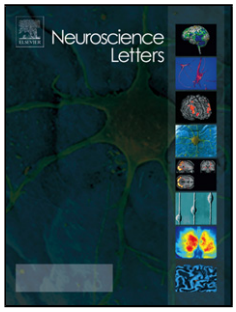
DOI:
10.1016/j.neulet.2015.08.036

Document Version
Peer reviewed version



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PII: S0304-3940(15)30106-3
DOI: http://dx.doi.org/doi:10.1016/j.neulet.2015.08.036
Reference: NSL 31509

To appear in: *Neuroscience Letters*

Received date: 30-3-2015
Revised date: 31-7-2015
Accepted date: 20-8-2015

Please cite this article as: Shuping Tan, Yizhuang Zou, Til Wykes, Clare Reeder, Xiaolin Zhu, FudeYang, Yanli Zhao, Yunlong Tan, Fengmei Fan, Dongfeng Zhou, Group cognitive remediation therapy for chronic schizophrenia: A randomized controlled trial, Neuroscience Letters http://dx.doi.org/10.1016/j.neulet.2015.08.036

Group cognitive remediation therapy for chronic schizophrenia: a randomized controlled trial

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Highlights

- CRT significantly improved cognitive flexibility, memory and social function.
- Improvement of cognitive function did not predict social function change.
- CRT is an effective and promising therapy for patients with schizophrenia in china.

Abstract

Individual-level Cognitive Remediation Therapy (CRT) has been shown to be effective for cognitive improvement and social function amelioration. Here, we aimed to test the efficacy of group-based CRT in Chinese subjects with schizophrenia. One-hundred and four inpatients were randomly assigned to either 40 sessions of small-group CRT therapy or therapeutic contact-matched Musical and Dancing Therapy (MDT). Cognitive and social functioning, as well as clinical symptoms, were evaluated over the course of treatment. Specifically, cognitive function was evaluated using a battery of cognitive measurements, clinical symptoms were evaluated using the Positive and Negative Syndrome Scale, and social function was evaluated using the Nurse's Observation Scale for Inpatient Evaluation-30. All patients were evaluated pre- and post-treatment. Forty-four individuals in the CRT group and 46 in the MDT group completed all of the planned treatments and analyses. Cognitive functions, especially cognitive flexibility and memory, showed significant improvement in the CRT group over the course of the study. The MDT group also showed improvement in several cognitive flexibility assessments, but the degree of improvement was significantly greater in the CRT group. Several social-function factors exhibited a significant improvement in the CRT group, but not in the MDT group. Cognitive function improvement correlated positively with social function without predicting social function change. We conclude that group-based CRT is an effective and promising therapy.

Keywords: Schizophrenia; Cognitive Remediation Therapy; Cognitive deficits

1. Introduction

Cognitive impairment is a core feature of schizophrenia [4, 16], and deficits affecting processing speed, attention/vigilance, working memory, and executive function correlate with poor functional outcomes [3, 19, 29]. Antipsychotic agents significantly control clinical symptoms, especially positive symptoms. However, these agents, whether typical or atypical, produce little or no remediation of cognitive deficits in schizophrenia [6, 15, 31]. Because of this shortcoming, many non-drug therapies, most notably neurocognitive approaches such as Cognitive Remediation Therapy (CRT), have been developed [12, 32, 35]. CRT is a novel rehabilitation method that aims to teach patients "thinking" skills in order to produce improvement in cognitive processes such as attention, working memory, and executive function [9, 21, 33, 35]. Accumulating evidences have validated the efficacy of CRT [10, 22, 33, 34]. Moreover, most studies have found significant functional outcome improvements accompanying changes in the level of cognitive functioning [8, 28, 37]. Prior studies confirming the efficacy of CRT [20, 24, 30] have almost entirely used individual-level CRT (i.e. one therapist and one participant per session). Although increasing evidence indicates a face-to-face approach is effective in improving cognition and social function in schizophrenia [26, 35], it is difficult to transfer this method to routine clinical therapy due to an insufficient supply of therapists. To remove this translational bottleneck, a group-based variation of CRT appears promising, especially in China, home to about 10 million patients with schizophrenia [25] who all might benefit from CRT. However, to date, evidence on the clinical effects of group-based CRT for this disorder is limited. The present study was therefore undertaken.

