Adherence of stroke patients with an online brain training programme: the role of health professionals' support.

M.M. Wentink\textsuperscript{1,2,4,7}, J. Meesters\textsuperscript{1,4}, M.A.M. Berger\textsuperscript{2}, A.J. de Kloet\textsuperscript{1,2}, E. Stevens\textsuperscript{6}, G.P.H. Band\textsuperscript{5}, C.H. Kromme\textsuperscript{1,4}, R. Wolterbeek\textsuperscript{4}, P.H. Goossens\textsuperscript{1,3,4}, T.P.M. Vliet Vlieland\textsuperscript{1,3,4}.

1. Sophia Rehabilitation, The Hague, The Netherlands
3. Rijnlands Rehabilitation Centre, Leiden, The Netherlands
4. Department of Orthopaedics, Rehabilitation Medicine and Physical therapy, Leiden University Medical Centre, Leiden, The Netherlands
5. Leiden Institute for Brain and Cognition, Leiden, The Netherlands
6. Helen Dowling Institute, Bithoven, The Netherlands
7. Faculty of Health, Amsterdam University of Applied Sciences, Amsterdam, the Netherlands

Corresponding author
Manon Wentink (PhD student)
Sophia Rehabilitation, Vrederustlaan 180, 2543 SW The Hague, The Netherlands
Phone: +31 70 3593703
Email: m.wentink@sophiarevalidatie.nl
Abstract

Background. Computer-based cognitive rehabilitation (CBCR) is used to improve cognitive functioning after stroke. However knowledge on adherence rates of stroke patients is limited.

Objective. To describe stroke patients' adherence with a brain training programme using two frequencies of health professionals’ supervision.

Methods. This study is part of a randomized controlled trial comparing the effect of the brain training programme (600 minutes playtime with weekly supervision) with a passive intervention in patients with self-perceived cognitive impairments after stroke. Patients randomized to the control condition were offered the brain training after the trial and received supervision twice (vs weekly in intervention group). Adherence was determined using data from the study website. Logistic regression analyses were used to examine the impact of supervision on adherence.

Results. 53 patients allocated to the intervention group (group S8; 64% male, mean age 59) and 52 patients who were offered the intervention after the trial (group S2; 59% male, mean age 59) started the brain training. The median playtime was 562 minutes (range 63-1264) in group S8 vs. 193 minutes (range 27-2162) in group S2 (p<0.001, Mann Whitney U).

Conclusions. The overall adherence of stroke patients with a brain training was low and there are some implications that systematic, regular interaction with a supervisor can increase training adherence of stroke patients with a restitution-focused intervention performed at home.

Keywords: stroke, adherence, cognitive rehabilitation, supervision, support, brain training.

This work was supported by the Fonds Nuts Ohra under Grant [number 1202-006] and Revalidatiefonds under Grant [number 2011184].
Introduction

Although stroke mortality rates in the past two decades have decreased, according to the World Health Federation stroke is still the second leading cause of death in the world. In 2010, the absolute number of people with first stroke was 16.9 million and the number of stroke survivors was 33 million [1]. Among the survivors of stroke, 22 to 50% [2,3] experience cognitive impairment, such as aphasia, neglect, reduced processing speed and impaired attention [4], with direct consequences for dependency in activities of daily living and functional outcomes [5].

Neurorehabilitation after stroke is focused on compensational strategy training and restitution-focused training [6]. Compensational training aims to compensate for the lost function by using remaining intact functions. Restitution-focused treatments consist of frequent repetition or stimulation of the affected function by high-intensity training [7,8]. Therefore, therapists often prescribe intensive exercise regimes for patients [9]. However, a study found that only 31 percent of patients actually performed exercises as recommended [10].

