Augmented cognitive behavioral therapy for post stroke depressive symptoms

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Augmented Cognitive Behavioral Therapy for Poststroke Depressive Symptoms: A Randomized Controlled Trial

Joyce A. Kootker, MSc,a Sascha M.C. Rasquin, PhD,b,c Frederik C. Lem, MD,d Caroline M. van Heugten, PhD,e,f Luciano Fasotti, PhD,g,h Alexander C.H. Geurts, PhDa,g

Abstract

Objective: To evaluate the effectiveness of individually tailored cognitive behavioral therapy (CBT) for reducing depressive symptoms with or without anxiety poststroke.

Design: Multicenter, assessor-blinded, randomized controlled trial.

Setting: Ambulatory rehabilitation setting.

Participants: Patients who had a Hospital Anxiety and Depression Scale-depression subscale (HADS-D) score >7 at least 3 months poststroke (N = 61).

Interventions: Participants were randomly allocated to either augmented CBT or computerized cognitive training (CCT). The CBT intervention was based on the principles of recognizing, registering, and altering negative thoughts and cognitions. CBT was augmented with goal-directed real-life activity training given by an occupational or movement therapist.

Main Outcome Measures: HADS-D was the primary outcome, and measures of participation and quality of life were secondary outcomes. Outcome measurements were performed at baseline, immediately posttreatment, and at 4- and 8-month follow-up. Analysis was performed with linear mixed models using group (CBT vs CCT) as the between-subjects factor and time (4 assessments) as the within-subjects factor.

Results: Mixed model analyses showed a significant and persistent time effect for HADS-D (mean difference, Δ0.4.6; 95% confidence interval, Δ0.5.7 to Δ0.3.6; P < .001) and for participation and quality of life in both groups. There was no significant group × time effect for any of the outcome measures.

Conclusions: Our augmented CBT intervention was not superior to CCT for the treatment of mood disorders after stroke. Future studies should determine whether both interventions are better than natural history.
of stroke, a psychological treatment approach seems warranted. Because cognitive behavioral therapy (CBT) is aimed at changing irrational cognitions and negative thoughts, its effects may endure after treatment, and chances of relapse of symptoms may be smaller compared with pharmacotherapy. In addition, the side-effect profile of psychological treatment is favorable compared with medication. However, psychological treatments of post-stroke mood disorders have not yet yielded convincing results.

To our knowledge, only 1 randomized controlled trial has been reported investigating psychological treatment of poststroke depressive symptoms. This study yielded inconclusive results regarding the effectiveness of CBT. As the authors acknowledged, this work was a pioneering study with several methodologic weaknesses that compromised its quality. For instance, cognitive impairments were not considered in the inclusion criteria, and the therapy content was insufficiently adjusted to the cognitive consequences of stroke. In addition, the training of therapists was limited. Other researchers argued that to optimize the effectiveness of CBT in patients with stroke, cognitive and emotional impairments and limited awareness of deficits should be taken into account. It was also recommended that CBT should be augmented with real-life activity training to help patients and their caregivers set and attain realistic goals aimed at social participation, taking into account their motor and cognitive impairments.

In addition, anxiety symptoms should be recognized and addressed in CBT treatment because these are often associated with depressive symptoms after stroke. In a pilot study, we already assessed the feasibility of a CBT intervention aimed at reducing depressive symptoms in stroke survivors. Three of 5 participants showed positive results on mood and quality of life immediately after treatment, and these positive results were retained at 3-month follow-up. These findings justified the conduct of a multicenter randomized controlled trial as part of the Restore4Stroke study in The Netherlands.

In the present study, we hypothesized that patients treated with individually tailored augmented CBT would show a larger decrease in depressive symptoms and more improvement in social participation and quality of life than those receiving computerized cognitive training (CCT). CCT was selected as the comparator intervention to control for Hawthorne effects, in the expectation that CCT might improve cognition but not mood.

Methods

Participants

Participants were recruited over a period of 18 months from January 2012. They were screened for eligibility by their treating physicians and psychologists during regular outpatient visits in the following 7 participating rehabilitation centers or hospital rehabilitation departments in The Netherlands: Groot Klimmendaal, Arnhem; St Maartenskliniek, Nijmegen; Adelante, Hoensbroek; Roessingh, Enschede; VieCuri, Venlo; Tolbrug, ’s Hertogenbosch; and ViaReva, Apeldoorn. Participants were eligible when they met the following inclusion criteria: they should (1) have sustained any type of clinically confirmed stroke at least 3 months earlier; (2) a score >7 on the Hospital Anxiety and Depression Scale-depression subscale (HADS-D); (3) be ≥18 years; (4) have only mild cognitive impairments (Mini-Mental State Examination score >27 out of 30) and score positively on the communication-related items of the National Institutes of Health Stroke Scale; and (5) poststroke major depression requiring a start with medication.

