Cognitive adaptation training combined with assertive community treatment: A randomised longitudinal trial

Jens Peter Hansen a,b,⁎, Birte Østergaard b, Merete Nordentoft c, Lise Houngsaard b

a Mental Health Services in the Region of Southern Denmark — Esbjerg, Denmark
b Research Unit of Nursing, Institute of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense C, Denmark
c Psychiatric Center Copenhagen, Bispebjerg, Capital Region Psychiatry and Faculty of Health Sciences, University of Copenhagen, Denmark

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Abstract

Background: Cognitive adaptation training (CAT) targets the adaptive behaviour of patients with schizophrenia and has shown promising results regarding the social aspects of psychosocial treatment. As yet, no reports have appeared on the use of CAT in combination with assertive community treatment (ACT). Our purpose was to evaluate the effect of CAT in comparison with ACT, focusing on social functions (primary outcome), symptoms, relapse, re-hospitalisation, and quality of life of outpatients with schizophrenia.

Methods: The trial was a parallel, randomised, multicentre trial conducted in three centres treating patients with a first episode of schizophrenia disorder. A total of 62 outpatients diagnosed as having schizophrenia were randomly assigned to CAT + ACT or ACT alone. The CAT was conducted in the patient’s home and included instruction in prompting for specific actions. The treatment lasted for 6 months, and the patients were assessed at baseline and at 6- and 9-month follow-ups.

Results: The results of mixed-effects regression models indicated no significant differences between intervention group and control group at 6 and 9 months in any outcome [Global Assessment of Functioning at 6 months (p=0.32) and the Health of the Nation Outcome Scales social subscale at 6 months (p=0.30)].

Conclusion: The results from this trial differ from previous CAT trials because use of CAT showed no significant effects. However, the low number of participants may have been responsible for these results. Thus, additional studies are needed to determine whether the use of some elements of CAT can help to make ACT more economically effective.

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1. Introduction

Approximately 75% to 85% of patients with schizophrenia have cognitive impairments (Johnson-Selfridge and Zalewski, 2001; Kurtz et al., 2005; Pfammatter et al., 2006). Impairments have a negative influence on patients’ ability to maintain work, contact with friends, and independent living and functioning social relationships (Green et al., 2000). Although antipsychotic treatment can decrease cognitive impairment, it cannot eliminate these problems (Peuskens et al., 2000). It therefore seemed relevant to develop compensatory strategies for the remaining cognitive impairments.

Cognitive adaptive training (CAT) has shown promising effects on patients with schizophrenia in terms of an enhanced level of social functioning, decreased relapse rates, and higher compliance compared to treatment as usual. CAT is designed to bypass cognitive deficits by rearranging the environment to support and sequence appropriate behaviours (Velligan et al., 2008b).

CAT has so far only been tested in comparison with groups receiving active comparator conditions and treatment as usual (i.e. standard medication follow-up provided by a community outpatient clinic). In the setting for the present trial, assertive community treatment (ACT) was already the standard treatment and included a low case load for the team members who attempted to provide all the psychiatric and social care the patients required at home (Marshall and Lockwood, 1998).

We combined CAT with ACT to investigate whether CAT would show the same promising effects on patients with schizophrenia in this setting. Although CAT and ACT both use support as an essential element in intervention, CAT and ACT interventions differ in both ideas and methods. CAT places the primary focus on cognitive impairment and the strategies to bypass these (Velligan and Bow-Thomas, 2000), where ACT focuses on helping the patient to live in the community with a disease (McGrew et al., 1994; Burns, 2010). CAT uses individual training on social abilities (Velligan and Bow-Thomas, 2000), where ACT uses support and contacts in the environment to help the patient in regard to symptoms, social problems and daily living (McGrew et al., 1994; Burns, 2010).
To our knowledge the trial was the first trial on the effect of CAT in an ACT setting. The trial was also the first to target patients with first-onset of psychoses.

The aim of the trial was to evaluate the effect of CAT + ACT versus ACT alone, with focus on social functions, symptoms, relapse, re-hospitalisation, and quality of life of outpatients with schizophrenia.