Recently, computer-based cognitive rehabilitation (CBCR) programmes, especially serious brain games, have emerged as a tool for restitution-focused treatment in stroke patients. It is expected that serious brain training helps patients in recovering from a stroke by making training more fun, as monotony of repeated motions is decreased and direct feedback about performance is provided [9,11,12]. However results about the effect of restitution-focused computer training are still conflicting [13,14,15]. Studies are often hampered by low adherence rates [16,17,18,19], although this is one of the main requirements for success of an intervention as well as improved patient outcomes [20]. Laver et al. (2015) concluded in their review that studies should provide more detail in their reporting of adherence of stroke patients with CBCR interventions [15]. Moreover, the impact of the extent of supervision on stroke patients’ adherence with restitution-focused interventions is unknown. It was found in a review of Kelders et al. (2012) that frequency of interaction with a counselor was a significant predictor for adherence with web-based health interventions in different patient groups (p < 0.001) [21].

The goal of this study was to contribute to a better understanding of the impact of supervision on stroke patients’ training adherence with restitution-focused interventions, as a potential factor to increase adherence, ultimately leading to better treatment outcomes for those recovering from stroke. The aim of the study was to describe stroke patients' adherence with a
home-based 8-week brain training programme (Lumosity Inc.®) by comparing two frequencies
of health professional’s supervision. The hypothesis of the study was that a CBCR training with
more supervision would lead to higher training adherence in stroke patients [21].
Materials & Methods

Study design

The present study on adherence was part of a randomized controlled trial (RCT) evaluating the effectiveness of an 8-week CBCR programme on cognitive functioning, quality of life (QoL) and self-efficacy as compared to a passive intervention [22]. In this study no effect of the CBCR programme were found on cognitive functioning, quality of life or self-efficacy when compared to the control group, except for very limiting effects on working memory and speed. A profile of the study is shown in Figure 1.

The current study compares patients in the original intervention group who received supervision eight times during the CBCR intervention period (S8) vs. the original control group who underwent the CBCR intervention after the original RCT and received supervision twice during the intervention period (S2). For the present analysis the data from all patients who agreed to take part in the programme were used.

Patients in the S2 group received weekly information about stroke during the period that the S8 group received their intervention. The information provision was not interactive, it provided unidirectional information about brain differences between men and woman, the influence of stress on brain function and possible difficulties with living with a damaged brain. No new information was provided in these brain facts that were not already extensively addressed during previous rehabilitation treatment. Each week, during a period of 8 weeks, new information (text or a video clip) was added to the website. The study was approved by the Medical Ethical Review Board of The Leiden Medical Centre (P 12.190). The CONSORT (Consolidated Standards of Reporting Trials) guidelines were used for adequate reporting of the study [22].

Recruitment and inclusion

Inclusion criteria for participation in the study were: age between 45 and 75 years, diagnosed with stroke 12-36 months ago, having self-perceived cognitive impairments (extracted
from a checklist accompanying the recruitment letter), having access to the Internet, being able
to visit the rehabilitation centre and having time to participate. Exclusion criteria were:
antidepressant use; receiving actual treatment for cognitive impairments; severe aphasia; lack of
computer skills; not being proficient in Dutch; participants with psychological disorders in need
of treatment; patients with physical disorders known to impact cognition. Patients were recruited
from the participating rehabilitation centers.

The recruitment procedure is described in more detail in a previous report [23]. In total,
142 patients meeting the inclusion criteria were screened for eligibility, of whom 53 were
eventually randomised to the S8 group and 57 patients to the S2 group. 50 patients (94%) in the
treatment group and 57 patients (100%) in the control group completed the study. Of the S2
group, 52 accepted the offer to participate in the programme after the trial was completed. A
flow chart of the inclusion is shown in Figure 2.

Intervention
The CBCR intervention was a home-based brain training programme with a duration of 8
weeks. The duration of 8 weeks for both the intervention and the follow-up were based on
clinical expertise by the research team and the health professionals involved in the project team.
All participants received a user identification and password to log on to a website providing
access to the brain training (www.spelenderwijsbeter.nl). The training software was supplied by
Lumosity Inc.®. This programme was selected because it targets multiple cognitive domains and
adapts the level of difficulty of games to a patients’ own abilities. In total, 16 games were used
targeting five cognitive domains: attention, speed, memory, flexibility and problem solving.