2. Methods

2.1 Participants

All participants were recruited from the Beijing Huilongguan Hospital. The inclusion criteria were:

- Diagnosis of schizophrenia according to the Diagnostic and Statistical Manual, 4thed. [1] by two attending psychiatrists;
- Duration of illness of 2 years or more;

- Age 20–60 years;
- Evidence of cognitive impairment;
- Completion of at least 6 full years of education;
- Clinical condition stable for at least 1 month.

Participants were excluded for:

- Difficulty in communicating effectively with therapists;
- Substance abuse, as defined by the DSM-IV;
- History of organic brain disorder or other severe organic disorder.

All participants provided written informed consent, and the protocol was approved by the Beijing Huilongguan Hospital Ethics Committee.

2.2 Procedure

One hundred and four participants fulfilled all criteria and were randomly assigned to the CRT (n = 52) or the Music and Dance Therapy (MDT) groups (n = 52). A random number table was used to generate lots that were drawn for sealed envelopes, which assigned the participants to the CRT or MDT groups (see consort flow chart in Fig. 1).

All participants were assessed before and after 10 weeks of treatment. Neurocognitive function, clinical symptoms, and social functioning were evaluated. Neurocognitive tests were carried out by two clinical psychologists, who had at least 5 years' experience with psychometric testing. Clinical symptom rating (Positive and Negative Syndrome Scale, PANSS) was conducted by two attending psychiatrists. Social function assessment was carried out by four senior nurses, who had at least 5 years' experience in psychiatric nursing. All eight raters were blind to group assignment.

2.3 Measures

The following measures were administered:

2.3.1 Clinical assessment

The Chinese version of the PANSS [39] was used for symptom assessment. In addition to the

total score, three subscales were calculated: positive, negative, and general psychopathology.

2.3.2 Neurocognitive assessment

(ⅰ) Stroop Neuropsychological Screening Test: This is a paper version of the ubiquitous Stroop test, key measurables being the reaction times for correctly naming 30 items in the following three categories: the color of colored circles printed in red, yellow, blue, or green; the word information of words printed in the same four colors; and the color information of words printed in the same four colors. The words were color names that were different from the color of the ink in which the word was printed. **Two skilled clinical psychologists used a professional stopwatch to measure the reaction times.**

(ⅱ) Category Fluency Test (CFT): Participants were asked to provide as many different names of fruits or animals as possible in one minute, the score being the number of such names provided.

(ⅲ) Verbal Fluency Test (VFT): Participants were asked to provide as many different Chinese common words as possible in one minute consisting of two to four Chinese characters beginning with a cue character provided by the test giver. For example, if the latter were "工", which means "working," participants could use it to make a word such as "工人," or "worker." In each test, five cue characters were given sequentially and the score was the total number of valid words generated.

(ⅳ) Trail Making Test-A: The key measurable was the time required to draw a trail in numerical order through a set of numbers running from 1 to 25, where the numbers were randomly placed. **Time required to perform Trail Making Test-A was also recorded using a professional stopwatch.**

(ⅴ) Logical Memory Test: Wechsler Memory Scale-Revised: Immediate-recall total score and delayed-recall total score.

(ⅵ) Benton Visual Retention Test (BVRT) [7], Form C: Participants were asked to reproduce 10 simple geometric designs in turn from memory. The key measurables were numbers of right and wrong responses.

(vii) Digit Span (Wechsler Adult Intelligence Scale-Revised): Administered according to the standard WAIS-R instructions. The key measurable was the age-scaled score.

2.3.3 Social functioning assessment

A Chinese version [18] of the Nurse's Observation Scale for Inpatient Evaluation (NOSIE)-30 [14] was used to evaluate participant behavior and social functioning. The measurables comprised a total score, a positive-factor score, and a negative-factor score.

