Computer-Based Cognitive Rehabilitation in Patients with Visuospatial Neglect or Homonymous Hemianopia after Stroke

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Objectives: The purpose of this pilot study was to investigate the feasibility and effects of computer-based cognitive rehabilitation (CBCR) in patients with symptoms of visuospatial neglect or homonymous hemianopia in the subacute phase following stroke. *Method:* A randomized, controlled, unblinded cross-over design was completed with early versus late CBCR including 7 patients in the early intervention group (EI) and 7 patients in the late intervention group (LI). EI received CBCR training immediately after inclusion (m = 19 days after stroke onset) for 3 weeks and LI waited for 3 weeks after inclusion before receiving CBCR training for 3 weeks (m = 44 days after stroke onset). *Results:* CBCR improved visuospatial symptoms after stroke significantly when administered early in the subacute phase after stroke. The same significant effect was not found when CBCR was administered later in the rehabilitation. The difference in the development of the EI and LI groups during the first 3 weeks was not significant, which could be due to a lack of statistical power. CBCR did not impact mental well-being negatively in any of the groups. In the LI group, the anticipation of CBCR seemed to have a positive impact of mental well-being. *Conclusion:* CBCR is feasible and has a positive effect on symptoms in patients with visuospatial symptoms in the subacute phase after stroke. The study was small and confirmation in larger samples with blinded outcome assessors is needed.

Key Words: Visuospatial neglect—homonymous hemianopia—stroke—cognitive rehabilitation

Introduction

Visuospatial neglect (VN) and homonymous hemianopia (HH) are common lateralized visuospatial symptoms occurring after stroke.[1] VN represents an inattention to the contralateral visual field relative to the lesioned hemisphere, causing patients to be predominantly aware of visual stimuli within the ipsilateral visual field.[2,3] HH represents a blindness in half of the visual field of both eyes contralateral to the damaged hemisphere.[4] Both VN and HH significantly reduce quality of life of affected patients as well as the ability to be self-reliant in everyday tasks such as driving and reading,[5,6] which makes it highly relevant to develop helpful rehabilitative strategies. However, no intervention has yet proven efficacious beyond doubt in the rehabilitation of VN[7] or HH.[8]

Computer-based cognitive rehabilitation (CBCR) is a supplementary rehabilitation method in which patients practice various cognitive tasks on a computer screen or similar electronic device. The aim of CBCR is to train various cognitive functions. As a rehabilitation tool, it has the advantage of being both cheap and flexible, and only few and mild side effects of CBCR have been reported from earlier studies, including mental fatigue and eye irritability.[9] Furthermore, earlier research suggests that training with dynamic visual stimuli is more effective in the rehabilitation of VN than static visual stimuli, and that moving stimuli might be crucial to modulate patients' visual attention.[10,11] In this context, CBCR is an advantageous rehabilitation method compared to paper and pen

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rehabilitation methods. However, great scientific debate remains about the effects of computerized "brain training"'[12] and the literature regarding CBCR as a rehabilitation tool for lateralized visuospatial symptoms after stroke is very limited.[13]

Current research concerning the effects of CBCR on rehabilitation of other cognitive domains such as executive functions has often been implemented in the chronic phase after stroke with limited evidence of positive effects.[4] However, preclinical research suggests that cognitive rehabilitation is most efficacious when administered in the subacute phase where it can boost the effects of spontaneous remediation.[14] Cohort studies with stroke patients support these findings.[15] It is therefore hypothesized that an effect of CBCR on symptoms of VN and HH after stroke is most likely to be identified if administered in the subacute phase.

Because this pilot study aimed to explore the feasibility and effects of CBCR on visuospatial symptoms in the subacute phase after stroke, both patients with VN and HH were included, even though this contributed to a more heterogeneous sample.

CBCR was compared to no intervention in a controlled, randomized, nonblinded cross-over trial.