The minimum requested total playtime was 600 minutes. Patients were encouraged to
complete at least one session a day (approximately 15-20 minutes) on at least 5 days per week.
Each session, random selections of three games were assigned to the participant, each game
lasting about five minutes. Patients were able to play longer after finishing the training session.
Furthermore, participants were instructed to complete an extra game session when they missed
one game session and/or were not able to play 5 days a week. With each game, all patients
started at the same level of difficulty. The difficulty level was then raised or lowered depending
on the performance in the previous round of the respective game. The software provided
feedback about game scores and how much games were completed. Patients could receive
reminders for training by e-mail or a text message for mobile phone.

**Supervision**

During the training period, patients from the S8 group received digital support by a
supervisor. Supervisors were three health care providers (a psychologist, physical therapist and
occupational therapist) from the two rehabilitation centers that participated in the study. The
supervision consisted of a short meeting with their own supervisor at the first assessment day in
the rehabilitation centre. Moreover, digital support was provided to patients weekly during the 8-
week training period by their supervisor by telephone if training adherence was lower than five
times a week.

A structured plan with instructions and a timeline was provided to the supervisors.
Moreover, during a meeting at the start of the intervention and evaluations during the
intervention these instructions were discussed with the supervisors. Supervisors were instructed
that contact was aimed at: (1) providing assistance needed to solve problems impairing a patient
to play (e.g. help with software problems, explaining game instructions, install a reminder for
training appointments, etc.), (2) providing strategies to achieve or improve adherence by using
the Plan-Do-Check-Act method and (3) encourage patients to increase training frequency by
using motivational interviewing. Moreover, patients were able to contact their supervisor
themselves by email or telephone anytime they needed assistance, for instance in case of
problems with training software or questions about a certain game.

Patients from the S2 group received supervision twice during the training period: a short
meeting with their supervisor at the start of the brain training and contact by telephone once,
after 4 weeks of training. They were encouraged to contact the supervisor by email or telephone
in case they experienced difficulties using the training.

**Assessments**

The main outcome of interest in the current study was training adherence during the intervention
period. Moreover, patient characteristics were used to determine which variables predict
adherence. These data were retrieved from medical records and online questionnaires.
Adherence
Training adherence was measured by registering the patients’ frequency of logging on to the
website of the study during the total training period of 8 weeks and for each week. This was done
in order to determine whether patients played 40 times in total (five times a week during 8
weeks) as was required. Data were automatically recorded by the software of the website and
therefore gathered independently of the provider of the software. In addition, the patients’
playtime, expressed as the minutes played during the 8-week training period for all cognitive
domains together and for each cognitive domain (attention, memory, speed, flexibility, problem
solving) were registered. These data were provided by Lumosity Inc.®. Logging into the brain
training and not playing any game was not registered as playtime.

Patient characteristics
Demographic characteristics included gender, age (years) and level of education (low:
primary and lower vocational education; middle: secondary and middle vocational education;
high: higher vocational and university education) [24]. In addition, living situation
(alone/together with spouse or other(s)), daily functioning (dependent/independent) and
participation in paid work (yes/no) were recorded. Stroke characteristics included the affected
hemisphere (left/right/other), type of stroke (infarction/hemorrhage), time between stroke and
enrollment and length of stay in the rehabilitation center (in months).
Physical and psychological characteristics included Health related quality of life
(HRQoL), measured with a Dutch version of the short Stroke Specific Quality of Life
Questionnaire (SSQoL) with higher scores indicating better quality of life (range 12-60) [25],
self-perceived cognitive failures, measured with a Dutch version of the 25-item Cognitive
Failures Questionnaire (CFQ) with higher scores indicating less cognitive failure (range 0-100)
[26] and self-efficacy, measured with a Dutch version of the general self-efficacy scale (SES)
with higher scores indicating greater self-efficacy (range 10-40) [27,28].

Analysis
Patients' baseline characteristics and adherence with the CBCR programme were
analysed using descriptive analyses. Data were presented as the number with percentage, median
with the range or mean with SD. It was tested if variables were normally distributed by means of
the Kolmogorov-Smirnov normality-test. Differences between the S8 group and S2 group were
analysed with independent t-tests, Mann-Whitney U tests or Chi-square test, where appropriate.

