapy group | Standard neglect therapy group |
|------------------------------------|-----------------------------|--------------------------------|
| Number                             | 10                          | 10                             |
| Sex (M/F)                          | 8/2                         | 6/4                            |
| Age (years)                        | 61.3 (15.2)                 | 60.7 (12.45)                   |
| Etiology                           | 5 infarcts, 5 hemorrhages   | 4 infarcts, 6 hemorrhages      |
| Post-stroke interval (days)        | 138.4 (192.1)               | 84 (33.86)                     |
| Contralesional paresis (% present) | 100                         | 100                            |
| Upper extremity                    | 100                         | 100                            |
| Lower extremity                    | 80                          | 70                             |
| Letters cancellation test (CoC)    | 0.42 (0.28)                 | 0.49 (0.29)                    |
| Bells test (CoC)                   | 0.38 (0.29)                 | 0.34 (0.3)                     |
| Copying task (N omitted)           | 4.4 (1.51)                  | 4.3 (1.64)                     |
| Line bisection (EWB)               | 0.33 (2.5)                  | 0.23 (0.17)                    |

Data are presented as mean (SD); CoC, Centre of Cancellation<sup>18</sup>; EWB, Endpoint weightings bias<sup>25</sup>.

The inclusion criterion for this study was the presence of spatial neglect as a result of brain damage caused by right hemispheric stroke. In addition to clinical behavioral observations, diagnostic criteria had to be met in at least two of the following four neglect tests: The Letter Cancellation Test<sup>20</sup>, the Bells Test<sup>21</sup>, a Copying Task<sup>22</sup>, and a Line Bisection Task<sup>23</sup>. Since the effects of changing the presentation format and size from paper-pencil procedures to digital formats with regard to neglect behavior and severity indices were observed to have no effect on the quantification of spatial neglect<sup>24</sup>, all four neglect tests were performed on a Samsung S7+ tablet with screen dimensions 285x185mm. The severity of spatial neglect in the cancellation tasks was determined by calculating the center of gravity of the target stimuli marked in the search fields, i.e. the Center of Cancellation (CoC; <sup>18</sup>). A CoC value  $\geq 0.08$  indicated left-sided spatial neglect<sup>18</sup>. The Copying Task consisted of a complex scene consisting of four objects (fence, car, house, tree), points were assigned based on missing details or whole objects. One point was given for a missing detail, two for a whole object. The maximum number of points is therefore eight. A score higher than 1 (i.e.  $> 12.5\%$  omissions) indicated spatial neglect<sup>22</sup>. In the Line Bisection Task<sup>23</sup>, patients were presented with four different line lengths eight times each, i.e. 32 lines in total. The cut-off value for spatial neglect was an ‘endpoint weightings bias (EWB)’ value  $\geq 0.07$ <sup>25</sup>.

## 2.2 The “Negami” App

The “Negami” App was developed for use on a tablet but could also be used on a mobile phone<sup>16</sup>. For the present experiment, we used an Apple iPad Pro 12.9” 3<sup>rd</sup> generation. The app allowed to add (augment) a virtual element (origami bird) to the video stream produced by the camera of the tablet. More detailed information on the technical implementation and design of the app can be found in Stammler et al. (2023). The “Negami” app provides two different tasks (Task A “Follow the bird”, Task B “Find the bird”; see Fig. 1) that each participant performed in succession while using arm movements in combination with trunk rotations (for more detailed descriptions of the tasks and difficulty levels see supplementary material). An example patient performing the *Negami* tasks can be seen here: [https://youtu.be/fyZ\\_PVWljp4](https://youtu.be/fyZ_PVWljp4) or in Stammler et al. (2023) at Multimedia Appendix 2. Users of the *Negami*-App can hold the tablet either ambidextrously from the right and left (cf. Fig. 1) or centrally from the top or bottom while performing the tasks. An optional Velcro hand strap can be attached to the back of the tablet to relieve the strain of holding the tablet with one hand.



**Figure 1.** (A) Task A “Follow the bird”. The patient has the task to follow the flying origami bird and to keep the bird within the orange/blue circle. (B) Task B “Find the bird”. The patient has to search for the bird that has been hidden by the therapist somewhere in the surrounding room (here: at the corner located at the foot of the stairs) and has to transfer it into the orange/blue circle.