Method

This study is described using the CONSORT guidelines for reporting of randomized trials.[16] The study has been approved by the Danish National Committee on Health Research Ethics (ID nr.: H-15005253) as well as the Danish Data Protection Authority (ID nr.: 2012-58-0004, local ID nr.: BBH-2015-030, I-Suite nr.: 03698).

Study Design

The trial consisted of 2 intervention groups: An early- and a late intervention group (EI and LI), with an allocation ratio of 1:1. The EI group received 3 weeks of CBCR training as a supplement to usual care immediately after inclusion in the trial followed by 3 weeks of usual care. The LI group started out with 3 weeks of usual care followed by 3 weeks of supplementary CBCR. Usual care primarily consisted of physiotherapy, ergotherapy, and speech therapy depending on the individual patient's needs. This cross-over design was used because CBCR had already been implemented into care but with no specific timing of the intervention. We set out to test if early application of the intervention was preferable to later application. The effects were assessed with a neuropsychological test battery designed to assess visuospatial and visuoperceptual symptoms outlined below. The test battery was administered at baseline, after 3 weeks at cross over and after 6 weeks at the end of the trial. The course of the trial for each participant is presented in Table 1.

Randomization Procedure

We planned to include 20 patients into the trial as a pilot sample to generate hypotheses for further study. Therefore, 20 c envelopes were prepared by the person responsible for data collection with 10 notes labeled 1 (for the EI group) and 10 notes labeled 2 (for the LI group). All envelopes were sealed and mixed together by the person responsible for data collection, and all patients themselves drew 1 envelope freely from the pile at inclusion. Envelopes from patients who were excluded from the trial after inclusion were not put back. The period of data collection was 12.10.2015-29.09.2017, and ended before all 20 planned patients were included; therefore, a total of 18 patients were included in the trial.

Inclusion of Patients

Patients were included from the Stroke Unit at Bispebjerg Hospital, Copenhagen which has a well-defined catchment's area of app. 350,000 inhabitants from urban Copenhagen for stroke rehabilitation.

Patients were included if they met the following criteria: (1) subacute phase after cerebral stroke (3-42 days post ictus), (2) symptoms of VN or HH described in the patient journal by a doctor or neuropsychologist, (3) capable of giving informed consent both verbally and in writing, (4) no known comorbid diseases which could influence their rehabilitation such as neurodegenerative diseases or severe psychiatric comorbidity, and (5) judged by a doctor or neuropsychologist to have a cognitive level of functioning making them capable of completing 3 weeks of CBCR training.

Table 1. *Course of the trial for patients in the EI and LI group*

Group	At inclusion	Week 1-3	End of week 3	Week 4-6	End of week 6
1 (EI)	Assessment with neuropsychological test battery	*CBCR intervention* + usual care	Assessment with neuropsychological test battery	Usual care	Assessment with neuropsychological test battery
2 (LI)	Assessment with neuropsychological test battery	Usual care	Assessment with neuropsychological test battery	*CBCR intervention* + usual care	Assessment with neuropsychological test battery

Abbreviations: EI, early intervention; LI, late intervention.

Patients were excluded if they did not meet the above inclusion criteria or did not provide informed consent. It was not an exclusion criterion if patients had other cognitive or physical symptoms because of the stroke, as long as they were able to carry out the CBCR training and give an informed consent.

Description of Intervention

In this trial, a Danish version of the French CBCR program "Scientific braintraining PRO" was selected for use. The program consists of exercises for several cognitive domains, and 5 exercises were selected from the domains of "visuospatial abilities" and "visual attention" to constitute the intervention for this pilot trial. For a full description of the exercises, see Appendix 1. Each exercise in the program consists of 9 levels of difficulty. The program encourages patients to advance a level up every time they solve a task more than 75% correct 2 times in a row. All patients were instructed to train for 30-45 minutes every second day for 3 weeks during the intervention period. The amount of daily training was chosen based on earlier training sessions with hospitalized patients which indicated that this was the realistic amount of training patients could overcome besides usual care.