Logistic regression analyses were used to examine the impact of the extent of supervision
on training adherence. Adherence (high and moderate versus low) was dichotomized to be used
as dependent variable. Moderate/ high adherence was defined as \( \geq 300 \) minutes, as this was half
of the required amount of total playtime (600 minutes). Low adherence was defined as \(<300
minutes of total playtime. All cognitive domains were included. The impact of supervision
(group S8/ group S2) was included as independent variable, while adjusting for the following
potential confounders: age, sex, educational level, type of stroke, affected hemisphere, cognitive
failure (CFQ), quality of life (QoL) and self-efficacy (SES). Moreover, multiple logistic
regression analyses with a stepwise backward selection procedure were executed in order to
determine which variables predict adherence. Variables with the highest \( P \) value were removed
one by one from the prediction model, until all remaining variables were \( P<0.05 \). All analyses
were performed with the SPSS statistical software package (version 21).
Results

Patient characteristics
The analysis on adherence concerned 53 patients who were allocated to group S8 and 52 patients in group S2, who agreed to participate in the CBCR programme after the trial ended (Figure 2). Characteristics of the 105 patients included in the study are presented in Table 1. The mean age of all patients was 59 (range 46-74) and 66 (63%) of the patients were male. Patient characteristics were similar for group S8 (baseline) and group S2 (t=16 weeks), except for more patients who had had a haemorrhage in group S8 (21/53; 40%) compared to group S2 (11/52; 21%) (p=0.04).

[Table 1 near here].

Adherence
A number of 21 out of the 105 (20%) included patients failed to complete any game. Reasons for not playing at all, as recorded by the supervisor, were: technical problems with the computer (n = 6), lack of motivation (n = 6), health problems (n = 4), vacation (n = 3), hospital stay (n = 1), finding training too difficult (n = 1). From the remaining 84 patients who completed at least one training session, 46 patients (87%) were in the S8 group and 38 (73%) in the S2 group (p<0.01, Chi-Square). Data about adherence for both groups are presented in Table 2.

The median total play time was 424 minutes (range 27-216; 71%) in the total population. The median playtime in group S8 was 528 min (range 63-1264; 88%) vs. 193 min (range 27-2162; 32%) in group S2 (p<0.001 Mann Whitney U). In the total group, 24 out of 84 patients (29%) played ≥600 minutes. In groups S8 and S2, 19/53 (36%) and 5/52 (10%), of the patients played ≥600 minutes (p<0.001, Chi-Square). The median frequency of logging into the website during the training period was 66 (1-164) in group S8 and 47 (1-318) in group S2 (p<0.001 Mann Whitney U). A number of 7 patients from group S2 did not receive interaction with their supervisor after 4 weeks of brain training, since they did not respond to any of the calls.

The Odds Ratio of being in the moderate and high adherence group was 3.4 [95% CI 1.98 – 5.96] (p=0.00) for patients who received weekly supervision (group S8), −0.9 [95% CI 0.86 – 1.02] (p=0.06) for older age (each year of life), 1.65 [95% CI 0.78 – 3.46] (p=0.19) for higher
self-perceived quality of life (SSQoL), 1.0 [95% CI 0.99 – 1.05] (p=0.26) for higher subjective cognitive failure (CFQ), 1.1 [95% CI 0.92 – 1.08] (p=0.50) for higher self-efficacy (SES) and 1.8 [0.67 – 4.60] (p=0.25) for patients with a high educational level.

[Table 2 near here].
Discussion

The aim of this study was to compare two different types of support on training adherence in chronic stroke patients. This study found that only 24 out of 105 patients (23%) were able to complete the required amount of playtime (600 minutes) of brain training. Training adherence was significantly higher for the patients in group S8 (median 528 minutes, range 63-1264) compared to patients in group S2 (median 193 minutes, range 27-2162). A small proportion of patients (5/52, 10%), who had interaction with a supervisor twice (group S2), were able to complete the training. Therefore, there are some implications that systematic, regular interaction with a supervisor can increase stroke patients’ training adherence with a restitution-focused intervention performed at home.

