Psychiatry Research xxx (2011) xxx–xxx

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

The pilot study of a Neuropsychological Educational Approach to Cognitive Remediation for patients with schizophrenia in Japan

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ARTICLE INFO

Article history:
Received 7 September 2010
Received in revised form 7 July 2011
Accepted 8 July 2011
Available online xxxx

Keywords:
Schizophrenia
Cognitive remediation
Cognitive function
Neuropsychological Educational Approach to Cognitive Remediation (NEAR)

ABSTRACT

The main aim of this study is to demonstrate the feasibility and efficacy of a Neuropsychological Educational Approach to Cognitive Remediation (NEAR) in Japan on cognitive function. This multi-site study used a quasi-experimental design. 51 patients with schizophrenia or schizoaffective disorder participated. The NEAR program consisted of two one-hour computer sessions per week and an additional group meeting session lasting 30 to 60 min once a week. The subjects completed 6 months of NEAR sessions before being assessed. Moreover, taking into consideration the possible practice effect, we assessed 21 control patients twice with an interval of 6 months. We assessed cognitive function by using Japanese version of Brief Assessment of Cognition in Schizophrenia (BACS-J). Consequently, NEAR group showed significant improvement in overall cognitive function, and in comparison with control group, these findings were generally similar except for motor speed. Though there are not a few limitations about the present study, this study indicated that NEAR is feasible in Japan just as well as in Western countries.

1. Introduction

It is widely accepted that cognitive dysfunction in schizophrenia plays a major role in determining social function (Green et al., 2000). Although there have been numerous reports that indicate the effectiveness of atypical antipsychotics (AAPs) on cognitive function, the size of the effect of AAPs is generally about 0.2–0.5 standard deviations (S.D.) (Woodward et al., 2005; Keefe et al., 2007), while the extent of cognitive dysfunction in schizophrenia is about 1–1.5 S.D. below the level of healthy populations (Bilder et al., 2000; Heinrichs, 2004). To bridge this gap, other treatment methods, such as cognitive remediation, have been considered in Western countries.

In Japan, the “Services and Supports for Persons with Disabilities Act” was established in 2006. Although disabled persons' employment, deinstitutionalization, and socialization were promoted by this law, there are actually many people with psychiatric illnesses, including patients with schizophrenia, who still suffer from social dysfunction. With the aim of alleviating the many difficulties that they encounter in their lives, cognitive remediation therapy for patients with schizophrenia has gradually been launched in Japan (Nemoto et al., 2009).

We have become interested in one of the cognitive remediation therapies, namely, a Neuropsychological Educational Approach to Cognitive Remediation (NEAR) (Medalia and Freilich, 2008; Medalia et al., 2009), which is theoretically based on neuropsychology, educational psychology, learning theory, and cognitive psychology. After participating in one-week clinician training of NEAR, we started implementing NEAR in Japan. NEAR is an evidence-based approach to cognitive remediation specifically developed for use with psychiatric patients. NEAR is a group-based treatment that provides a positive learning experience to each and every client, to promote independent learning, and to promote optimal cognitive function in everyday life. Sessions are structured in a way to enhance intrinsic motivation and learning. The main aim of this study is to demonstrate the feasibility and efficacy of NEAR in Japan by assessing its effectiveness on cognitive function using neuropsychological indices as a primary endpoint.

2. Methods

This multi-site study used a quasi-experimental design. All participants were recruited from five psychiatric hospitals in the western region of Japan called ‘San-in’ district and were subjected to NEAR in each hospital. All participants were recruited on the basis of consecutive referrals.

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doi:10.1016/j.psychres.2011.07.020

Table 1
Baseline demographic variables.