## 2.3 Procedure

### 2.3.1 Intervention

Over a period of 2 weeks, the neglect patients of the *Negami* therapy group received five training sessions per week, using the *Negami* app. Each session lasted about 25 minutes. They completed Task A in the first half and Task B in the second half of each training session. The

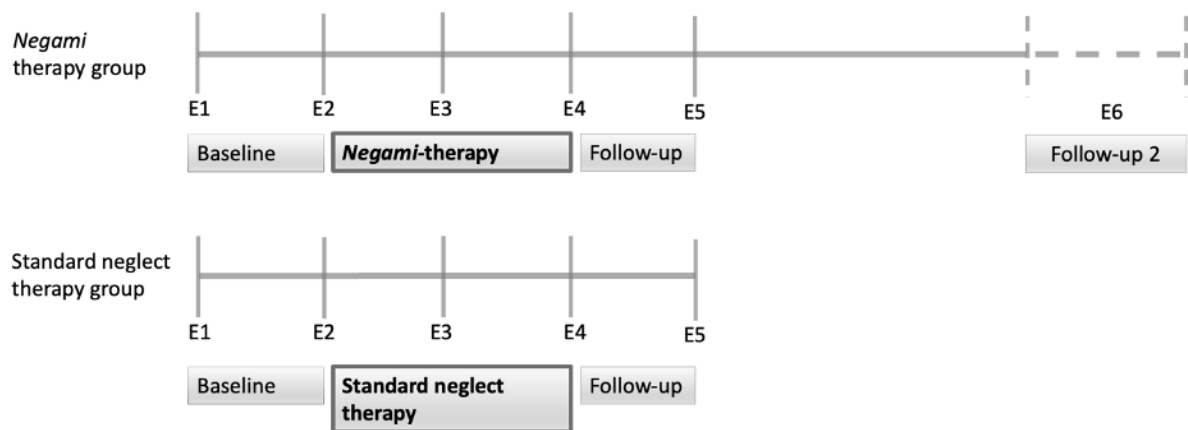
first training session always started with the lowest difficulty level. If the difficulty level was increased in the course of the training, the training session on the following day always started with the training level at which the training was stopped the day before. The criterion for success in advancing to the next difficulty level was that the task was successfully completed three times in a row. The return to a lower difficulty level was indicated when the task was not solved two times in a row. In order to avoid patient frustration when the tasks were not solved, Task A was automatically terminated after 30 seconds if the bird completed its trajectory and the patient did not manage to transfer it into the circle. For Task B, the task was automatically terminated after 90 seconds. The termination was scored as an unsolved task. The neglect patients of the standard neglect therapy group received the standard treatment for neglect of the respective rehabilitation institution by the corresponding neuropsychologist. This treatment consisted in all facilities of five training sessions per week, performing a standard smooth pursuit eye movement training and visual exploration therapy. For smooth pursuit eye movement training, patients were presented with clouds of dots on a computer screen that moved slowly at 5-10°/s from ipsilesional to contralesional. The patients had to follow the moving dots with their eyes. For visual exploration therapy, exercises such as reading and copying tasks, image description and search tasks were performed which required the patients to actively orient themselves to their contralesional side. Each session lasted about 25 minutes.

### 2.3.2 Diagnostic examinations

Before and after intervention both groups were examined five times overall (cf. Fig. 2), using the four diagnostic neglect tests (Letter Cancellation, Bells Test, Copying Task, Line Bisection Task) described above. In addition, a fifth test was developed and performed in all but the first two (due to ongoing development) included patients. Similar to *Negami* Taks B (see above), in this latter diagnostic task the patient was instructed to find the hidden bird. However, in this task (termed ‘Exploration Test’) no bird was hidden but exploratory movements of the patient were recorded, allowing to calculate mean dwell time of the corresponding viewing angle degree of the space surrounding the neglect patient.

Two of the five diagnostic examinations were performed before the start of intervention, allowing to control for spontaneous recovery (Fig. 2; E1 and E2). After the first week of training, a third examination was performed (Fig. 2; E3). After the end of the intervention, the patients of both groups were examined two further times: immediately after and one week after the end of the training (Fig. 2; E4 and E5). Additionally, the *Negami* therapy group was examined at a time interval of one to two months after completion of training (Fig. 2; E6).