2. Materials and methods

The trial was a randomised multicentre trial of 62 outpatients allocated to CAT + ACT or ACT alone. The patients were included consecutively from three outpatient clinics in Southern Denmark specialising in the treatment of patients with schizophrenia. The patients completed baseline assessment before randomisation into one of two groups: CAT + ACT or ACT alone group. After randomisation, the patients were treated for 6 months and then the patients were followed up for an additional 3 months. The environmental supports (e.g., signs, text message-systems) remained in use in the CAT + ACT group after the 6-month treatment period. Assessments of symptoms and functioning were conducted at baseline, at 6, and 9 months.

2.1. Patients

From 1 January 2009 to 31 July 2010, 66 patients with a diagnosis in the schizophrenia spectrum (ICD codes in the F2 category) who had been treated for more than 1 year at a psychiatric clinic treating patients with a first episode of schizophrenia disorder and who received psychotherapeutic medication and psychosocial treatment were included in the trial. Patients living at an institution, patients who did not speak or understand Danish, and patients who did wish to participate were excluded.

The patients were identified through contact to the centres. The eligible patients were informed of the possibility of taking part in the project by a member of the primary staff. The patients were given details of the trial by the first author in the patients' homes. The trial was approved from the local ethics review board (S-20080037), and all included patients signed an informed consent and could withdraw without account.

2.2. Blinding

Group assignment was blinded only for the assessors. The assessors were independent of the research team, were involved only in follow-up interviews, and were kept blinded to treatment allocation. The patients were told not to give the assessors information about their group assignments.

2.3. Randomisation

The included patients were centrally randomised to CAT + ACT or ACT alone. The randomisation was carried out through a centralised telephone voice response randomisation. The allocation sequence was computer generated, and stratified for each of the three centres and for social functioning assessed using The Health of the Nation Outcome Scales’ (HoNOS) items 9–12 (social problems subscale). The allocation sequence was concealed until the voice response call.

2.4. Intervention and control arm

All the patients received ACT with regular contact with a physician, a community mental health nurse, and a social worker. The treatment included medications and weekly contact with professionals (often in patients' homes). Additionally, all patients received treatment according to the concept described in the OPUS trial (Thorup et al., 2005) including psychoeducation, and social skill training in groups and psychosocial intervention with relatives.

Additionally, patients in the intervention arm received training regarding the solving of concrete problems related to daily life using tools such as schedules, schemes, and signs. The intervention was conducted in the patients' homes in accordance with a revised CAT manual every 14 days for a period of 6 months. All the interventions were provided by the same person who was responsible for the revisions of the CAT manual. This person had long experience in treating patients with schizophrenia and was theoretically prepared in conducting CAT by scientific immersion in cognition and training during a PhD course. The intervention was based on assessment of neurocognitive function using the Frontal Systems Behavior Scale (FrSBe) (Velligan and Bow-Thomas, 2000) and the Wisconsin Card Sorting Test CV4 (WCST) (Heaton et al., 1993). The executive functions were assessed using WCST (contrary to a composite assessment in the original CAT treatment). Patients who completed fewer than four categories or had more than 15% perseverative errors on the WCST were categorised as having poor executive functions (Thurston-Snoha and Lewine, 2007; Rodriguez-Jimenez et al., 2008). Patients who had increased scores on apathy received environmental prompts (i.e. automatic short message service (SMSs)) to initiate and complete daily activities. Patients who had increased scores on the disinhibition subscales received help to organise belongings and remove distracting objects from the environment so that they could focus on their daily activities. Patients with high scores on the executive subscale received extensive support and a stronger and clearer indication from environmental cues. Patients with no increase in subscale score received environmental prompts and tools to support daily activities as needed.

2.5. Assessments

At trial entry and at 6 and 9 months, the following information was collected.

2.5.1. Primary outcome

The global social functioning was assessed using the Global Assessment of Function (GAF-F) (Startup et al., 2002). The specific social functioning was assessed using HoNOS social problems subscale. The instrument assesses problems with relationships, activities of daily living, living conditions, occupations, and activities (Wing et al., 1998).