All patients were instructed 1:1 with the trainer on how to use the program at the beginning of the intervention period, but after this instruction, the patients had the primary responsibility for their own training with the CBCR program. All patients were contacted once a week (by phone if they were discharged from the hospital within the intervention period) to follow-up on their training and to support them if it was evident from their online training profile that they did not make progress. Participants were provided with free access to the CBCR program during their intervention period.

Assessment

A neuropsychological test battery was designed to assess all patients at inclusion, after 3 weeks at cross over and after 6 weeks at the end of the trial for each participant. The primary outcome assessed the development in lateralized visuospatial symptoms and the secondary outcomes assessed the development in related visuospatial and visuoperceptual abilities as well as mental well-being. The neuropsychological test battery consisted of the following tests:

Primary Outcome

Test of lateralized visuospatial symptoms with Cognitive Assessment at Bedside with iPad (CABPad). The CABPad consists of computerized versions of several neuropsychological tests. The used test from the CABPad in this trial was The Butterfly Test: A modified, computerized version of the broadly used neuropsychological test: Star cancellation, which is designed to uncover lateralized visuospatial symptoms.[17] A score closer to 0 indicates less severe or no VN, and a score further from 0 indicates more severe VN. A score of 0.67 was considered cutoff for VN to the left and a score of −0.60 was considered cutoff for VN to the right.

Secondary Outcomes

- The WAIS-IV Block design test is designed to assess visuospatial- and visuoconstructional abilities without graphomotoric involvement. Raw scores are calculated into scale scores from 1 to 20. A higher score represents better visuoconstructional ability.
- The drawing test Mental Status Undersøgelse (MSU) is designed to assess visuospatial- and visuoconstructional abilities with graphomotoric involvement. The patient is asked to copy 4 increasingly difficult drawings (a cross, a star, a cube with perspective, and a house with perspective). A score between 0 and 12 points is obtained based on the correctness of the patient's copies of presented drawings, with a maximum of 3 points per drawing. The lower the score, the lower the visuospatial and constructional abilities. Depending on age, a score between 7 and 9 indicates a deficit (older patients need a lower score to be considered within the normal range).[18]
- The Street completion test is designed to assess visual synthesis and visual closure. The patient is presented with 20 pictures of increasingly incomplete objects and is instructed to figure out what the object in the picture is. A score between 0 and 20 is obtained based on how many objects the patient correctly recognizes. A score below 10 indicates visuoperceptual difficulties. The cutoff is higher for people with a higher educational level.[19]
- The Symptom Checklist-90-Revised (SCL-90-R) is a mental well-being questionnaire consisting of 90 questions assessing the extent and severity of psychopathological symptoms. The test results in various mental well-being scores. The score used from the SCL-90-R in this study is the Global severity index which is an index of the overall extent and severity of present symptoms. A lower score reflects better mental well-being.

Statistical Analysis

This pilot study is based on a small sample of 18 patients. Therefore, data are not expected to be normally distributed and nonparametric statistical models were used for statistical analysis. Specifically, Willcoxon signed-rank test has been applied in statistical analysis of the development within groups, and the Mann-Whitney

test has been applied in statistical analysis of the differences in development between groups. Pearson's correlation coefficient is used as the measure of effect sizes.

Correction for multiple comparisons was not made due to the exploratory and hypothesis generating nature of the study. Statistical analysis was performed by IBM SPSS Statistics version 24, CA, USA.

Results

Characteristics of Included Patients

Patients' characteristics are presented in Table 2. A total of 18 patients were included in this trial. Among these, 4 patients were excluded during their course of the trial (Nr. 4, 11, 12 and 14). One patient was excluded due to a hospital-transfer to the other end of the country, which made retesting too difficult logistically. One patient was excluded because the patient did not train during the CBCR-intervention period, and 2 patients were excluded because they did not wish to continue with the training throughout the intervention period. Therefore, a total of 14 patients completed the study: 7 in each group. The EI group started the CBCR intervention directly after inclusion and baseline assessment, on average 19 days post ictus. Patients in the LI group were on average included 23 days post ictus and did not receive the CBCR intervention for the first 3 weeks of the study period. Therefore, the LI group started CBCR training averagely 44 days post ictus.