2.4 Therapy

The CRT protocol was based on a Chinese version of the CRT manual, originally derived from an English version of *Frontal/Executive Function Program (Revised)* [5, 34]. This therapy consists of three modules: 1) the "Cognitive Shift Module," addressing flexibility in thinking and information-set maintenance; 2) the "Working Memory Module", addressing working memory capacity, which has participants work with two to five information sets at a time; and 3) the "Planning Module," which training the ability for self-ordered, goal-oriented, set/schema formation, manipulation, and planning [23, 38].

Participants received 40 hourly sessions at an average rate of 4 per week. Four therapists, after standard CRT therapy training, helped the participants finish the CRT tasks, which were mainly done with pencil and paper. Each therapist conducted testing of 3–4 participants simultaneously with the details of the process varying with individual performance in treatment. To minimize errors, the therapist also discussed information-processing strategies and how to regulate, organize, and monitor behavior. As described in other reports [12, 33], many therapeutic techniques such as errorless learning, verbal indicating, and scaffolding were used to ensure therapeutic effects.

Patients randomized into the control group, MDT, had the same number of therapeutic sessions as the CRT group. MDT therapy had two different activities: playing music (learning to play a fairly easy instrument, namely the xylophone) and dancing (learning to dance).

2.5 Data Analyses

Primarily, a series of intent-to-treat analyses were used to examine all outcome variables.

Repeated-measures ANOVA was employed to find main effects of CRT vs. MDT on all outcome variables. To better understand the clinical significance of outcome improvements, effect size (ES) for a given variable was calculated as the difference after treatment between CRT and MDT groups divided by the pooled standard deviation.

Finally, a series of correlation tests were used to investigate the correlations among the pre-post changes in cognitive domains, clinical symptoms, and social functions. If evidence of a correlation between two outcomes was found, such as cognitive improvement and social functioning changes, a stepwise regression model was calculated in which initial function scores were entered first, to test the hypothesis that some cognitive changes may be predictors of social function improvement and clinical symptom amelioration.

3. Results

3.1 Demographic characteristics

During treatment, eight participants in the CRT group (1 discharged, 2 clinically aggravated, and 5 refusing to continue after 2–10 sessions of treatment) and six participants in the MDT group (2 discharged, 1 clinically aggravated, and 3 refusing to continue after 2–8 sessions of therapy) dropped out. Ultimately, 44 participants in the CRT group and 46 participants in the MDT group completed the study and provided adequate data for analysis. At study entry, there was no significant intergroup difference in any demographic feature, cognitive function, or clinical symptom (Table 1).

3.2 Cognitive Function

Within-group paired *t*-testing showed that six of ten cognitive variables improved significantly after treatment in the CRT group, while only four improved in the MDT group. After treatment, performance on the Trail Making–A, VFT, Stroop-word color, BVRT-correct, and BVRT-wrong tests improved significantly in the CRT group compared to the MDT group, as assessed by repeated-measures ANOVA (Table 2).

3.3 Symptomatology

The PANSS total scores, PANSS negative scale, and PANSS general psychopathology scale

showed significant improvements (within-group paired *t*-test) after treatment in both the CRT and MDT groups. There was no group difference in the total score or in any of the subscales of the PANSS after treatment (Table 3).

3.4 Social functioning

The total and general negative NOSIE scores within the CRT group showed significant improvements after treatment. A significant group difference in total NOSIE scores, with general negative and general positive subscale scores exhibiting significant group trends, was also found. There was no significant change in the total score or in any subscale of NOSIE in the MDT group after treatment (Table 3).

3.5 Correlations among improvements in cognitive, clinical symptom, and social functioning

Correlation testing revealed several significant positive correlations: cognitive functioning improvement and clinical symptom alleviation, i.e., VFT vs. general psychopathology scale of PANSS ($r = 0.48$, $p < 0.01$); cognitive functioning improvement and social functioning enhancement, i.e., VFT vs. total score of NOSIE ($r = 0.37$, $p < 0.05$); and clinical symptom alleviation and social functioning enhancement, i.e., general psychopathology scale of PANSS vs. general negative scale of NOSIE ($r = 0.39$, $p < 0.05$). Stepwise regression modeling revealed that neither cognitive improvement nor clinical change was involved in the social functioning model.