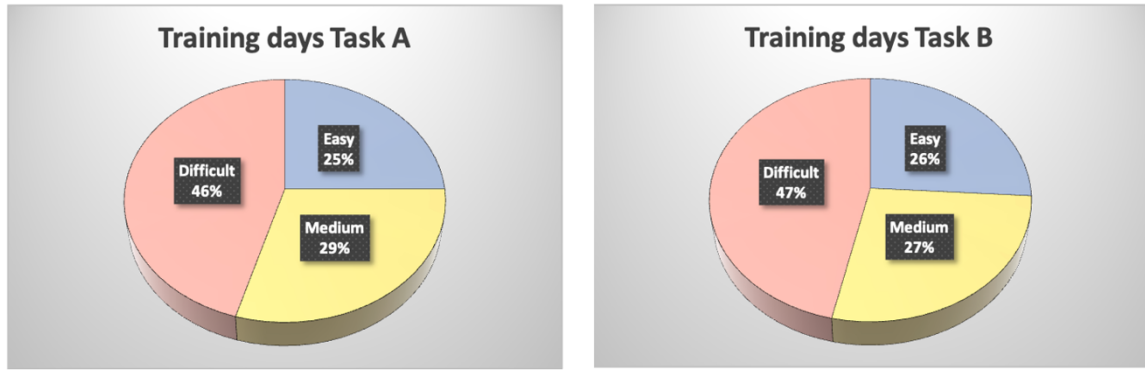
**Figure 2.** Experimental design. Five diagnostic examinations (E1 to E5) were performed weekly in both the *Negami* therapy group and the standard neglect therapy group. Additionally, the *Negami* group was examined at a time interval of one to two months after completion of training.

### 3. Results

#### 3.1 Descriptive results of the training with *Negami*

Patients from the *Negami* therapy group completed most days of the two-week training period at the highest level of difficulty (cf. Fig. 3). With the last training session 8 of 10 patients from the *Negami* group reached the difficulty level "difficult" in Task A; two of 10 patients reached the level "medium". Within the two-week training period, three of the patients from the *Negami* group had to return once to a lower difficulty level because they did not solve Task A at a certain level of difficulty two times in a row. On average, for Task A, difficulty level "medium" was reached after 2.8 (SD=0.92) training days and the difficulty level "difficult" after 4.9 (SD=2.2) days.

In Task B, 9 of the 10 patients from the *Negami* group reached the level "difficult" with the last training session; one of 10 patients made it to the level "medium". None of the patients had to return to a lower difficulty level during the period of therapy. On average, the difficulty level "medium" in Task B was reached after 3.3 (SD=1.49) training days and the difficulty level "difficult" after 6.2 (SD=2.2) days.

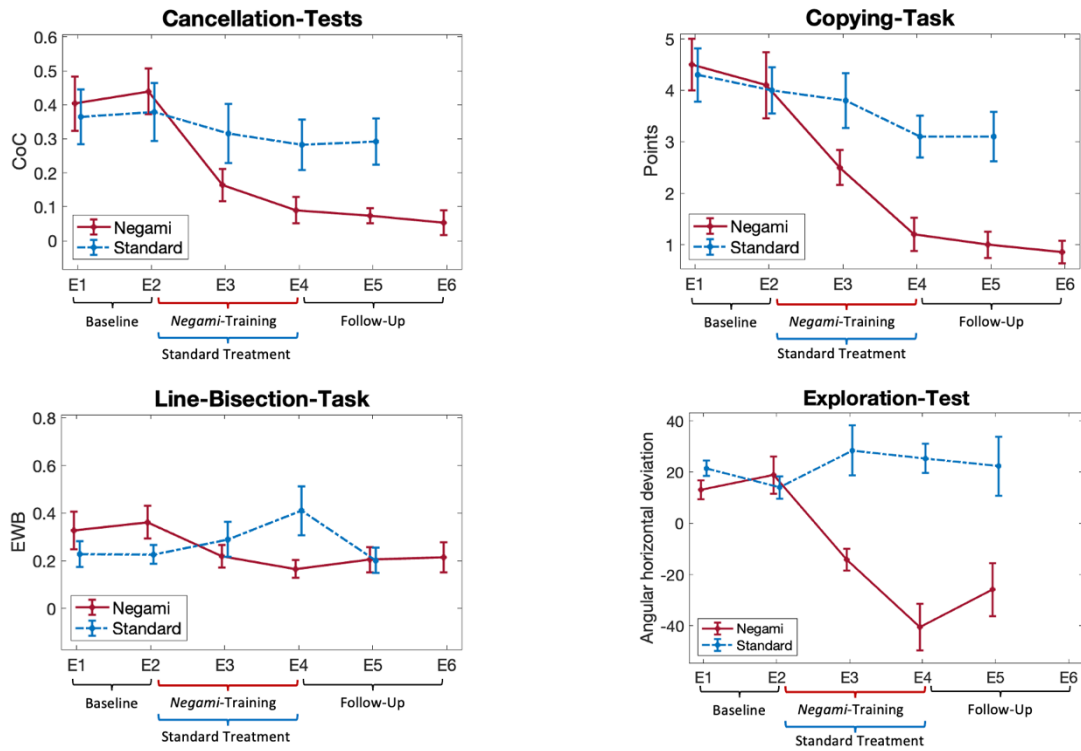


**Figure 3.** Relative number of training days that ended with the three difficulty levels ‘easy, medium, difficult’ of Tasks A and B of the *Negami* app. Since each of the 10 patients received 10 training sessions, the maximum number is 100 days.