The observation of non-adherence to a CBCR training programme in patients with stroke is in line with findings of other studies [16,17,18,19]. The adherence rate for all patients found in the current study was 29% (36% in group S8 vs. 10% in group S2), but cannot be compared to those studies because of lack of adequate reporting of training adherence [15]. Compared to an average adherence rate of 50% found in a review of 101 publications about Web-based interventions in different areas (chronic conditions, lifestyle and mental health) adherence was low [21], which confirms non-adherence with CBCR programmes is a problem among patients with stroke.

Although a number of patient characteristics were examined with respect to their association with training adherence, apart from the extent of supervision, no other predictors were found in the current study. Therefore it remains unclear for which patients with stroke a CBCR programme in its current form is most suitable. The intensity of training (600 minutes within 8 weeks) might be too demanding for stroke patients. It should be further investigated if lower intensity of training can improve adherence among patients with stroke.

The current study has a number of limitations. First, patients in the S8 group were allocated to the intervention group during the RCT and probably received in general more attention (outside the weekly contact) compared to patients from group S2. Second, interactions between the supervisors and patients were not logged (e.g. topics of conversation and duration of contacts) and could therefore not be verified. It cannot be truly concluded that patients who received more support from supervisors showed greater levels of adherence than those who received very little support.
Third, there should be the same time difference between being informed about the study and the start of the intervention in both groups. Patients in the S8 group started the training straight away when it was still exciting and novel, while patients in the S2 group had to wait 16 weeks when excitement could have waned. On the other hand, those patients were probably still motivated to participate in the brain training, given the option to start the training themselves (self-selection). Moreover, the control group has been given some information about stroke at the time when the intervention group was underwent the brain training procedure. This passive intervention could have had limited impacts on the patients. But the information was very general and previously received by patients during their rehabilitation process.

In conclusion, the overall adherence with an online brain training was low and it seems that serious brain training is not suitable for all initially motivated chronic stroke patients. Moreover, despite a number of methodological limitations in the study design, this study provides ground to further investigate the effect of the extent of supervision on training adherence of stroke patients with restitution-focused training. Although only little or no effects were found on cognitive functioning, self-efficacy and quality of life of the restitution-focused brain training in the overall study [23], this seems important since low adherence rates undermine the effect of interventions. A future study is recommended comparing three groups operating simultaneously with one intervention group receiving weekly support, a second intervention group receiving only two episodes of support and a control group.

**Declaration of interest**

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.
References


Figure 1. Study profile

- Weekly contacts with a supervisor during the 8-week training period (58)
- Contacts with a supervisor twice (57)
Figure 2. Flow of inclusion

Enrollment

Patients invited for participation (n=889)
  Response (n=146)

Patients assessed for eligibility by telephone (n=142)

Patients excluded (n=31)
  Reasons:
  - Medication for depression n=5
  - Aphasia n=5
  - No time to participate n=6
  - Illiteracy n=2
  - No internet access n=5
  - CVA >40 months ago n=6
  - <45 and >75 years old n=2

Patients after assessment for eligibility (n=115)

Random allocation

Allocated to intervention group (n=57)

Allocated to control group (n=58)

Withdrawal prior to baseline assessment (t0) (n=4)

Baseline assessment (n=53)

Baseline assessment (n=57)

Follow-up

Participation in trial at:
  T0 (n=50)
  T8 (n=50)

Participation in trial at:
  T0 (n=57)
  T8 (n=57)

1 Reason for drop-out:
  Too much stress (n=2)
  Malignancy (n=1)

Were offered the intervention after the trial ended (n=57)

Patients that continued participation at:
  T16 (n=52)
  T24 (n=52)

Patient that did not wish to continue participation (n=5)

Analysis

Analysed (n=52)
Table 1. Baseline characteristics of patients with stroke who participated in an 8-week CBCR programme, presented for all patients and per group.