4. Discussion

As expected, the present study showed there was significant improvement in many cognitive performance measures after CRT treatment. Although performance on several cognitive tests also improved in the MDT group, the benefits conveyed by CRT were considerably greater in these instances. MDT was implemented here as an alternative non-pharmacological therapy to control for Hawthorne effects. This therapy is commonly prescribed for persons with mental disorders in China. Indeed, cognitive test performance did improve with MDT, suggesting that therapeutic contact and amusement activity may have some benefit for cognitive function. However, other cognitive variables such as Trail-Making A and BVRT changed little with MDT. This indicates that these non-specific factors have a relatively small effect on neurocognition in schizophrenia.

Therefore, the distinct advantages of CRT in improving performance on a range of cognitive tests revealed here cannot be attributed to practice or to intensive therapeutic input, but rather are mainly attributable to specific effects of CRT. These findings replicate the main results of prior studies of CRT efficacy [10, 12, 17, 35]. Our results further suggest that small-group-based CRT has effects comparable to face-to-face, individualized CRT in improving cognitive function even for severe disability and long disease duration inpatients with schizophrenia. These results thus demonstrated that group-based CRT is an effective alternative to one-on-one CRT with greater scope and efficiency (one therapist can treat 3–4 participants simultaneously). This is especially relevant for psychiatric practices in China given the vast number of patients in need of such treatment.

CRT treatment was associated with significant improvement in the PANSS total scores and two PANSS subscales. However, a similar pattern was observed in the MDT group, and no significant difference was found between the two groups. Therefore, CRT's impact on clinical symptoms was small and non-specific. This is consistent with prior studies concluding that CRT has little impact on clinical symptoms as measured by PANSS [2]. After CRT treatment, the total and general negative NOSIE scales were significantly improved. This finding is also well-precedented [10, 23] and indicates that CRT not only has therapeutic effects on cognitive function, but also on social function. Many studies have established that cognitive function correlates with social function in schizophrenia [11, 27]. In present study, a significant positive correlation between cognitive flexibility (VFT test) and social function was found. However, this cognitive improvement did not predict social function change in further regression analysis; this result is in closer accordance with prior research [27]. These contradictory results of correlation and regression analysis may reflect the complex relationship between cognitive and social function [28].

In summary, given that we adopted a less focused and intensive therapeutic mode—small-group therapy versus one-on-one—and recruited participants with severe disability, relatively advanced ages, and comparatively longer disease durations, these results were especially encouraging. Combined with previous research, the present results indicate that CRT is an effective and promising therapy for improving cognitive function and social outcomes for

participants with schizophrenia, even those with severe disability.

Despite these promising findings, the present study has several limitations. First, because the durability of cognitive and social-function benefits obtained from neurocognitive treatment is considered particularly important, many earlier studies have shown that the effect of these therapies can last 6 to 24 months [10, 13, 23], the lack of follow-up data in the present study is therefore an obvious limitation. Future studies should evaluate the durability of effects. Second, earlier research suggests that CRT could improve the self-esteem of participants with schizophrenia at post-treatment [36] and the present study lacks self-esteem data. Investigations of participants' subjective experience should be included in future studies.

Disclosure Statement

There are no conflicts of interest to report.

Role of the funding source

This study was partially supported by Beijing Municipal Science & Technology Commission grant (No. D0906001040191, Z141107002514016), Beijing Natural Science Foundation grant (No. 7102086), and Fund for Capital Medical Development and Research grant (No. 2011-2013-02).

Acknowledgements

The authors thank the patients, clinical psychiatrists, and nursing staff of Beijing Huilongguan Hospital for their participation and collaboration. The authors also thank the anonymous reviewers for their helpful comments.