### 3.2 Control for spontaneous recovery and confounding variables

Figure 4 gives an overview on the results of the *Negami* therapy group and the group with standard neglect therapy over all diagnostic examinations. In both groups, we found no significant differences between measurement time points E1 and E2 for all five neglect tests (*Negami* therapy group: dependent t-tests for all five neglect tests:  $p > 0.26$ ; standard neglect therapy group: for all five neglect tests  $p > 0.23$ ). This indicates that spontaneous remission could be excluded in both groups when treatment started. For the following analyses, we thus combined the two measurement time points E1 and E2 into one (‘baseline’) variable, separate for each of the five diagnostic neglect tests.

Further, the potential confounding variables age, sex, and post-stroke interval did not differ significantly between the two therapy groups (age:  $t(18)=0.1$ ,  $p=0.92$ ; sex  $\chi^2(1)=0.95$ ,  $p=0.33$ ; post-stroke interval  $t(18)=0.89$ ,  $p=0.4$ ), and therefore were not included in subsequent analyses.



**Figure 4.** Results in the Cancellation-Tests (performance in the Letter- and the Bells-Cancellation-Tests have been averaged for the sake of clarity), Copying-Task, Line-Bisection-Task, and the ‘Exploration Test’ for the *Negami* therapy group (*red*) and the group with standard neglect therapy (*blue*) over the different diagnostic examination time points (E1 to E6).

### 3.3 Treatment effects

We conducted ANOVAs of repeated measures with factors group (*Negami* therapy vs. standard neglect therapy) for diagnostic examination time points (baseline, E3, E4, E5), using IBM SPSS Statistics (Vers. 28; <sup>26</sup>). Statistical significance was defined as  $p < 0.05$ . Significant interaction effects were found in all five neglect tests (Letter-Cancellation-Test:  $F(3,54)=4.05$ ,  $p=0.01$ ,  $\eta^2=0.18$ ; Bells-Cancellation-Test: with Greenhouse-Geisser correction  $F(3,36)=6.49$ ,  $p<0.01$ ,  $\eta^2=0.31$ ; Copying-Task:  $F(3,54)=8.3$ ,  $p<0.01$ ,  $\eta^2=0.32$ ; Line-Bisection-Task: with Greenhouse-Geisser correction  $F(3,31)=3.4$ ,  $p=0.05$ ,  $\eta^2=0.17$ ; ‘Exploration Test’:  $F(3,39)=5.35$ ,  $p=0.03$ ,  $\eta^2=0.29$ ).

For post-hoc analyses, pairwise t-tests were conducted to examine the within-subject factors with a Bonferroni- corrected significance level of  $p < 0.0125$ . For the *Negami* therapy group, pairwise t-test comparisons for ‘baseline’ versus time point E4, i.e. the examination right after termination of the intervention, revealed significant differences in four of five diagnostic neglect tests (Letter-Cancellation-Test:  $t(9)=4.95$ ,  $p<0.01$ ,  $d=0.2$ ; Bells-Cancellation-Test:  $t(9)=5.7$ ,  $p<0.01$ ,  $d=0.19$ ; Copying-Task:  $t(9)=6.02$ ,  $p<0.01$ ,  $d=1.63$ ; Line-Bisection-Task:  $t(8)=3.75$ ,  $p=0.01$ ,  $d=0.2$ ). A clear numerical, but no significant difference was found for the

'Exploration Test' ( $t(6)=4.47$ ,  $p=0.02$ ). For the group with standard neglect therapy, comparisons for 'baseline' versus time point E4 revealed one significant improvement in the Copying-Task ( $t(9)=2.4$ ,  $p=0.01$ ,  $d=1.38$ ). No significant differences were observed for the other four examination tests (Letter-Cancellation-Test:  $t(9)=1.88$ ,  $p=0.05$ ; Bells-Cancellation-Test:  $t(9)=0.98$ ,  $p=0.35$ ; Line-Bisection-Task:  $t(9)=-1.92$ ,  $p=0.04$ ; 'Exploration Test':  $t(8)=-1.49$ ,  $p=0.09$ ).

To examine if there was any significant change in neglect behavior between the first and the second week of training, i.e. between E3 and E4, further paired t-tests were performed. In the *Negami* therapy group only the 'Exploration Test' revealed a significant difference ( $t(6)=3.18$ ,  $p=0.01$ ;  $d=21.88$ ; all other four diagnostic examination tests:  $p>0.02$ ). In the standard neglect therapy group, the only significant difference between E3 and E4 was found for the Copying-Task ( $t(9)=2.69$ ,  $p=0.01$ ,  $d=0.82$ ; all other four diagnostic examination tests:  $p>0.22$ ).