The study design and methods were previously published and approved by the Medical Ethical Committee of Nijmegen (The Netherlands) and by the executive boards of all participating rehabilitation institutes. The adjusted time points of assessment were approved post hoc by the same medical ethical committee.

Procedure

After referral to the primary investigator (J.A.K.), participants were enrolled based on the inclusion and exclusion criteria. Oral and written informed consent was obtained by the primary investigator (J.A.K.). Subsequently, patients were randomized to either 4 months of augmented CBT or an equal period of CCT. Interventions were given in the same 6 rehabilitation institutions where patients were treated.

All outcome measures were collected at 4 time points. Initially, we intended to measure at baseline, immediately posttreatment, and 6 and 12 months posttreatment. Because of a lower than expected inclusion rate, the timing of the assessments was adjusted to baseline (t0), immediately posttreatment (t1), and 4 (t2) and 8 months (t3) posttreatment (fig 1). All assessments took place in the rehabilitation institute where the patient was treated. Baseline assessments were performed by the primary investigator (J.A.K.). From t1, all outcome assessments were performed by research assistants who were not involved in the administration of the interventions and who were blinded to treatment allocation of the participants. When patients mentioned the content of their intervention to the assessor, this was reported, and the subsequent assessment was performed by a different, still blinded, assessor.

Randomization

Stratified block randomization (block size 4) was performed by a randomization program for each participating rehabilitation institution separately. Main factors that were expected to affect outcomes were selected for minimization (ie, rehabilitation institute, patients’ anxiety level [Hospital Anxiety and Depression Scale-anxiety subscale score ≤7 vs >7]). As a result, for each participating institute, patients with high anxiety scores and those with low anxiety scores were equally allocated to either the experimental or nonexperimental group.

Interventions

Both interventions were administered during a 4-month time period, with a minimum of 13 and a maximum of 16 sessions. Each session consisted of two 20- to 25-minute blocks divided by a 10- to 15-minute break. Therefore, each session lasted
approximately 1 hour. The CBT intervention was administered by a certified health care psychologist (therapist) who had ample experience in treating depression and stroke rehabilitation in general. All therapists were additionally trained by the primary investigator (J.A.K.) to master the specific aspects of the current CBT intervention. Goals for attaining daily life activities were primarily set together by the patient and the therapist using pictures from the Activity Card Sort.21 Concurrently with the psychological sessions, the CBT intervention was augmented with 3 sessions of occupational therapy or movement therapy. During these sessions, an occupational or movement therapist helped patients with establishing and attaining goals aimed at meaningful activities and social participation. These goals were attuned to the content of the psychological sessions. In the case of a baseline Hospital Anxiety and Depression Scale-anxiety subscale score >7, the protocol was extended with an additional (fourth) occupational therapy/movement therapy session aimed at relaxation techniques, as provided by the Dutch Heart Foundation.22 To implement the recommendations made by Broomfield et al.,10 therapists were continuously reminded to use concrete, repetitive, accessible, slow, and structured communication strategies, as proposed by Judd.23 A detailed description of the applied CBT intervention has been published elsewhere.14

Cointerventions

During the study, patients were requested to minimize cointerventions by other therapists and to refrain from starting new medication. Any existing (psycho)pharmacologic treatment was continued. All cointerventions were registered in a booklet at each assessment.

Assessments

Baseline assessments consisted of the following characteristics: age (years), sex (male or female), employment (yes or no), time since stroke (months), stroke type (ischemic, hemorrhagic, or other), affected hemisphere (left, right, or other), mobility (Stroke Impact Scale mobility subscale25), comorbidity (Cumulative Illness Rating Scale26), level of independence (Stroke Impact Scale25), comorbidity (Cumulative Illness Rating Scale26), level of independence (Barthel Index20), and cognition (Mini-Mental State Examination18). Except for comorbidity, higher scores reflect better outcomes on the scales mentioned.