A total of 5 patients needed an additional follow-up after initial instructions in the CBCR program because of problems with 1 or more exercises during the intervention period (4 patients from the EI group and 1 from the LI group), and the remaining 9 patients did not need further assistance after introduction to the program.

Baseline Characteristics for Early Intervention Group and Late Intervention Group

As is evident from Table 3 below, no significant differences between the EI and LI group were present at baseline regarding age, education, and time of inclusion after stroke or any of the outcome measures. On the basis of this, the EI and LI groups are considered comparable at baseline. However, even though there were no significant differences between the average age in the EI group and LI group, patients in the LI group are averagely 9 years older than in the EI group. It is possible that this difference is not significant because of low power due to the small sample, and it cannot be ruled out that this age difference can impact the results.

Accumulated Training Time and Development in the CBCR Program

As is evident from Table 4, no significant differences were found between the EI and LI groups on accumulated training time or improvement within the trained CBCR program after the intervention. On the basis of this, the EI and LI groups are considered comparable after the CBCR intervention.

Results within Groups: Comparison of Baseline, Cross Over and after the Intervention

Within group developments on the different outcome measures are presented below in Table 5. The corresponding baseline characteristics are presented in Table 3. The results are presented for the development from baseline to cross over after 3 weeks, and from cross over to the end of the trial after 6 weeks.

As presented in the table, there was a significant reduction in lateralized visuospatial symptoms measured with

Table 2. *Characteristics of included patients*

ID	Sex	Group	Age	Earlier strokes	Subacute stroke	Symptom	Education	Inclusion post ictus
1	F	Early	53	Several bilateral	R. posterior	L VN	10 years	12 days
2	M	Early	63	No	R. posterior	L HH	9 years	14 days
3	F	Early	71	No	R. medial	L VN	17 years	33 days
5	M	Early	49	No	L. posterior	R HH	13 years	19 days
6	F	Early	69	Several bilateral	Several bilateral	R VN	12 years	40 days
7	M	Late	74	Several bilateral	L. posterior	L VN	9 years	35 days
8	F	Late	81	One: R. Medial	R. medial	L VN	13 years	35 days
9	M	Late	73	No	R. medial	L VN	12 years	38 days
10	F	Late	66	One: L. Medial	R. posterior	L HH	15 years	7 days
13	M	Early	71	One: L. Anterior	L. medial	R VN	12 years	3 days
15	M	Late	62	No	R. medial	L VN	9 years	12 days
16	M	Late	78	No	Several bilateral	R VN	13 years	23 days
17	F	Late	51	No	R. medial	L VN	11 years	8 days
18	F	Early	40	No	R. medial	L VN	17 years	11 days

Abbreviations: HH, Homonymous Hemianopia; L, Left; R, Right; VN, Visuospatial Neglect.

Table 3. *Baseline characteristics for EI versus LI*

N = 14	Early	Late	Significance level
Age	m = 60 (40-71, SD = 12.15)	m = 69 (51-81, SD = 10.53)	*P* = .128
Education (years)	m = 13 (9-17, SD = 3.13)	m = 12 (9-15, SD = 2.22)	*P* = .620
Inclusion post ictus (days)	m = 19 (3-40, SD = 13.11)	m = 23 (7-38, SD = 13.48)	*P* = .710
CABPAD butterfly	m = 1.04 (.06-2.71, SD = 1.04)	m = 1.06 (.04-2.78, SD = .99)	*P* = 1.000
Street test	m = 7.14 (1-13, SD = 4.45)	m = 7.71 (3-17, SD = 7.71)	*P* = .900
Drawing test MSU	m = 6.71 (3-9, SD = 2.43)	m = 5.57 (0-11, SD = 3.60)	*P* = .456
Block design	m = 6.00 (2-10, SD = 3.87)	m = 5.57 (2-9, SD = 3.10)	*P* = .805
SCL-90-R	m = 51.29 (36-67, SD = 11.47)	m = 54.43 (48-64, SD = 5.41)	*P* = .535

Abbreviations: CABPad, Cognitive Assessment at Bedside with iPad; SCL-90-R, Symptom Checklist-90-Revised.