To examine the differences between the two patient groups, t-tests were performed for each diagnostic examination time point. Results were summarized in Table 2. No significant differences between the two groups were observed at 'baseline' for all five diagnostic tests. Significant differences were observed from the first week of therapy onwards. At diagnostic examination E3, significant differences were observed for the 'Exploration Task'. At diagnostic examination E4, the Bells-Cancellation-Test, the Copying-Task, and 'Exploration Test' differed significantly between the two groups, favoring the *Negami* therapy group. At diagnostic examination E5, this was again the case, now for all neglect tests but the Line-Bisection Task.

Sensitivity analyses using a mixed model approach yielded comparable results.

**Table 2.** Between-group comparisons for each diagnostic examination time point for all five neglect tests.

|           | Letter-Cancellation                             | Bells-Cancellation                              | Copying-Task                                    | Line-Bisection-Task            | 'Exploration Test'                              |
|-----------|---|---|---|--------------------------------|---|
| Base-line | t(18)=0.4,<br><i>p</i> =0.35                    | t(18)=0.47,<br><i>p</i> =0.65                   | t(18)=0.21,<br><i>p</i> =0.42                   | t(17)=1.58,<br><i>p</i> =0.07  | t(15)=-0.33,<br><i>p</i> =0.75                  |
| E3        | t(14)=-1.09,<br><i>p</i> =0.15                  | t(13)=-2.02,<br><i>p</i> =0.32                  | t(18)=-2.05,<br><i>p</i> =0.03                  | t(17)=-0.78,<br><i>p</i> =0.22 | t(13)=-3.9,<br><i>p</i> <0.01*, <i>d</i> =25.26 |
| E4        | t(18)=-1.7,<br><i>p</i> =0.05                   | t(12)=-2.68,<br><i>p</i> =0.01*, <i>d</i> =0.18 | t(18)=-3.64,<br><i>p</i> <0.01*, <i>d</i> =1.17 | t(17)=-2.11,<br><i>p</i> =0.03 | t(15)=-5.81,<br><i>p</i> <0.01*, <i>d</i> =23   |
| E5        | t(11)=-2.65,<br><i>p</i> =0.01*, <i>d</i> =0.18 | t(12)=-3.22,<br><i>p</i> =0.01*, <i>d</i> =0.15 | t(18)=-3.84,<br><i>p</i> <0.01*, <i>d</i> =1.22 | t(17)=0.46,<br><i>p</i> =0.48  | t(15)=-2.87,<br><i>p</i> <0.01*, <i>d</i> =34.6 |

\*= Significant mean differences between groups at the Bonferroni-corrected significance level of 0.0125.

### 3.4 Follow-up examinations

Three patients were unable to participate in the follow-up examination due to relocation far beyond our catchment area, change of contact details, and death in one patient. Pairwise t-comparisons showed no significance for the *Negami* therapy group between time points E4 and E5 for all five neglect tests (all *p*>0.29) as well as between E5 and the follow-up examination E6, again for all neglect tests performed (all *p*>0.35). This indicates that the improvements due to *Negami* therapy remained stable. Unfortunately, for the 'Exploration Test' the latter comparison could not be performed due to missing data at E6 for all subjects. This was caused by an update of the app that was supposed to implement cloud-based data storage (see below discussion). Unfortunately, the update deleted the last collected data, resulting in an irrevocable data loss for the 'Exploration Test' of E6. In the group with standard neglect therapy, no significant difference was found between time points E4 and E5 for all five neglect tests (all *p*>0.06).

## 4. Discussion

This study investigated the effectiveness of an AR therapy app for the treatment of spatial neglect after stroke. Two groups, an experimental *Negami* group and a group receiving standard neglect therapy, were compared in a randomized control trial. Both groups were studied in

parallel over a five-week period. Both improved significantly under therapy relative to baseline. While the *Negami* therapy group improved in four of the five neglect tests used, the standard therapy group showed improvement only in the Copying-Task. Both these improvements were still seen one week after the end of therapy. The *Negami* therapy group received a second follow-up examination at a time interval between one to two months after completion of training. The improvement remained stable even at this later time point. When we compared the *Negami* therapy group versus the standard neglect therapy group, we found that the improvement of the *Negami* group was significantly superior. The benefit was already evident after one week of therapy (E3) and was also seen after its end. Right after the end of the two weeks training period (E4), the *Negami* therapy group performed better in three neglect tests and one week after the training (E5) in even four of the five neglect tests. Thus, the present results demonstrate not only the efficacy of treating spatial neglect with the *Negami* app but also indicated that the therapy with *Negami* appears to be superior to the standard neglect therapy approach.