2.5.2. Secondary outcome

Social needs were assessed using the Camberwell Assessment of Need (CANSAS) items 1–5 and 11–24 (Andresen et al., 2000). Symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1988). Quality of Life was assessed using Lehman Quality of Life Interview, Brief Version (L-QoLI) (Melle et al., 2005).

Data on hospitalisation recorded as the number of hospitalisations, the number of bed-days, and the reasons for hospitalisation were collected from the hospital records.

2.6. Inter-rater reliability

Two investigators trained in the outcome assessments did the assessments. After more than 15 completed interviews, the investigators were assessed for reliability. The reliability test was conducted on the basis of eight PANSS interviews in which investigators did individual ratings. We calculated the intraclass correlation coefficient (ICC) for each item to control test–retest reliability. The ICC was considered positive for group comparison (ICC = 0.89).

2.7. Statistical methods

Differences in functional outcome over time by intervention group and controls were assessed using multilevel mixed-effects linear regression analysis with unstructured variance matrix where the baseline values of the outcomes were used as covariates. p values...
above 0.05 were considered significant. Skewed variables were power transformed if possible; otherwise the variables were transformed into dichotomous responses. Missing values were replaced using multiple imputation (m = 20) (Schafer and Graham, 2002). This approach assumes that the distribution of missing data could be estimated from the information from previous interviews under the assumption that data were missing at random. The model was checked using residual plots and the Shapiro–Wilk test. For time to readmission, we used a stratified Cox regression to relax the assumptions of proportional hazards. Survival times were plotted in a Kaplan–Meier survival curve. All analyses in the 62 patients were done on the principle of intention to treat. The analyses were conducted in the statistical software programme Stata 11.

2.8. Power calculation

When the trial was planned, we considered social functioning to be the primary outcome. We expected a mean reduction in HoNOS social subscale from 8 to 6 points, with a standard deviation of 3.5 in both groups. With a 0.05 level of significance and 90% power, 65 patients were required for each study group. Thus, we planned an inclusion of 164 patients, with compensation for 20% attrition during follow-up. However, only 62 patients were randomised because of exclusions and refusals. The reduced group size gave us the ability to detect a difference of 3 points between groups on the HoNOS social subscale.

3. Results

3.1. Baseline characteristics

The flow chart for the trial is presented in Fig. 1. Of the 366 eligible patients, 300 were excluded: 59 patients did not fulfil the inclusion criteria, 29 met the exclusion criteria (20 living at institutions, 6 did not understand Danish, and 3 lived with someone included in the study), 191 refused to participate, and 21 could not participate (19
moved or were discharged from treatment centres and 3 were evaluated to be too psychotic to undergo baseline assessments. Before randomisation 4 patients dropped out, leaving 62 patients for randomisation and analysis. After randomisation, 6 patients in the CAT+ACT group and 4 patients in the ACT alone group withdrew consent. Additionally, at the 6-month follow-up, 1 patient in the ACT alone group and 1 patient in the intervention group could not be located, and at the 9-month follow-up, 6 patients in ACT alone group could not be located.

Table 1 summarises the demographic and some of the baseline variables by treatment group. The clinical characteristics were similar except for the percentages of perseverative errors and differences between centres. Patients in the intervention group had a higher percentage of perseverative errors [14% (SD=7)] compared to the patients in the intervention group [10% (SD=10)]. The patients from one centre had a higher mean age [25.4 years (SD=11.1)] than in the two other centres [22.1 years (SD=1.7) and 26.6 years (SD=4.8)]. The times from onset of schizophrenia to randomisation were likewise longer at this centre [8.3 years (SD=7.8)] than at the other two centres [2.0 years (SD=0.22) and 1.9 years (SD=0.86)]. The HoNOS social subscale scores were higher at this centre [6.3 (SD=3.5)] than at the two other centres [4.8 (SD=4.3) and 4.0 (SD=3.5)].