Table 4. *Accumulated training time and improvement in the CBCR program after the intervention*

	Early intervention group (training weeks 1-3)	Late intervention group (training weeks 3-6)	Significance level
Training time (min)	m = 515 (210-855, SD = 258)	m = 446 (190-659, SD = 191)	*P* = .710
Improvement in CBCR-program (level 1-9)	m = 6.0 (3.4-9, SD = 2.32)	m = 6.7 (5.4-9, SD = 1.20)	*P* = .460

Abbreviations: CBCR, computer-based cognitive rehabilitation.

Table 5. *The development in outcome measures within groups*

	Mean week 3	Significance level week 1-3	Effect size	Mean week 6	Significance level week 3-6	Effect size
Early group						
CABPad butterfly	m = .29 (−.83-2.33, SD = 1.00)	*P* = .018*	r = .89	m = .43 (−.50-3.12, SD = 1.28)	*P* = .735	r = .13
Street test	m = 10 (6-14, SD = 3.42)	*P* = .039*	r = .77	m = 11.14 (6-16, SD = 4.1)	*P* = .066	r = .69
Drawing test MSU	m = 9.29 (4-12, SD = 3.40)	*P* = .017*	r = .90	m = 9.86 (5-12, SD = 3.02	*P* = .854	r = .07
Block design	m = 8.57 (5-12, SD = 2.51)	*P* = .041*	r = .77	m = 9 (5-12, SD = 2.45)	*P* = .461	r = .28
SCL-90-R	m = 52.29 (43-67, SD = 9.27)	*P* = .684	r = .15	m = 51 (37-61, SD = 7.64)	*P* = .674	r = .16
Late group						
CABPad butterfly	m = .70 (−.07-2.82, SD = 1.02)	*P* = .237	r = .44	m = .25 (−1.19-2.42, SD = 1.15)	*P* = .116	r = .59
Street test	m = 8.57 (4-15, SD = 4.24)	*P* = .443	r = .29	m = 9.71 (5-16, SD = 4.35)	*P* = .131	r = .60
Drawing test MSU	m = 7.71 (0-8, SD = 4.07)	*P* = .044*	r = .76	m = 8.57 (1-12, SD = 4.35)	*P* = .034*	r = .80
Block design	m = 8.43 (2-12, SD = 3.36)	*P* = .026*	r = .84	m = 9.71 (7-11, SD = 1.50)	*P* = .343	r = .36
SCL-90-R	48.43 (39-61, SD = 7.46)	*P* = .027*	r = .83	m = 51.86 (36-60, SD = 8.86)	*P* = .498	r = .26

* is used to highlight significant results defined as results below *P* = 0.05.

the CABPad butterfly test in the EI group during their intervention period (*P* = .018, r = .89). Furthermore, the EI group experienced a significant development on all secondary outcome measures during their intervention period, except SCL-90-R (*P* = .684, r = .15). There was no significant development in any of the outcome measures from week 3 to 6 when the EI group only received usual care. The LI group did not experience significant development in lateralized visuospatial symptoms measured with the CABPad butterfly test from week 1 to 3 when they only received usual care (*P* = .237, r = .44). However, they experienced a significant development in 3 of the secondary outcome measures: Drawing test MSU (*P* = .044, r = .76), block design test (*P* = .026, r = .84), and SCL-90-R (*P* = .027, r = .83). During week 3-6 when the LI group received CBCR training they did not experience a