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Figure Caption

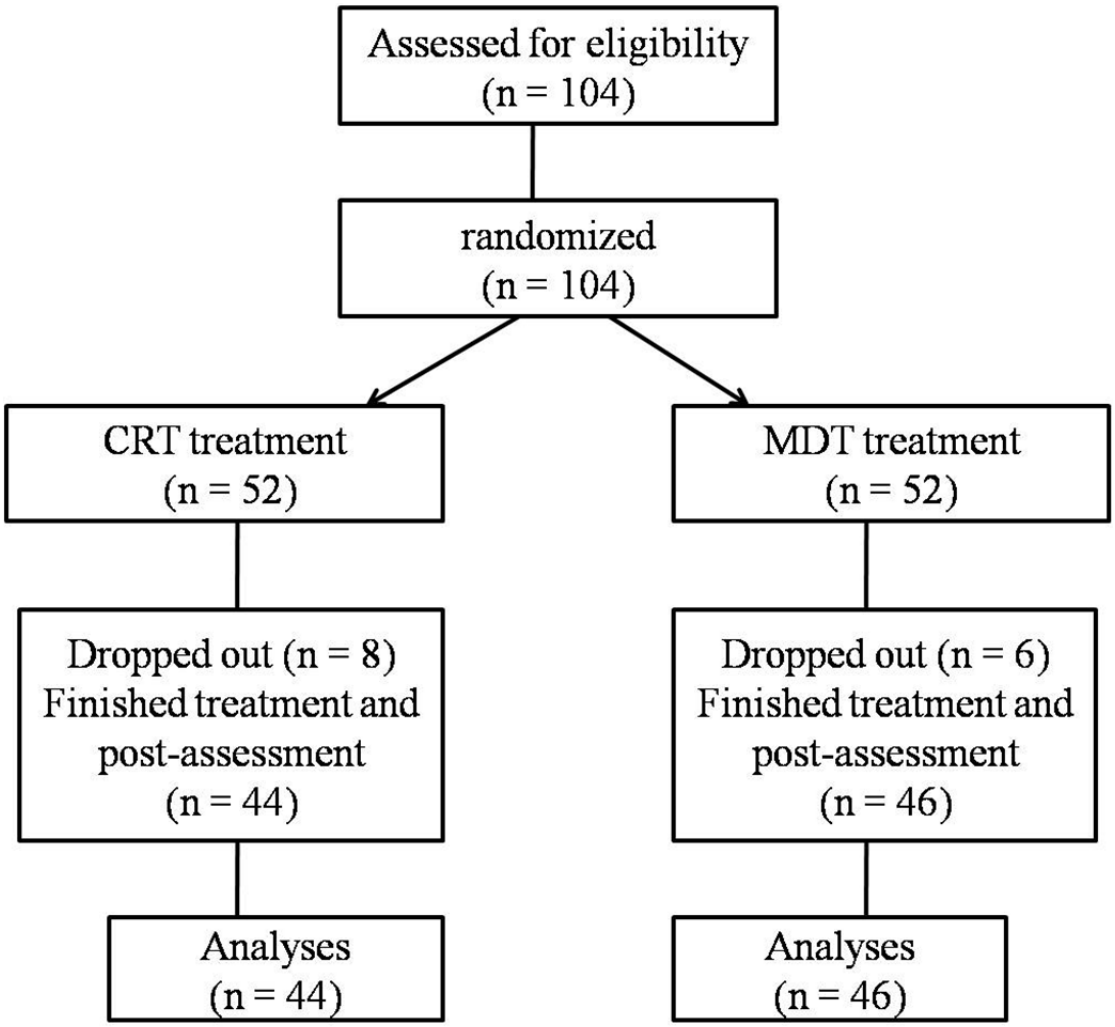

Fig. 1. CONSORT flow chart.

Fig. 1. CONSORT flow chart.

Tables

Table 1. Demographic and clinical characteristics of participants at entry to the study

Characteristics	CRT group (n = 52)	MDT group (n = 52)
Sex (male: female)	27:17	27:19
Mean age (SD), year	46.77 (7.18)	46.09 (5.52)
Mean education level (SD), year	9.70 (1.85)	10.13 (2.42)
Mean illness duration (SD), year	23.95 (8.18)	21.51 (6.50)
Years in hospital (SD), year	9.95 (7.52)	9.53 (6.61)
WAIS-R (intelligence quotient, IQ)	80.16 (14.04)	79.57 (13.86)
Mean (SD) PANSS score		
Positive Scale	14.31 (4.66)	12.74 (4.15)
Negative Scale	20.24 (4.67)	19.43 (4.93)
Total Scale	67.26 (11.32)	65.57 (11.34)
Neuroleptic medication use		
Atypical rate	52.23%	52.32%
Atypical dose[a] (mg)	221.23 (129.34)	234.42 (189.31)
Typical dose[a] (mg)	346.31 (173.23)	331.32 (178.25)
Mean dose[a]	280.32 (162.15)	275.15 (140.41)

CRT, Cognitive Remediation Therapy; MDT, Music and Dancing Therapy; WAIS-R, Wechsler Adult Intelligence Scale—revised.