The primary outcome was the severity of depressive symptoms as assessed with the HADS-D. The Hospital Anxiety and Depression Scale has been specifically validated to assess depressive symptoms in patients with stroke.17 Secondary outcomes were the Hospital Anxiety and Depression Scale-anxiety subscale for symptoms of anxiety, the Post Stroke Depression Rating Scale for assessing the more qualitative aspects of mood,27 coping assessed with the Utrecht Proactive Coping Competence Scale,28 quality of life assessed with the Stroke Specific Quality of Life scale,29 social participation assessed with the Utrecht Scale for Evaluation of Rehabilitation-Participation,30 and subjective well-being assessed with a life satisfaction questionnaire (Life Satisfaction questions).31 Except for the Hospital Anxiety and Depression Scale and Post Stroke Depression Rating Scale scores, higher scores reflect better outcomes.

Statistical analyses

This study was originally powered on the HADS-D at 4 months posttreatment (ie, t2), without accounting for improved precision.

Fig 1  Flowchart of the Restore4Stroke Trial for depressive symptoms after stroke (Consolidated Standards of Reporting Trials diagram). t0, baseline; t1, immediately posttreatment; t2, 4 months posttreatment; t3, 8 months posttreatment.

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because of repeated measures (at t1 and t3). To obtain a power of 80% with an α level of 5%, we originally aimed to include a total of 106 participants. In this calculation, adjustments for baseline values (ie, t0) and posttreatment values (ie, at t2) and a dropout rate of 15% were taken into account. Due to the lower than expected inclusion rate, we investigated whether accounting for the additionally repeated measures at t1 and/or t3 could provide sufficient power. Using the method described by de Hoop, we calculated that including an extra posttreatment value (ie, t1) would provide sufficient power with half the originally planned subjects. This was discussed with and approved by the medical-ethical committee. As a consequence, a minimal number of 53 participants was needed.

Median and ranges or numbers and percentages were used for descriptive statistics in the case of continuous and categorical variables, respectively. After confirming normative distribution of the dependent continuous variables, we used linear mixed models for repeated measures to study the differences between groups for each outcome (dependent variable). The independent fixed variables were group (CBT vs CCT), baseline score, time point of measurement (t0–t3), the minimization factor Hospital Anxiety and Depression Scale- anxiety subscale score >7, and the interaction term between point of measurement and group. The participating institute was treated as a random variable. We present the baseline-adjusted mean differences between groups at each time point with 95% confidence intervals (CIs). The effects of the intervention on the primary and secondary outcome measures were analyzed according to the intention-to-treat principle using SAS 9.2 for Windows and IBM SPSS Statistics 20 for Windows. Data analysis was performed by an independent statistician who was blinded to group allocation.

Results

Participants

Figure 1 presents the patient flow throughout the study. Trial inclusion took place from January 2011 until August 2012, and ended according to prior agreements with the medical ethical committee. Out of 163 referred patients, 61 ultimately participated. Of these, 31 patients were assigned to the CBT intervention and 30 patients were assigned to the CCT intervention. Incomplete interventions occurred once in the CBT group (change in protocol by psychologist) and 4 times in the CCT group (related to suicidal thoughts: n=1; dissatisfaction with intervention: n=2; no reason/not specified: n=1). Fifty-two patients completed the posttreatment assessment, of whom 44 completed the last follow-up. Patient characteristics are listed in table 1.

Control of bias

More than 95% of all assessments were performed according to the protocol. Some exceptions were as follows: extra pauses (t0, n=1), missing page in assessment booklet (t1, n=1), Utrecht Proactive Coping Competence Scale questionnaire too difficult to understand (t1, n=1), and Utrecht Proactive Coping Competence Scale questionnaire and Life Satisfaction questions filled in at home because of time constraints (t1, n=1). Assessor unblinding by the patient occurred in 13% of the t1 assessments, 10% of the t2 assessments, and 9% of the t3 assessments. In the CBT group, 1 patient had sought contact with a psychologist outside the trial for additional anxiety therapy (t1) and 1 patient had started antidepressants (t2). In the CCT group, 1 patient commenced with antidepressants at t1.

Interaction effects and group differences

Table 2 presents the primary and secondary outcomes by point of measurement for each group. Changes in the HADS-D were never significant between groups (fig 2). No group differences after treatment were found for any of the primary or secondary outcomes. Therefore, a parallel line model is presented for all variables in table 3.

Time effects

Table 3 depicts the estimated mean differences between points of measurement, adjusted for baseline values, for all outcomes, and for both groups together. A posttreatment effect was found for the primary outcome, HADS-D (mean difference, −4.6; 95% CI, −5.7 to −3.6). The overall time effect of the HADS-D from posttreatment to 8-month follow-up was not significant. However, the HADS-D showed a significant increase from posttreatment to 4-month follow-up (mean difference, 1.1; 95% CI, 0.2−1.9), followed by a significant decline from 4-month to 8-month follow-up (mean difference, −1.4; 95% CI, −2.1 to −0.7) for both groups.