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=105)</th>
<th>Group 1 (n=53)</th>
<th>Group 2 (n=52)</th>
<th>Between groups (P-value)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years; median (range)</td>
<td>59 (46-74)</td>
<td>59 (46-74)</td>
<td>59 (46-73)</td>
<td>0.85</td>
</tr>
<tr>
<td>Sex, male;</td>
<td>66 (63)</td>
<td>34 (64)</td>
<td>32 (62)</td>
<td></td>
</tr>
<tr>
<td>Type of stroke:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarction, n (%)</td>
<td>68 (67)</td>
<td>29 (55)</td>
<td>41 (79)</td>
<td></td>
</tr>
<tr>
<td>Haemorrhage, n (%)</td>
<td>34 (32)</td>
<td>21 (40)</td>
<td>11 (21)</td>
<td>0.04</td>
</tr>
<tr>
<td>Unknown ‡, n (%)</td>
<td>3 (6)</td>
<td>3 (5)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Location of stroke:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemisphere left, n (%)</td>
<td>50 (48)</td>
<td>23 (43)</td>
<td>27 (52)</td>
<td></td>
</tr>
<tr>
<td>Hemisphere right, n (%)</td>
<td>50 (48)</td>
<td>26 (49)</td>
<td>24 (46)</td>
<td>0.21</td>
</tr>
<tr>
<td>Basal ganglia, n (%)</td>
<td>3 (3)</td>
<td>3 (6)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Unknown ‡, n (%)</td>
<td>2 (2)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Time from stroke onset to</td>
<td>25 (8.2)</td>
<td>26 (9.1)</td>
<td>25 (7.5)</td>
<td>0.32</td>
</tr>
<tr>
<td>randomization in months; mean (SD)</td>
<td>5.8 (3.6)</td>
<td>6 (3.6)</td>
<td>5 (3.4)</td>
<td>0.23</td>
</tr>
<tr>
<td>Time spent in rehabilitation centre in</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>months; mean (SD)</td>
<td>36 (34)</td>
<td>17 (32)</td>
<td>19 (36)</td>
<td></td>
</tr>
<tr>
<td>Low, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate, n (%)</td>
<td>33 (32)</td>
<td>18 (34)</td>
<td>15 (29)</td>
<td>0.94</td>
</tr>
<tr>
<td>High, n (%)</td>
<td>36 (34)</td>
<td>18 (34)</td>
<td>18 (35)</td>
<td></td>
</tr>
<tr>
<td>Living alone, n (%)</td>
<td>26 (25)</td>
<td>13 (25)</td>
<td>13 (25)</td>
<td>0.84</td>
</tr>
<tr>
<td>Independent in daily functioning, n (%)</td>
<td>101 (96)</td>
<td>52 (98)</td>
<td>54 (95)</td>
<td>0.35</td>
</tr>
<tr>
<td>Participation in paid work, n (%)</td>
<td>32 (31)</td>
<td>14 (26)</td>
<td>18 (35)</td>
<td>0.33</td>
</tr>
<tr>
<td>Subjective cognitive failure‡;</td>
<td>63 (20)</td>
<td>63 (19)</td>
<td>63 (20)</td>
<td>0.62</td>
</tr>
<tr>
<td>median (IQR)</td>
<td>3.7 (2.5)</td>
<td>3.7 (2.4)</td>
<td>3.8 (2.4)</td>
<td>0.57</td>
</tr>
<tr>
<td>Quality of life‡; median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-efficacy‡; median (IQR)</td>
<td>30 (15)</td>
<td>28 (14)</td>
<td>30 (15)</td>
<td>0.83</td>
</tr>
</tbody>
</table>

*Differences between the groups were analysed with independent t-tests, Mann-Whitney U tests or Chi-square test, where appropriate.

‡ No data were available for medical status.

¥ Low: lower technical and vocational training; median: secondary technical and vocational training; and high: higher technical and vocational training and university.

# Measured with the Cognitive Failures Questionnaire (CFQ); range 0-100; higher scores indicating less cognitive failure.

~ Measured with the Stroke Specific Quality of Life Questionnaire (SSQoL); range 12-60; higher scores indicating better quality of life.