[a] means dose of chlorpromazine equivalents (mg).

Table 2. Repeated measures ANOVA for mean (S.D.) scores on Cognitive function by group (CRT and MDT) for baseline and post-treatment.

Outcome Measure	CRT Group (n = 44)				MDT Group (n = 46)				Group by Time Interaction		Effect Size
	Baseline		Post-treatment		Baseline		Post-treatment				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	P	d
Cognitive Flexibility											
Trail Making–A	82.95	35.12	61.81[a]	28.87	85.22	41.99	80.10	39.12	9.530	0.003	0.651
CFT	18.59	6.30	19.39	5.79	17.52	5.91	17.54	5.66	0.362	0.549	0.127
VFT	20.09	7.51	21.05	8.10	19.85	9.21	16.28[a]	8.07	9.186	0.003	0.639
Stroop-color circle	31.43	19.74	23.66[a]	9.46	33.20	15.31	28.04[a]	10.52	0.706	0.403	0.176
Stroop-colored word	33.73	22.35	22.80[a]	11.36	35.30	16.20	30.85[a]	14.54	2.810	0.097	0.366
Stroop-word color	52.82	20.12	46.52[a]	14.17	50.65	16.78	55.91	17.90	12.444	0.001	0.742
Memory											
Digit Span-total	11.09	2.22	10.93	2.25	10.11	1.78	10.09	1.99	0.130	0.720	-0.076
BVRT-correct	4.05	1.88	6.26[a]	1.82	4.61	2.01	5.07	1.70	20.924	0.000	1.006
BVRT-wrong	10.13	4.80	5.62[a]	3.18	9.27	4.29	8.30[a]	3.95	17.580	0.000	0.912
Logical Memory	4.33	1.49	4.60	2.04	3.63	2.11	4.09	1.88	0.167	0.684	-0.089

CRT, Cognitive Remediation Therapy; MDT, Musical and Dancing Therapy; CFT, Category fluency test; VFT, Verbal fluency test; BVRT, Benton Visual Retention Test.

[a] within group paired–t test, $p<0.05$.

Table 3. Repeated measures ANOVA for mean (S.D.) scores on Clinical symptom (PANSS) and social functions by group (CRT and MDT) for baseline and post-treatment.

Outcome Measure	CRT Group (n = 44)				MDT Group (n = 46)				Group by Time Interaction		Effect Size
	Baseline		Post-treatment		Baseline		Post-treatment				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	P	d
Clinical symptoms											
PANSS Total	67.26	11.32	59.76[a]	10.17	65.57	11.34	58.14[a]	10.50	0.001	0.977	0.000
PANSS Positive	14.31	4.66	12.93	3.31	12.74	4.15	12.00	4.19	0.575	0.451	-0.175
PANSS Negative	20.24	4.67	17.29[a]	4.44	19.43	4.93	16.49[a]	4.01	0.000	0.992	0.002
PANSS general psychopathology	29.76	4.99	27.12[a]	4.15	29.06	5.91	25.77[a]	3.83	0.300	0.586	0.124
Functions											
NOSIE Total	155.51	30.41	161.78[a]	20.20	169.51	33.70	163.95	27.42	4.208	0.044	0.465
NOSIE General Negative	24.81	16.18	22.32[a]	10.92	20.78	16.61	23.80	14.96	3.780	0.056	0.440
NOSIE General Positive	52.32	19.42	56.11	12.59	62.29	20.26	59.76	15.23	3.250	0.075	0.409

CRT, Cognitive Remediation Therapy; MDT, Musical and Dancing Therapy; PANSS, positive and negative score; NOSIE, Nurse's Observation Scale for Inpatient Evaluation.

[a] within group paired–t test, $p<0.05$.