	NEAR group	Control group
Number of patients		
Sch:Schizophrenia	Sch:48	Sch:21
SchAf:Schizoaffective disorder	SchAf:3	SchAf:1
Gender	Male:31, Female:20	Male:14, Female:8
Mean age	36.1 ± 10.6 y.o.	41.1 ± 12.4 y.o.
Years of education	13.5 ± 2.5 years	12.5 ± 2.6 years
Duration of illness	13.8 ± 9.8 years	16.1 ± 10.8 years
Age at onset of illness	22.3 ± 6.6 y.o.	22.6 ± 6.3 y.o.
Total number of hospitalizations	2.8 ± 3.1 times	4.6 ± 5.2 times
Total months of hospitalization	19.4 ± 29.4 Months	39.3 ± 65.8 months
Mean dosage of antipsychotics (Chlorpromazine equivalent dose)	634.5 ± 364.9 mg/day	699.2 ± 569.2 mg/day
Treatment settings (Outpatient or inpatient) *	Outpatients:42 Inpatients:9	Outpatients:12 Inpatients:10
NEAR attendance rate	0.90 ± 0.11	
BACS-J z score; Verbal memory**	−1.09 ± 0.92	−2.00 ± 1.05
BACS-J z score; Working memory	−0.95 ± 0.95	−1.30 ± 1.08
BACS-J z score; Speed	−1.60 ± 1.37	−2.25 ± 1.74
BACS-J z score; Verbal fluency	−0.47 ± 1.00	−0.71 ± 0.89
BACS-J z score; Attention and speed of information processing	−1.24 ± 0.88	−1.56 ± 0.77
BACS-J z score; Executive function	−0.57 ± 1.42	−1.56 ± 2.15
[EX]**	−0.79 ± 0.59	−1.10 ± 0.59
BACS-J composite score**	−1.65 ± 1.27	−2.61 ± 1.51

* $p<0.05$ Fisher's exact test.
** $p<0.05$ Student's t test.
[EX] = −log[2 − (Executive function BACS-J z score)].

2.1. Subjects (Table 1)

After a complete explanation of the study, informed consent was obtained from the participants. The protocol of this study was approved by the Ethics Committee of Tottori University. Inclusion criteria were outpatients or inpatients (a) with a diagnosis of schizophrenia or schizoaffective disorder made by two experienced psychiatrists according to DSM-IV-TR criteria, (b) between 13 and 65 years old, (c) able to sit for a one-hour session, (d) willing to participate in the study, and (e) being recommended by their doctors. Exclusion criteria were patients (a) with active substance or alcohol abuse or having left detox within 1 month, or (b) with traumatic head injury within the past 3 years.

Sixty-two patients were referred and eleven patients dropped out of the program midway through it (the dropout rate was 17.4%). Among these eleven patients, five patients dropped out owing to a lack of motivation and five patients dropped out because of relapse of psychotic symptoms. One patient found a job and left the program. Six of the patients who withdrew left the program within the first half of the 6-month trial. Finally, fifty-one patients with schizophrenia or schizoaffective disorder completed the NEAR program. The NEAR program consisted of two one-hour computer sessions per week and an additional group meeting session lasting 30 to 60 min once a week. The subjects completed approximately six months of NEAR sessions before being assessed for the efficacy.

Moreover, we assessed 22 control patients twice with an interval of six months, taking into consideration a possible practice effect, which may have affected the scores of neuropsychological tests. They did not receive any cognitive training program including NEAR. As for the clinical backgrounds, the treatment settings were significantly different between the two groups, with more inpatients being included in the control group than in the NEAR participant group.

In each computer session, patients engaged with some educational computer software that was related to various domains of cognitive function, including attention, memory, and executive function, taking into account the profiles of the patients' cognitive impairments. The software available in Japan is not identical to that in Western countries; however, it appeared to cover the relevant cognitive domains (Table 2).

The main aim of the group meeting sessions was to contextualize the computer training into their everyday activities. The process should lead to enhancing motivation and generalization of cognitive skills to real-life activities.

One of our co-authors is certified as a supervisor of NEAR and she supervised NEAR sessions periodically. In order to use consistent methods across sites, all clinicians participated in one-week clinician training of NEAR, and they attended trimonthly meetings.