From the observation that there was still significant improvement between the first and the second week of *Negami* training, as well as in the standard therapy group, one can deduce that the therapy interval should not be less than at least two weeks. Nevertheless, further studies are pending to assess more precise statements about frequency, extent and duration of therapy.

Effective treatment by exploration training has been shown in several controlled studies, but so far only with small numbers of patients (for review see <sup>27-30</sup>). An interesting extension of the principle of active exploration training has been the use of virtual reality (VR). Immersive <sup>31-33</sup> and non-immersive <sup>34-36</sup> VR therapy methods have been tested successfully in (individual) neglect patients. However, the problem of VR methods in general is that a mostly expensive dedicated hardware (e.g., head-mounted display [HMD]) is required <sup>37</sup> and that side effects such as dizziness, fatigue, or irritated eyes can occur, termed ‘cybersickness’ <sup>38,39</sup>. Augmented reality (AR) could be a solution to these problems, since already existing end devices (tablets, cell phones) can be used to run the app and no sensory mismatch is evoked that leads to cybersickness. In fact, when older subjects used the *Negami* app, no or only very minor side effects were observed <sup>15</sup>.

In the field of AR, another AR-based application for neglect patients has been developed in addition to the *Negami* app. The app asks patients to search for virtual images virtually attached to the walls of the real environment <sup>40</sup>. While both apps have been shown to increase patient motivation for treatment <sup>15,40</sup>, the present study is the first that provides first findings about the efficacy of such an AR app in treating spatial neglect. Increasing patients’ motivation

is especially important considering that motivation for rehabilitation significantly affects clinical outcomes <sup>41</sup>. This could be one of the reasons why in the present study the *Negami* training group improved significantly more than the patients who received the standard neglect therapy.

A big advantage of apps such as *Negami* is that it also can be used after an inpatient stay at a rehabilitation facility in the home setting. In order to maintain and consolidate the positive results after rehabilitation training after discharge, promotion of interventions in the home environment is of crucial importance <sup>42</sup>. Besides the advantage of maintaining symptom improvement, *Negami* also has the prerequisites to use it for telerehabilitation. By implementing cloud-based synchronization of patient and user management, it ensures that all data collected on the device is automatically synchronized with the cloud when an internet connection is active. Patients can therefore practice from home using the *Negami* app, while therapists and clinicians can access the processed tasks regardless of location to track the patient's progress and adjust the difficulty level accordingly.

## **5. Limitations**

One limiting factor of the present study is the relatively small sample size. We were able to include a total of 20 patients. Ten patients each were assigned to either the experimental *Negami* therapy group or the standard neglect therapy group. Having demonstrated the positive efficacy of *Negami* on neglect behavior in this study, future studies need to verify our findings in larger patient samples and, in addition, should examine its effects on activities of daily living.

## **6. Conclusion**

Two weeks of training with *Negami* in patients with unilateral neglect after stroke significantly improved spatial neglect. Thus, *Negami* can be used as an effective alternative or addition to the current standard neglect therapy and may even be superior to it.

## **7. Conflict of Interest**

The authors declare that there is no conflict of interest.