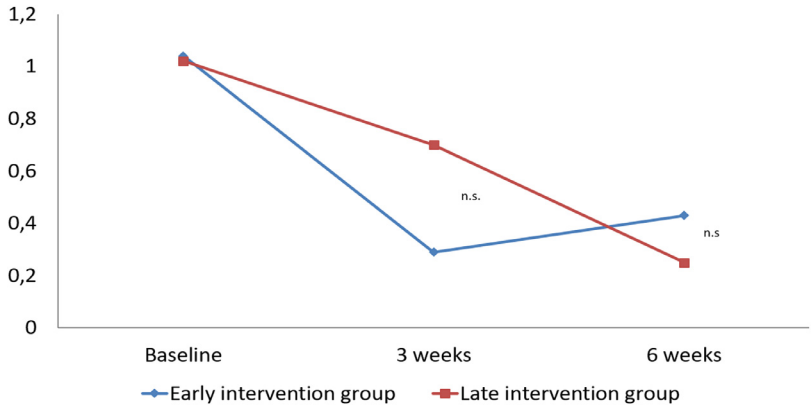

Figure 1. *Development on the CABPad butterfly test for the LI and EI group (lower score indicates less VN).*

significant development in lateralized visuospatial symptoms measured with the CABPad butterfly test as the EI group did during their CBCR intervention ($P = .116$, r = .59). Furthermore, a significant development was only present for 1 secondary outcome, the drawing test MSU ($P = .034$, r = .80).

When the development in lateralized visuospatial symptoms measured with the CABPad butterfly test is analyzed during the course of the entire trial between baseline and the end of week 6, the difference in symptoms for patients in the EI group is not significant ($P = .273$). The difference in lateralized visuospatial symptoms between baseline and the end of week 6 is significant for the LI group ($P = .018$). The development on the primary outcome measure CABPAD butterfly test is also presented in Figure 1.

Results between Groups: Comparison of the Development for Early and Late Intervention Group

Development between groups on the different outcome measures is presented below in Table 6. There was no significant difference in the development of the CABPad butterfly test between groups from week 1 to 3 ($P = .383$, r = .26) or between week 3 and 6 ($P = .259$, r = .46). The development on the primary outcome measure CABPAD butterfly test is also presented in Figure 1. Furthermore, there was no significant difference between the 2 groups on any of the secondary outcomes except the SCL-90-R from week 1 to 3, in which the LI group had a significantly more positive score than the EI group ($P = .017$, r = .62).

Discussion

Main Results and Their Coherence with Existing Literature

Both the EI and the LI groups improved during the intervention period in visuospatial functions, and the LI group improved on 2 measures of visuospatial and visuoperceptual functioning within the usual-care period. There was also a trend toward more improvement during early intervention.

The EI group experienced a significant reduction in lateralized visuospatial symptoms during their CBCR-intervention period from week 1 to 3. The LI group did not experience the same effect during this period in which they only received usual care. This supports the assumption that CBCR as a supplement to usual care is more effective than usual care alone for lateralized visuospatial symptoms. These results are in line with earlier studies exploring the effects of CBCR on visuospatial symptoms after stroke.[20–25] However, not all existing studies support the positive effects of CBCR in the rehabilitation of lateralized visuospatial symptoms after stroke.[26] Furthermore, earlier studies generally suffer from several

Table 6. *The development in outcome measures between groups*

	EI versus LI week 1-3, significance level	Effect size	EI versus LI week 3-6, significance level	Effect size
CABPad butterfly	$P = .383$	r = .26	$P = .259$	r = .46
Street test	$P = .259$	r = .33	$P = .383$	r = .36
Drawing test	$P = .902$	r = .05	$P = .209$	r = .53
Block design	$P = 1.000$	r = .02	$P = .620$	r = .20
SCL-90-R	$P = .017$*	r = .62	$P = .383$	r = .36

* is used to highlight significant results defined as results below P = 0.05.

methodological limitations and should therefore be interpreted cautiously.[13] This pilot study, however, also suffers from methodological limitations, primarily due to the small sample size and somewhat heterogeneous sample, which are further outlined in the section below. Larger trials conducted in more homogenous samples will help clarify the effects of CBCR on visuospatial symptoms after stroke.