A posttreatment effect was also observed for the Hospital Anxiety and Depression Scale-anxiety subscale (mean difference, −2.6; 95% CI, −3.6 to −1.5). Post Stroke Depression Rating Scale (mean difference, −3.4; 95% CI, −4.9 to −2.0), Utrecht...
Specific Quality of Life Scale (mean difference, 0.3; 95% CI, 0.0–0.6), but not for the Utrecht Proactive Coping Competence Scale. However, the Utrecht Proactive Coping Competence Scale showed a significant change from posttreatment to 8-month follow-up (mean difference, 0.1; 95% CI, 0.0–0.2), as did the Post Stroke Depression Rating Scale (mean difference, −0.9; 95% CI, −0.2 to 0.4) and Level Satisfaction questions (mean difference, 0.2; 95% CI, 0.0–0.5).

Discussion

The aim of our study was to evaluate the effectiveness of individually tailored CBT for reducing depressive symptoms with or without anxiety after stroke. The results of our multicenter randomized controlled trial indicate that there was significant and persistent improvement of depressive and anxiety complaints after treatment; however, this was independent of the type of intervention. In addition, the subjective ratings of patients’ participation level (Utrecht Scale for Evaluation of Rehabilitation-Participation satisfaction subscale) increased after treatment, as did quality of life (Stroke Specific Quality of Life Scale) and life satisfaction (Life Satisfaction questions).

Fig 2 Mean scores for CCT and CBT patient groups at all assessment time points.
Estimated mean differences (95% CIs) between points of measurement for both the CBT and CCT groups, using linear mixed model for repeated measurements while adjusting for baseline values

<table>
<thead>
<tr>
<th>Time Differences</th>
<th>Overall Group Difference After Treatment Period</th>
<th>8-mo Follow-Up/C0</th>
<th>8-mo Follow-Up</th>
<th>4-mo Follow-Up/C0</th>
<th>Overall Group Difference After Treatment Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.6 (2.1 to 7.1)</td>
<td>1.1 (0.2 to 2.0)</td>
<td>0.7 (0.0 to 1.4)</td>
<td>0.0 (0.0 to 0.0)</td>
<td>1.1 (0.2 to 2.0)</td>
</tr>
<tr>
<td>Posttreatment</td>
<td>-2.6 (-3.6 to -1.6)</td>
<td>-1.2 (-2.1 to -0.3)</td>
<td>-0.7 (-1.6 to 0.2)</td>
<td>-0.1 (-0.2 to 0.0)</td>
<td>-0.7 (-1.6 to 0.2)</td>
</tr>
<tr>
<td>4-mo follow-up</td>
<td>-0.4 (-1.3 to 0.5)</td>
<td>0.0 (-0.1 to 0.1)</td>
<td>0.1 (0.0 to 0.2)</td>
<td>0.2 (0.0 to 0.4)</td>
<td>0.0 (-0.1 to 0.1)</td>
</tr>
</tbody>
</table>

**Table 3**

NOTE: Values are presented as mean (95% CI). The interaction between time and group never reached the level of statistical significance. Therefore, a parallel line model is presented for all variables. Ranges are as follows: HADS-A: (0-21); HADS-D: (0-21); LS2: (0-13); PSDRS (0-5); UPCC (0-4); USERP (0-100, each subscale).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline</th>
<th>Posttreatment</th>
<th>4-mo follow-up</th>
<th>8-mo follow-up-Posttreatment</th>
<th>8-mo follow-up-4-mo follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>HADS-D</td>
<td>-2.6</td>
<td>-1.2</td>
<td>-0.7</td>
<td>0.0</td>
<td>1.1</td>
</tr>
<tr>
<td>HADS-A</td>
<td>-3.4</td>
<td>-0.7</td>
<td>0.1</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>PSDRS</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>UPCC</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>SSQol</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>USERP</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Vocational activities</td>
<td>-1.6</td>
<td>-3.7</td>
<td>0.5</td>
<td>0.1</td>
<td>-0.2</td>
</tr>
<tr>
<td>Leisure activities</td>
<td>3.1</td>
<td>0.7</td>
<td>-0.7</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Satisfaction</td>
<td>2.9</td>
<td>-1.2</td>
<td>2.5</td>
<td>-0.4</td>
<td>-0.1</td>
</tr>
<tr>
<td>Restriction</td>
<td>1.3</td>
<td>0.7</td>
<td>-2.0</td>
<td>0.4</td>
<td>-0.1</td>
</tr>
</tbody>
</table>