Although the medications were changed throughout the whole period as little as possible, there were 16 patients whose medications needed to be changed because of clinical decisions. However, the change in the medication status of these 16 patients was only related to daily dosage levels.

2.2. Assessments

We assessed cognitive function using the Japanese version of Brief Assessment of Cognition in Schizophrenia (BACS-J) (Keefe et al., 2004; Kaneda et al., 2007). Z scores were calculated for each subcomponent score using means and standard deviations based on the dataset of 340 healthy control Japanese populations; however, it must be noted that age, sex, and socio-economic status of the healthy controls were not necessarily controlled with the patients in the present study. Composite scores were calculated by averaging all z scores of the six subcomponents (verbal memory, working memory, motor speed, verbal fluency, attention and speed of information processing, and executive functions), and then re-normed based upon the standard deviations (SD) of the average of those scores in the normative sample (SD = 0.6).

2.3. Statistical analysis

Two-tailed paired t-tests were performed for the assessment of change between the two measurements of BACS-J data, which were administered before (baseline) and after (post-treatment) the NEAR sessions. Each subcomponent score was normally distributed except for the executive function score. By performing a logarithmic transformation of the executive function score, the curve was modified to a normal distribution, described by [EX] = −log[2 − (Executive function BACS-J z score)]. Therefore, we used [EX] instead of "executive function BACS-J z score" for analysis.

Except for the treatment settings, baseline verbal memory, baseline [EX], and baseline composite scores, neither socio-demographic nor clinical variables differed significantly between the two groups (Table 1). Therefore, repeated measures analyses

Table 2
Sample educational computer software used in the computer sessions.

Task	Software	Activity	Target cognitive domain
The mail room	Monsters Inc.: Scream Team Training	Sort all the mail into the proper mailboxes before the clock hits 9 a.m.	Attention, speed
Lunch room	Monsters Inc.: Scream Team Training	Select food items and daily specials to serve to each monster in accordance with the figure presented on the lunch-order ticket.	Attention, speed
Moonfish	Finding Nemo: Nemo's Underwater World of Fun	Repeat the shape patterns made by the moonfish.	Working memory
Spark! Mejikara	Let's refresh your brain	Memorize the illustrations that appear one after another on the screen, and recollect them in order.	Working memory
Hustle memory	Let's refresh your brain	Memorize the character's clothes that are put on within ten seconds.	Visual learning and memory
Frippletration	Thinkin' Things 2	Visual and auditory memory matching game.	Visual / auditory learning and memory
Stocktopus	Thinkin' Things 3	Repeat trading items to get the items you need for your portfolio.	Working memory, executive function,
Build it	Factory Deluxe	Build up the presented goal product by selecting and using appropriate tools.	Executive function
The puzzles	Logical Journey Of The Zoombinis	Solve puzzles with various rules using as clues physical features of hair, eyes, nose, and feet of little creatures called Zoombinis.	Executive function

"Thinkin' Things 2", "Thinkin' Things 3", and "Factory Deluxe" were English versions; however, English ability was not necessary to accomplish the tasks. Other software programs were Japanese versions.

Please cite this article as: Ikezawa, S., et al., The pilot study of a Neuropsychological Educational Approach to Cognitive Remediation for patients with schizophrenia in Japan, Psychiatry Res. (2011), doi:10.1016/j.psychres.2011.07.020

Table 3
The result of paired *t* test on BACS-J data with NEAR participants.