From week 3 to 6 when the LI group received the CBCR intervention, they did not experience a significant reduction in lateralized visuospatial symptoms as the EI group did during their CBCR-intervention period. Furthermore, while the EI group experienced a reduction in all related visuospatial and visuoperceptual outcome measures during their CBCR-intervention period, such a reduction was only present on a single related measure—the drawing task—for the LI group during their CBCR-intervention period. This can be interpreted as evidence that CBCR is most effective for lateralized visuospatial symptoms and related visuospatial and visuoperceptual functions when administered early in the subacute phase after stroke.

Cognitive rehabilitation is suspected to be more efficacious in the early subacute phases after stroke compared to the chronic phases, because they presumably further enhance the spontaneous recovery processes of the brain after stroke.[27] However, preclinical studies imply that too early might do more harm than good: Hylin, Kerr, and Holden showed, that laboratory rats who are forced to use a paretic paw within the first 14 days after stroke suffer more neural damage than rats who begin forced rehabilitation at a minimum of 14 days after stroke.[28] Contrary, other preclinical studies show that rehabilitation initiated 5-7 days after stroke is still more efficacious than rehabilitation initiated 3 months or more after stroke,[14] and cohort studies of stroke patients support these conclusions.[15] As such, studies in human subjects are needed to conclude not only which intervention is best, but also at what point in time. Therefore, this study divided patients into an EI group and an LI group to explore the effects of earlier versus later rehabilitation. This study adds to this discussion by providing data which suggests, that cognitive rehabilitation for visuospatial symptoms is more efficacious when initiated early (averagely 19 days after stroke) versus late (averagely 44 days after stroke). These findings should be further explored by larger clinical trials.

The EI group did not experience any significant changes in mental well-being during the course of the trial. This can be interpreted as evidence that CBCR training does not have a negative impact on the mental well-being of patients. From baseline to cross over the patients in the LI group experienced a significant improvement in mental well-being which was not present in the EI group. The test at cross over was administered right before the patients in the LI group started training, which means it could reflect anticipation for the supplementary CBCR training these patients knew they would receive immediately afterwards. As such, this self-administered intervention may contribute to stabilizing mental well-being possibly by supporting empowerment.

Strengths and Limitations of this Study

The methodological strengths of this study are primarily constituted of its randomized and controlled design. However, in this study the outcome assessor was not blind to the group allocation of patients, which constitutes a known possible methodological bias.[29]

Furthermore, even though the EI group experienced a significant reduction in lateralized visuospatial symptoms during week 1-3 when they received the CBCR intervention and the LI group did not experience significant symptom reduction during the same period, the difference in symptom reduction between the 2 groups was not significant. There are some possible explanations for this. It is possible that even though CBCR seems to cause a significant reduction in lateralized visuospatial symptoms when the patients are compared to themselves before the intervention, the effects are too modest to create a significant effect when compared to the effect of guideline rehabilitation alone. Another possible explanation is that the effects shown in this study are modest because of a lack of statistical power due to the small sample. A low statistical power reduces the chances of identifying a possible effect provided an effect exists. A post hoc power analysis reveals a statistical power for the comparison analysis which equals: $\beta = .14$. This is way below the recommended statistical power of: $\beta < .80$.[30] As such, the modest effects identified in this study needs confirmation from studies with larger samples.

The effects found in this study should be confirmed in larger trials with blinded outcome assessors.

Conclusion

The results of this pilot study support that CBCR could be an effective rehabilitation intervention for lateralized visuospatial symptoms especially when administered early in the subacute phase after stroke compared to later in the subacute phase, but the effects are modest and are not maintained 3 weeks after ended training. CBCR does not seem to have a negative impact on the mental well-being of patients and this self-administered intervention may contribute to stabilizing mental well-being possibly by supporting empowerment. Confirmation of the effects found in this study is needed in trials with larger samples and a blinded outcome assessor.