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## Abbreviations

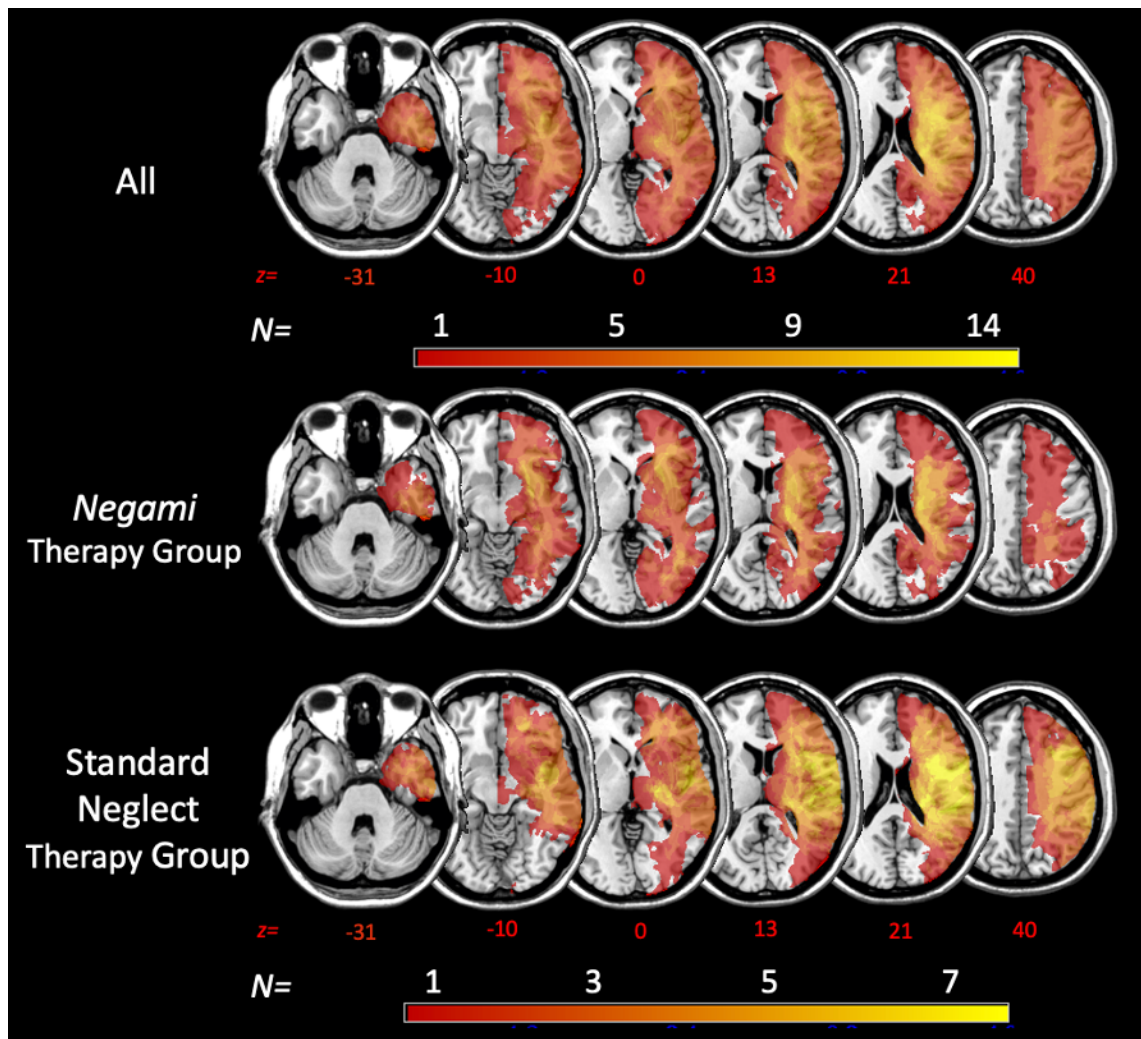
AR: Augmented Reality

CoC: Center of Cancellation

HDM: Head Mounted Display

VR: Virtual Reality

## Supplementary Material



**Figure 1.** Simple overlay plots. Overlaps of normalized acute lesions are shown for all patients ( $N = 20$ ) and for patients of the *Negami* Therapy Group ( $N = 10$ ) and the Standard Neglect Therapy Group ( $N = 10$ ) on the ch2-template in MNI space via MRICron<sup>1</sup>. Displayed axial slices refer to z-coordinates -31, -10, 0, 12, 21 and 40 mm. The color of the voxels represents the number of patients with damage to this voxel ( $N_{min} = 1$ ;  $N_{max} = 14$  or  $N_{max} = 7$ , respectively).

<sup>1</sup> Rorden C, Brett M. Stereotaxic display of brain lesions. *Behav Neurol.* 2000;12(4):191-200. doi:10.1155/2000/421719