	Baseline	Post treatment	*t*	*p*	Cohen's *d*
Verbal memory	−1.09±0.92	−0.13±0.99	8.80	<0.0001	1.01
Working memory	−0.95±0.95	−0.54±1.17	4.11	<0.0005	0.39
Motor speed	−1.60±1.37	−1.04±1.42	3.28	<0.005	0.41
Verbal fluency	−0.47±1.00	−0.14±1.10	3.41	<0.005	0.32
Attention and speed of information processing	−1.24±0.88	−0.99±0.96	3.19	<0.005	0.28
[EX]	−0.79±0.59	−0.55±0.55	3.02	<0.005	0.44
Composite score	−1.65±1.27	−0.79±1.33	8.96	<0.0001	0.67

[EX] = −log[2 − (Executive function BACS-J z score)].

of variance were performed on BACS-J data using 'group' (NEAR group, control group) and 'treatment settings' (inpatient, outpatient) as inter-individual factors, while 'time' (baseline, post-treatment) was used as an intra-individual factor. Moreover, in the analyses of verbal memory, [EX], and composite scores, baseline data were used as covariates.

3. Results (Tables 3, 4, Fig. 1)

3.1. The within-NEAR treatment change of BACS-J data

There were significant improvements in the scores of all subcomponents in BACS-J (Table 3).

3.2. In comparison with control patients

There were significant interactions between 'group' and 'time' in verbal memory, working memory, verbal fluency, attention and speed of information processing, [EX], and composite scores (Table 4). The improvement of these areas was significantly greater in the NEAR group than in the control group. There was no difference between groups in terms of the change in motor speed.

4. Discussion

In the present study, we found significant improvement for all cognitive domains related to BACS-J. According to the meta-analysis of the effectiveness of cognitive remediation in schizophrenia, neurocognitive benefit varied from small (Cohen's $d = 0.2$) to very large ($d = 1.2$) effect size (Medalia and Choi, 2009). Medalia et al. (2009) also suggested that heterogeneity of response to cognitive remediation might depend on instructional techniques, intellectual ability, and intrinsic motivation. In NEAR, instructional techniques are devised to enhance intrinsic motivation. It has already been shown that the use of NEAR educational software without an instructional approach did not achieve clinically meaningful change in neurocognitive capacity (Bellack et al., 2005; Dickinson et al., 2010). In our study, we complied with the principle of NEAR by attaching great importance to instructional approach and could find small to very large effect sizes in broad domains ($d = 0.28$–1.01). In comparison with the control group, the positive findings remained significant except for motor speed. NEAR approach proved to be a feasible psychosocial therapy, even in Japan with its different cultural background and with the use of software programs that differ from those in Western countries.

In BACS-J, motor speed was assessed by "Token Motor Task". The task requires the participants to put 100 plastic tokens into a container bimanually as quickly as possible within 60 s, and the outcome measure is the total number of tokens put in the container (Keefe et al., 2004). In the NEAR session, participants were engaged in the computerized learning tasks selected to address specific domains of cognitive function (Medalia et al., 2009); however, we may have failed to include those tasks that required considerable motor speed to perform in the session. This may explain why the NEAR participants were not able to achieve greater improvement in motor speed than the controls.

In this study, the two groups were heterogeneous in many points, and although several subcomponent scores of the BACS-J were significantly lower in the control group than in the NEAR group, correlations between baseline BACS-J data and the improvement in