3.2. Primary outcomes

The results indicated no significant differences in primary outcome GAF at 6 months (p = 0.32) or 9 months (p = 0.34) and no significant differences in HoNOS social subscale at 6 months (p = 0.30) and 9 months (p = 0.15). The non-significant mean improvement in GAF was 1.5 in favour of the intervention group, as illustrated in Fig. 2. Analyses of effect of time showed no significant improvements on GAF at 9 months for the CAT+ACT group (p = 0.42) or the ACT alone group (p = 0.36). The effect size on HoNOS was significant at 9 months for the ACT+CAT group (p = 0.004) and for the ACT alone group (p = 0.05).

3.3. Secondary outcome and control for confounders

The secondary outcome was not significantly different in the CAT+ACT group compared to the ACT alone group at any time for any outcome, as illustrated in Table 2. However, analyses of effect of time indicated a consistent improvement on some secondary outcomes, as illustrated in Table 3 and Fig. 2. After a Bonferroni correction (Altman, 1999) the analysis showed no significant differences in primary outcome GAF at 9 months for the CAT+ACT group (p = 0.42) or the ACT alone group (p = 0.36). The time from randomisation to relapse did not differ significantly between the groups according to analysis with the proportional hazards regression model (p = 0.75). The times to readmission illustrated in the survival curves for the treatment group over time are presented in Fig. 3. There were no significant differences in the time patients spent in hospital (p = 0.79).

The analysis showed no effect of confounders on either primary nor secondary outcomes. The list of confounders included age, sex, education, substance abuse, centre, occupational background, anti-psychotic medication (sort), diagnosis, years in centre, days at hospital in intervention period, contacts to psychiatrist, contacts to emergency ward, contacts to primary team member (PTM), and caseload for primary team member.

The patients included in this trial had similar social functioning (GAF > 40) compared to the patients who refused to participate (GAF < 38).

3.4. Fidelity

The fidelity of the delivered ACT was assessed according to McGrew et al. (1994) showing high fidelity on all items except a mean caseload at 13.8 (SD = 4.5) which is 3.8 over recommended caseload. A staff member’s caseload in the community mental health centres varied between 1:5 patients and 1:22 patients. The patients received 0.61 (SD = 0.26) visits a week, on average. The CAT treatment was delivered according to the CAT manual to all but three patients admitted to hospital part of the time for the intervention. The mean number of interventions was 8.1 (SD = 4.3). The interventions were applied to all areas described in the CAT manual with highest frequency regarding social skills (60%), work skills (33%) and medication management (27%). The tools used in the intervention included all the tools described in the manual with highest frequency regarding messages on mobile phones (37%) and use of schedules (37%)