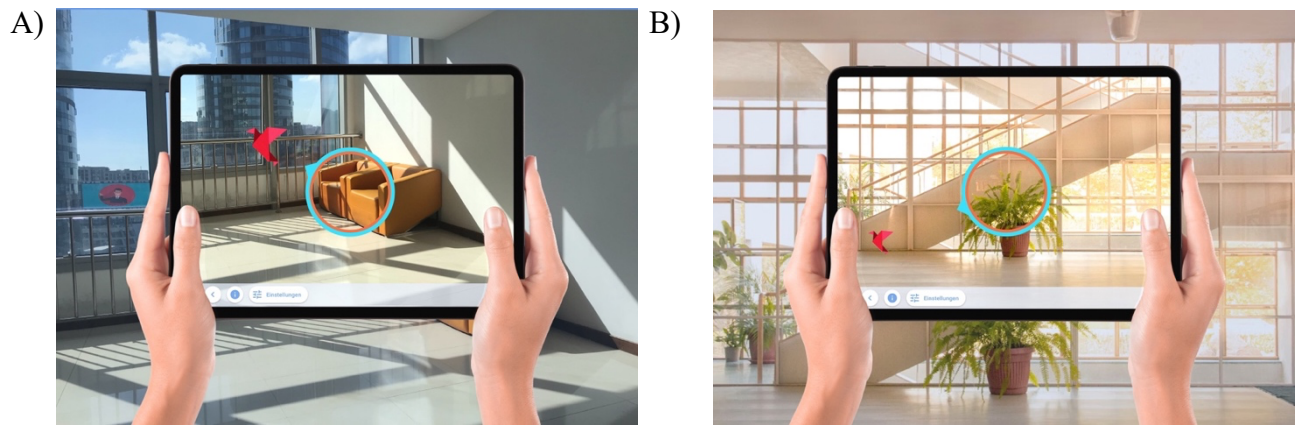
Task A: “Follow the bird”. The first task of the patient is to follow the virtual origami bird through real space. The patient's straight-ahead eye/head/body orientation is set as ‘0’. Beginning at set point ‘0’, the bird flies with sinusoidal movements towards one side of space (in neglect patients towards the neglected, contralesional side). While doing so, the patient sees an orange circle in the center of the screen (Fig. 2). The bird should be held in this circle while performing the task. As soon as the patient fails to successfully follow the bird and keep it in the circle during its flight, the patient is provided with an additional orientation aid: a blue compass needle appears showing the patient in which direction the bird is located (see Fig. 2A). The task is considered successfully completed as soon as the bird has finished its trajectory and the bird has been positioned centrally in the orange circle. During the performance the patient receives auditory feedback; every time the patient manages to get the bird into the orange circle, a short, bright tone is presented. If the patient manages to keep the bird continuously in the orange circle, the tone is presented every two seconds. When the task has been successfully completed, the patient receives feedback auditorily again through a different tone and visually through the change of the color of the circle to green.

With the end of a successful trial, the trail can be repeated or the difficulty level can be adjusted to easy, medium, or difficult (cf. Tab. 1). The difficulty levels are saved as templates.

**Table 1.** Difficulty levels provided with Task A “Follow the bird”.

| Level     | Maximum distance of the bird’s path | Speed of bird movement | Amplitude of bird movement |
|-----------|-------------------------------------|------------------------|----------------------------|
| Easy      | up to $\pm 35^\circ$                | 2.3°/sec               | 6.8°                       |
| Medium    | up to $\pm 55^\circ$                | 4.1°/sec               | 8.0°                       |
| Difficult | up to $\pm 85^\circ$                | 8.1°/sec               | 11.3°                      |

Angular degrees are participant’s space coordinates, starting from their straight-ahead eye/head/body orientation which is set as ‘0’. Sec, second.



**Figure 2.** (A) Task A “Follow the bird”. The patient has the task to follow the flying origami bird and to keep the bird within the orange/blue circle. (B) Task B “Find the bird”. The patient has to search for the bird that has been hidden by the therapist somewhere in the surrounding room (here: at the corner located at the foot of the stairs) and has to transfer it into the orange/blue circle.

Task B: “Find the bird”. In the second task of the “Negami” app, the therapist hides the virtual origami bird in the room surrounding the patient. For this purpose, the patient's straight-ahead eye/head/body orientation again is set as ‘0’. Starting from this location, the therapist hides the bird somewhere on the left/right side of the patient without the patient seeing it. The area in which the bird can be hidden by the therapist is predefined by the app, depending on the chosen difficulty level of the task (for more details see <sup>1</sup>). Once the therapist has positioned the bird in space, the patient is then instructed to find the bird and, once found, to position it centrally into the orange circle (cf. Fig. 2B). Should the patient show difficulties in finding the bird, it is possible to provide the patient with orientation assistance by turning on the blue compass needle. The task is successfully solved when the patient has found the bird and placed it in the center of the circle. According to Task A, the circle then turns green and the patient hears a bright tone signaling the successfully solved task. After successful completion the task can be repeated or changed in difficulty (cf. Tab. 2)

**Table 2.** Difficulty levels provided with Task B “Find the bird”.

| Level     | Extension of the area (along the horizontal dimension of the surroundings) within which the bird can be hidden |
|-----------|--|
| Easy      | 0° to -40° [or 0° to +40°]   |
| Medium    | -40° to -75° [or +40° to +75°]   |
| Difficult | -75° to -90° [or +75° to +90°]   |

Angular degrees are participant’s space coordinates, starting from their straight-ahead eye/head/body orientation which is set as ‘0’. Negative values indicate positions to the participant’s left, while positive values indicate positions to the participant’s right.

<sup>1</sup> Stammer B, Flammer K, Schuster T, Lambert M, Karnath H-O. Negami: An Augmented Reality App for the Treatment of Spatial Neglect After Stroke. *JMIR Serious Games*. 2023/2/27 2023;11:e40651. doi:10.2196/40651