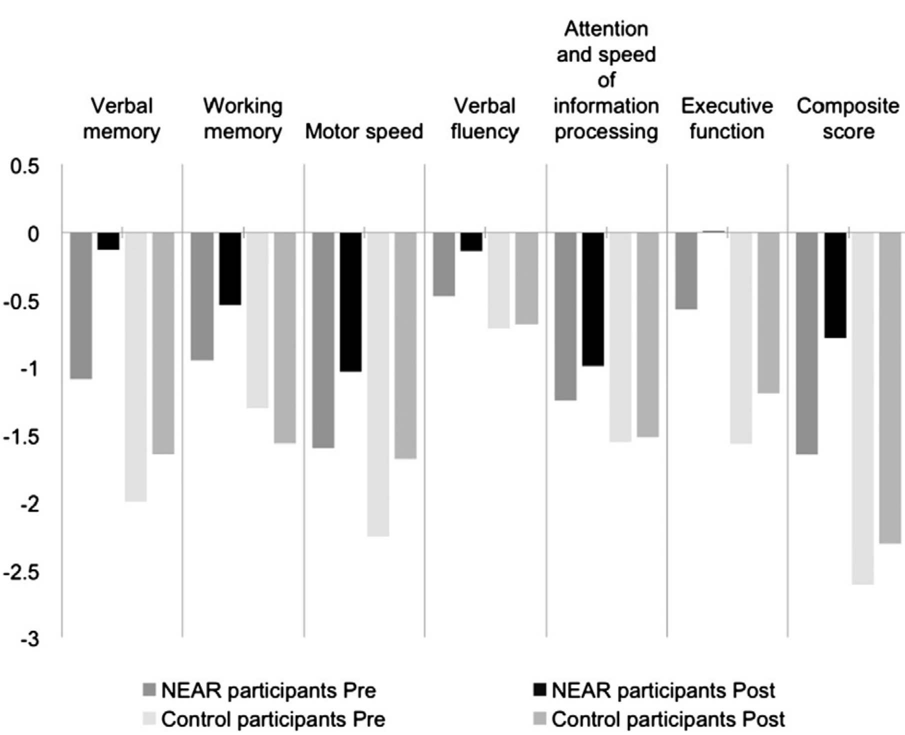

Fig. 1. Changes in cognitive function during 6 months period.

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Table 4
"Time × group" interaction effect on ANOVA with BACS-J data in comparison with control group.

	d.f.	*F*	*p*
Verbal memory#	1,69	16.1	<0.0005
Working memory	1,70	16.9	<0.0005
Motor speed	1,70	1.53	n.s.
Verbal fluency	1,70	4.39	<0.05
Attention and speed of information processing	1,70	5.79	<0.05
[EX]#	1,69	4.69	<0.05
Composite score#	1,69	19.1	<0.0001

# baseline data were used as covariates.
[EX] = − log[2 − (Executive function BACS-J z score)].

BACS-J data were negative ($r = -0.57$ to -0.06) in the NEAR group. This implies that the NEAR program is more effective when baseline neurocognition ability is weaker. Although it is possible that there was recruitment bias to include higher-function subjects in the NEAR group at baseline, it may be assumed that taking into account the difference in neurocognition would not negate the effect of NEAR.

There are several limitations of the present study. First, although only the difference in treatment settings between the NEAR participants and the controls appeared significant, clinical and demographic variables were not well matched between the two groups. Second, subjects were not randomly assigned to either of the groups. Third, some clinicians who managed the NEAR session also had to take a role as a tester of BACS-J. In order to resolve these issues, randomized control studies of NEAR program with testers being blinded to the treatment assignment are warranted. Moreover, while we focused on the neurocognitive effect of NEAR in Japan in the present report, we should also take into consideration its effectiveness on social function and/or quality of life in patients with schizophrenia.

Acknowledgements

The authors would like to thank Masato Kato, Kuniya Tamashiro, Izumi Nagata, Junya Sasaki, Yuichiro Hata, Seiji Katayama, Akira Iwasaki, Yu Hiroe, Miki Nakada, Maki Umebayashi, Kouko Yamada, Chiaki Komatsu, Mayumi Kurimura, Kanako Nakatani, Yukina Senda, Takafumi Shinkawa, Hironori Ohmiya, Kenji Matsumura, Junko Oka, and Maroko Yoshizawa for their support and assistance with this research.

Funding for this study was provided by a Scientific Research Grant-in-Aid for Development of Characteristic Education from the Japanese Ministry of Education, Culture, Sports, Science, and Technology (MEXT). MEXT had no further role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

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Please cite this article as: Ikezawa, S., et al., The pilot study of a Neuropsychological Educational Approach to Cognitive Remediation for patients with schizophrenia in Japan, Psychiatry Res. (2011), doi:10.1016/j.psychres.2011.07.020