**Table 3**

These results appear to be similar to those of Lincoln and Flannaghan, even though our CBT was of longer duration and higher intensity, was augmented with occupational or movement therapy, was provided by well-trained psychologists, and took cognitive impairments and anxiety complaints into account. Like our study, Lincoln and Flannaghan found no differences between intervention groups (ie, no intervention, attention placebo, CBT), however, they did find a small decline (3–4 points) in median score on the Beck Depression Inventory (range, 0–63) for each group immediately after the intervention period. Notably, the relative improvements that were observed in the present study were larger (ie, 3–4 points on the HADS-D; range, 0–21), which suggests that both treatments may have caused a beneficial effect.

As our study lacked a nonintervention group, it cannot be ruled out that any beneficial effect of either CBT or CCT was nonspecific or that HADS-D scores simply improved because of regression to the mean. However, the observed improvements were relatively large, whereas recent literature shows that depressive symptoms poststroke (measured with the Beck Depression Inventory) remain stable over the first 2 years. In addition, our Restore4Stroke consortium recently reported nonsignificant fluctuations in poststroke depressive symptoms (maximally 2-point change in HADS-D) over the first 2 years. These findings point toward the possibility that the observed decline in depressive symptoms after treatment in the present study may actually represent a beneficial effect of both CBT and CCT. This notion raises the question of what the effective component of CCT might be because we took care that cognitive trainers and psychological assistants were instructed not to address issues other than the cognitive training. Interestingly, in a recent evaluation of CCT, Akerlund et al showed that patients with acquired brain injury who suffered from depressive complaints demonstrated mood improvements after CCT, which suggests that cognitive training may improve mood through motivational mechanisms or perhaps through cognitive improvement. Irrespective of the underlying mechanism, it may be that such effects occurred in our study.

Unfortunately, at the initiation of our study, beneficial effect results of CCT on mood problems were not yet known.

Quality of life scores and satisfaction with life and with participation equally and persistently improved in both groups after treatment, as did anxiety level. Proactive coping did not immediately respond after the intervention, but it improved during follow-up, together with life satisfaction and qualitative aspects of mood. In a recent study from our Restore4Stroke consortium, change in depression scores was associated with subjective experience of participation, emphasizing that rehabilitation should focus on resuming occupational activities when treating depressive complaints after stroke. Although in the present study this approach was applied in the CBT intervention, it remains to be explained why we found no group differences for any of the secondary outcomes, and why CBT and CCT had similar effects.

**Study limitations**

Apart from the absence of a nonintervention group, the main limitation of this study is the relatively small patient sample and the recruitment through rehabilitation institutes, which limits the generalizability of our results. It is well known that recruiting patients with depressive symptoms for participation in research is notoriously difficult. Patients who did participate may have been more motivated than those who did not, which may have led to selection bias. This too would limit the generalizability of our
results. Although we did not reach the inclusion number as originally planned, the risk of false-negative outcomes for group by time interactions seems to be small because no trends were observed toward significant interactions. We were not able to directly compare our results with those of Lincoln and Flanagan because we used the HADS-D instead of the Beck Depression Inventory as a primary outcome. This choice was determined by the intention to prevent overestimation of depressive symptoms because of general symptoms (eg, fatigue) of stroke. Unlike the Beck Depression Inventory, the Hospital Anxiety and Depression Scale does not include fatigue as a symptom of depressed mood.

Conclusions

This randomized controlled trial showed persistent improvement of depressive symptoms, anxiety symptoms, quality of life, satisfaction with life, and participation after both CBT and CCT in patients with depressive complaints minimally 3 months after stroke. This finding implies that, for now, both types of interventions may be considered to improve depressive symptoms after stroke. Future research should determine whether both interventions are better than natural history and what underlying mechanisms are responsible for such effects.

Suppliers

a. Cogniplus; SCHUHFRIED.
b. SAS 9.2; SAS Institute.
c. IBM SPSS Statistics 20; IBM.

Keywords

Anxiety; Depression; Psychology; Rehabilitation; Stroke

Corresponding author

Joyce A. Kooiker, MSc, Reinier Postlaan 12, PO Box 9101, 6500 HB, Nijmegen, The Netherlands. E-mail address: joyce.kooiker@radboudumc.nl.

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