^ Measured with the General Self Efficacy Scale (GSES); range 10-40; higher scores indicating greater self-efficacy.
<table>
<thead>
<tr>
<th></th>
<th>All patients (n=84)</th>
<th>Group 1 (n=46)</th>
<th>Group 2 (n=38)</th>
<th>Between groups (P-value) ^</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total time played (minutes):</td>
<td>424 (27-2162)</td>
<td>528 (63-1264)</td>
<td>193 (27-2162)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total time played per cognitive domain (minutes), %:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention</td>
<td>58 (2-466) (14)</td>
<td>60 (3-408) (11)</td>
<td>37 (2-466) (19)</td>
<td>0.002</td>
</tr>
<tr>
<td>Speed</td>
<td>49 (1-139) (12)</td>
<td>53 (3-139) (10)</td>
<td>6 (1-48) (3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Memory</td>
<td>168 (4-646) (40)</td>
<td>232 (26-646) (44)</td>
<td>95 (4-645) (49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Flexibility</td>
<td>87 (4-1009) (21)</td>
<td>109 (6-349) (20)</td>
<td>50 (4-1009) (26)</td>
<td>0.001</td>
</tr>
<tr>
<td>Problem solving</td>
<td>53 (1-265) (13)</td>
<td>81 (1-265) (15)</td>
<td>7 (2-168) (3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Frequency of logging on to the website (number):</td>
<td>50 (1-318)</td>
<td>66 (1-164)</td>
<td>47 (1-318)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Presented as the median total play time (in minutes) with the range and percentage of the total play time, unless indicated otherwise.

^Differences between the groups were analysed with independent t-tests, Mann-Whitney U tests or Chi-square test, where appropriate.
Randomization

Group S8

Brain training*  No intervention

Group S2

Control intervention  No intervention  Brain training^  

Week 0  Week 8  Week 16  Week 24

*Weekly contacts with a supervisor during the 8-week training period (S8)
^Contacts with a supervisor twice (S2)
Figure 1

*Weekly contacts with a supervisor during the 8-week training period (S8)
*Contacts with a supervisor twice (S2)
Figure 2. Flow of inclusion

Enrollment

Patients invited for participation (n=889)
Response (n=146)

Patients assessed for eligibility by telephone (n=142)
Patients excluded (n=31)
Reasons:
Medication for depression n=5
Aphasia n=5
No time to participate n=6
Illiteracy n=2
No internet access n=5
CVA >40 months ago n=6
<45 and >75 years old n=2

Patients after assessment for eligibility (n=115)

Allocated to intervention group (n=57)

Allocated to control group (n=58)

Random allocation

Withdrawal prior to baseline assessment (t0) (n=4)
Baseline assessment (n=53)

Withdrawal prior to baseline assessment (t0) (n=1)
Baseline assessment (n=57)

Follow-up

Participation in trial at:
T0 (n=50)
T8 (n=50)

Reason for drop-out:
Too much stress (n=2)
Malignancy (n=1)

Participation in trial at:
T0 (n=57)
T8 (n=57)

Were offered the intervention after the trial ended (n=57)

Patient that did not wish to continue participation (n=5)

Patients that continued participation at:
T16 (n=52)
T24 (n=52)

Analysis

Analysed (n=52)
Figure 2

Enrollment

Patients invited for participation (n=889)
Response (n=146)

Patients assessed for eligibility by telephone (n=142)
Patients excluded (n=31)
Reasons:
Medication for depression n=5
Aphasia n=5
No time to participate n=6
Illiteracy n=2
No internet access n=5
CVA >40 months ago n=6
<45 and >75 years old n=2

Patients after assessment for eligibility (n=115)

Random allocation

Allocated to intervention group (n=57)
Withdrawal prior to baseline assessment (t0) (n=4)
Baseline assessment (n=53)

Allocated to control group (n=58)
Withdrawal prior to baseline assessment (t0) (n=1)
Baseline assessment (n=57)

Follow-up

Participation in trial at:
T0 (n=50)
T8 (n=50)
1 Reason for drop-out: Too much stress (n=2)
Malignancy (n=1)

Participation in trial at:
T0 (n=57)
T8 (n=57)

Were offered the intervention after the trial ended (n=57)

Patient that did not wish to continue participation (n=5)

Patients that continued participation at:
T16 (n=52)
T24 (n=52)

Analysed (n=52)

Analysis