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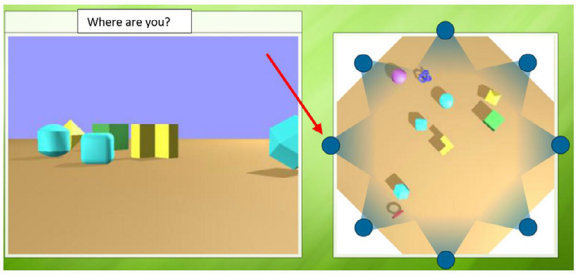
of the authors have any conflicts of interest to disclose regarding this work.

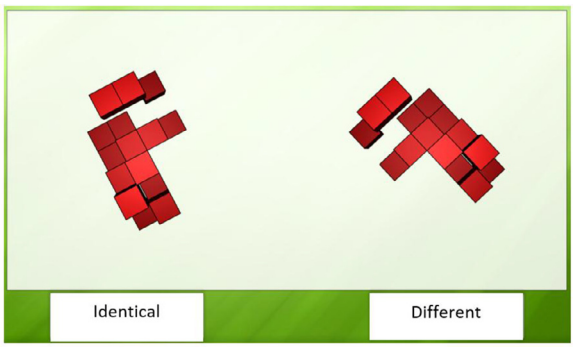
Appendix 1: Description of exercises

Exercise no. 1



In this exercise the patient is instructed to imagine that the left side of the above illustration is her field of view. On the right side of the illustration, the same scene is shown from above. The patient has to decide which of the blue observatory post she is located on based on the presented field of view. The correct observatory post is marked with a red arrow which is not present in the real exercise. The exercise shown here is from level 3 out of 9. As the levels increase, the number of possible observatory posts also increases, while the number of figures in the field of view decreases and get more similar colors.

Exercise no. 2



In this exercise the patient is instructed to decide if the 2 geometrical figures are identical and are rotated in various directions, or if they are different no matter how they are both rotated. The figures are different if they are either inverted or have unidentical components. In the illustration above the figures are inverted, and the correct answer is "different". The exercise shown here is from level 3, and as the levels increase the figures also become increasingly complex.

Exercise no. 3

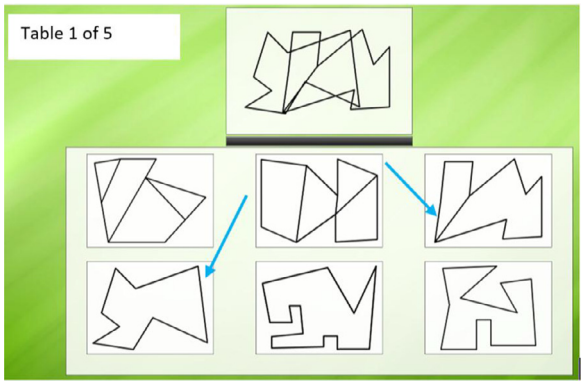
In this exercise the patient is instructed to decide if the presented hand is a right- or a left hand. The exercise illustrated above is from level 5. As the levels increase the hand is presented in increasingly unusual positions. In low levels the hand is presented without an object, at middle levels (as above) the hand is presented with an object and in high levels all hands are presented inverted.

Exercise no. 4

In this exercise the patient is initially introduced to a symbol, which has to be remembered. Then the patient is presented with a variety of symbols which are identical expect for the originally presented symbol. From level 3, a distracting symbol is introduced. The patient is instructed to identify the originally presented symbol, which is marked with a green arrow in the illustration above and avoid choosing the other symbols including the distracting symbol marked with a red arrow in the illustration above. The arrows are not included in the real exercise. Besides, the introduction of a distracting

symbol the exercise becomes more difficult with increasingly detailed symbols along with an increase in the number of overall symbols. The exercise illustrated above is from level 4.

Exercise no. 5



In this exercise, the patient is instructed to choose which 2 of the 6 bottom figures constitutes the target figure in the top of the illustration above. The 2 correct figures are pointed out with blue arrows in the illustration above. These arrows are not present in the real exercise. The exercise becomes more difficult through increasingly complex target figures and a larger number of similar figures to choose between. The exercise in the illustration is from level 4.

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