4. Discussion

In this trial comparing CAT+ACT versus ACT alone, we investigated whether patients receiving CAT might benefit with regard to social functioning, symptoms, admission to hospitals, and quality of life. To the best of our knowledge this is the first trial in an ACT setting. However, there are some limitations that have to be taken into consideration. (1) There were no assessments of conceivable contamination with CAT interventions in the ACT alone group. The contaminations were solely prevented by admitting the CAT intervention to the patients from a person outside the ACT team (the first author). (2) The CAT treatments were administered by a staff without practical training in CAT and without supervision from experienced CAT providers. (3) The low number of patients in the study may have resulted in accepting a false null hypothesis, giving a type II error. We planned to avoid this problem by calculating power to demonstrate significant results. However, the estimated number of patients was not reached because 300 had to be excluded; mostly patients who did not want to participate. Attention to refusers is crucial in trials involving patients with schizophrenia because many of these patients have difficulty making decisions (Candilis et al., 2008) and lack interest in research projects (Candilis et al., 2006). Thus, we included all centres in the region to get access to enough patients. However, the large number of patients refusing to participate made it impossible to conduct this project as originally planned. The high refusal rate might come from a practice where the patients were initially informed through the patient’s primary mental health worker. Most of the refusers did not want to meet the primary researcher. Thus, lack of sufficient support in making the decision to meet the primary researcher may have induced some refusals.
Despite the lack of power, the results showed a non-significant, infinitesimally small mean difference of 0.5 on the HoNOS social subscale in favour of CAT treatment. When we did a power calculation from the results, it gave an estimated population of 2.328 patients at 90% power to demonstrate significance. However, an improvement of 0.5 on the HoNOS social subscale would not be clinically relevant.
Previous results from studies of CAT have shown significant improvements in the CAT groups in comparison with the control groups (Velligan et al., 2008b, 2009). One trial has shown effect of CAT and Generic Environmental Supports (GES) on social functioning compared to treatment as usual (Velligan et al., 2008a). However, the differences in social functioning between the CAT group and the GES group were only reported significant on the Social and Occupational Functioning Scale (SOFAS) (p = 0.03) and not on the adaptive Multnomah Community Ability Scale (MCAS) (Velligan et al., 2008a). GES is a manual-driven series of environmental supports provided monthly by telephone calls regarding the use of checklist of everyday activities, pill containers, and reminder signs (Velligan et al., 2006). In the present trial, treatment as usual was more intensive than that in the GES group in regard to time spent with patients, in instructions in correct medication management, and adjusting the medication. Thus, the lack of significant results on primary outcome in the present trial is in accordance with previous results showing no significant differences between GES and CAT on MCAS. Additionally, the general social functioning in previous trial was assessed using the SOFAS instrument contrary to GAF in the present trial. The SOFAS instrument might be more sensitive to changes in adaptive functioning in regard to the treatment (Hilsenroth et al., 2000). Consequently, an assessment using adaptive instruments such as MCAS and more sensitive instruments like SOFAS might have generated significant differences between groups in this trial. In regard to previous OPUS studies, the improvement in mean GAF over time was smaller than in previous OPUS studies (Petersen et al., 2005). There was no significant change in symptoms between groups as in previous CAT studies. However, the positive symptoms on PANSS changed significantly over time in contrast to previous studies of CAT. The changes of positive symptoms over time were similar to the improvements in the intervention group in the OPUS study (Petersen et al., 2005).

The time to readmission to hospital was not significantly different between groups in this trial in contrast to previous CAT studies (Velligan et al., 2008b). However, the time to readmission was longer in this trial for both groups than the time to readmission in the intervention group in previous CAT studies. Drop-out analysis showed significantly more drop-outs among women than men (p = 0.013). More men than women were diagnosed as substance abusers. Thus, substance abuse and gender were included in all analyses of outcome. However, neither gender nor substance abuse had any effect on outcome. CAT + ACT did not improve social functioning and Quality of Life or reduce symptoms and readmission significantly compared to ACT alone treatment in this first trial of CAT added to ACT treatment. Therefore, we still do not know the most efficient compensatory treatment in regard to cognitive impairment in an ACT setting. Further studies on the effectiveness of combinations of ACT and CAT are needed to determine whether use of elements from CAT can improve functional outcomes in schizophrenia.

### Contributors
All authors participated in all stages of the preparation and completion of this article including design of the study, writing the protocol, literature searches, statistical analysis and writing the final manuscript.

### Conflict of interest
None disclosed for any of the authors.

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### Table 3
Significant changes over time for both groups.

<table>
<thead>
<tr>
<th>Measured parameter</th>
<th>6-months p-value of interaction</th>
<th>9-months p-value of interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>CANSAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>0.027</td>
<td>0.004</td>
</tr>
<tr>
<td>Intervention group</td>
<td>0.039</td>
<td>0.018</td>
</tr>
<tr>
<td>PANSS positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>0.019</td>
<td>0.007</td>
</tr>
<tr>
<td>Intervention group</td>
<td>0.026</td>
<td>0.013</td>
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<tr>
<td>L-QoL life in general</td>
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<td></td>
</tr>
<tr>
<td>Control group</td>
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<td>0.002</td>
</tr>
<tr>
<td>Intervention group</td>
<td>0.020</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Values are mean (SD) unless stated otherwise.

**CANSAS** = Camberwell Assessment of Need on unmet needs at items 1–5 and 11–24.

The p-values for CANSAS were analysed after transformation to dichotomous response, 0 = no unmet needs and 1 = one or more unmet needs.

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