



The Open Psychology Journal

Content list available at: www.benthamopen.com/TOPSYJ/

DOI: 10.2174/1874350101609010121



RESEARCH ARTICLE

Pilot Study of the Effects of Cognitive Remediation Therapy Using the Frontal/Executive Program for Treating Chronic Schizophrenia

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Received: August 24, 2016

Revised: October 14, 2016

Accepted: October 17, 2016

Abstract:

Introduction:

Cognitive Remediation Therapy is a new rehabilitation approach that has been created in order to improve cognitive functions such as attention, memory and executive function. We aimed to investigate the effects of one type of Cognitive Remediation Therapy, the Frontal/Executive Program, on cognitive function, social function, and psychiatric symptoms in the chronic phase schizophrenia patients.

Methods:

Seventeen participants who gave consent were randomly assigned to an intervention group (n=8) or control group (n=9). The intervention consisted of 44 sessions of FEP over a period of approximately six months. Cognitive function, social function, and psychiatric symptoms were evaluated before and after the intervention and before and after a roughly six-month long period for controls. Results: The present study showed improvements in Brief Assessment of Cognition in Schizophrenia-Japanese version composite score and subscales of verbal memory and working memory. Improvements were also observed in overall evaluation in the Schizophrenia Cognition Rating Scale-Japanese version, total Positive and Negative Syndrome Scale score and the Global Assessment of Functioning Scale score. FEP is considered to improve the performance of cognitive function tests and social function tests and psychiatric symptoms tests that are the target of this training.

Conclusion:

Intervention by Frontal/Executive Program improved cognitive function and psychiatric symptoms in patients with chronic schizophrenia with long disease duration who require large doses of medication. Significant effects of intervention were observed in overall patient, informant and interviewer evaluation in social function test. FEP is a training method the primary means pencil and paper, it is possible to inexpensively implement when compared to the other CRT that uses a computer. There is an advantage that less economic cost.

Keywords: Cognitive function, Cognitive Remediation Therapy, Frontal/Executive Program, Psychiatric symptoms, Schizophrenia, Social function.

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INTRODUCTION

Schizophrenia is a chronic disorder characterized by diverse symptoms, including both positive and negative symptoms. However, a well-established fact is that schizophrenia patients also manifest impairments in cognitive function that are independent of other symptoms [1, 2]. Cognitive impairment is thought to be central to the pathology [3], and in particular, the areas to be impaired in schizophrenia are attention, verbal memory, executive function and verbal fluency [4 - 6]. Furthermore, these cognitive impairments have been identified as having a great influence on patients' ability to reintegrate into society and function in daily life [7, 8]. Therefore, their improvement is also thought to be of critical importance. Although the mitigation and prevention of recurrence of psychiatric symptoms by anti-psychotic drugs is possible, the same effect on cognitive function or social dysfunction has not been observed [9].

Cognitive Remediation Therapy (CRT) has gained attention in the recent years for treating cognitive impairment. CRT is a behavioral intervention that was developed in order to improve the cognitive processes (attention, memory, executive function, social cognition or metacognition). It is defined as a comprehensive rehabilitation program for carrying out tasks with the objective of activating specific cranial nerve functions [10]. CRT effect research has increased since the 1990s [11]. CRT resulted in a gradual improvement of cognitive ability of schizophrenia patients in the meta-analysis, it revealed that these neurocognitive improvements will lead to the improvement of psychosocial functioning [12].

CRT programs have not been adequately standardized, and vary not only in strategy, such as bottom-up or top-down, and approach, such as computer-based or pencil and paper-based, but also in basic configurations, such as number of sessions and number of patients, and whether it combined with other rehabilitation programs [13].

The objectives of the present study were, therefore, to examine whether intervention using the Frontal/Executive Program-Japanese version (FEP-J) [14] as one type of CRT could improve cognitive function, social function, and psychiatric symptoms in patients with chronic schizophrenia. A study of the effectiveness of CRT is a new area that began research in the last decade in Japan. Many studies to the current have been implemented in public institutions, mainly university hospitals. Therefore, this study is Japan's first pilot study of intervention using the FEP-J in private colleges' psychiatric hospital.

MATERIALS AND METHODOLOGY

Subjects

All subjects were chronic schizophrenia inpatients and outpatients at the psychiatric department of Asahiyama Hospital. Inclusion criteria were age of 60 years or less, at least nine years of education, and schizophrenia meeting DSM-IV-TR diagnosis criteria [15]. "Chronic" was defined as three years or longer since onset. The exclusion criteria were dementia, drug addiction, alcoholism, organic brain disease, pregnancy, an IQ of ≤ 50 , acute-phase schizophrenia, schizophrenia without cognitive dysfunction, and absence of a signed informed consent form.

Study Design

The study protocol was approved by the Asahiyama Hospital ethics committee and the Hokkaido University graduate school Faculty of Health Sciences ethics committee. Written informed consent was obtained from all subjects.

The patients' cognitive function, social function, and psychiatric symptoms were evaluated within two-week periods before and after the entire duration of the 44 sessions for the intervention group and before and after a roughly six-month long period for the control group (treatment-as-usual). Evaluation took about two hours and was split into two days.

Participants in the intervention group were given 44 sessions of one-on-one FEP twice a week that lasted approximately one hour each. The FEP was developed by Delahunty *et al.* [16] and a Japanese version was created by Matsui *et al.* [14]. It is one of the CRT intended for schizophrenic patients, although the paper-and-pencil is the main medium also includes building blocks and hand exercises during a session. FEP is a CRT program that can be implemented at low cost.

As multiple trainers participated in the study, with each trainer working with a single patient, all trainers participated in joint study meetings once a week for a total of nine sessions. At the meetings, each trainer presented details of his or her sessions and FEP role-playing and video filming were used to increase shared understanding and perception towards FEP and reduce inter-trainer differences in intervention methods. All trainers are a clinical psychologist and

occupational therapist with a long clinical experience.

Evaluation

Psychiatric Symptoms

Psychiatric symptoms were assessed with the Positive And Negative Syndrome Scale (PANSS) [17] and the Global Assessment of Functioning Scale (GAF) [15].

Social Function

Social function was measured with the Schizophrenia Cognition Rating Scale-Japanese version (SCoRS-J) [18] and the Life Assessment Scale for the Mentally Ill (LASMI) [19]. The SCoRS is a scale recommended by the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Neurocognition Committee in the United States as a candidate with face validity for functional outcomes. The SCoRS-J is the Japanese version of a scale devised by Keefe *et al.* [20] that was created by Kaneda *et al.* [18]. It is based on interviews of the patient or informant and constructs from 20 items to assess the eight areas, such as memory, learning and attention, as well as an overall evaluation.

Cognitive Function

Cognitive function was measured with the Brief Assessment of Cognition in Schizophrenia-Japanese version (BACS-J) [21], the Wisconsin card sorting test (WCST) [22], and the Continuous Performance Test (CPT) [23]. The BACS-J is the Japanese version was made by Kaneda *et al.* [21] after it has been created by Keefe *et al.* [24]. It is a cognitive function evaluation for schizophrenia patients as an indicator of the six cognitive function area scores and composite score. The scores are compared to averages of healthy controls to calculate z-scores that are used in evaluation. The WCST is a task that involves sorting cards according to certain rules that change over time, reflecting functioning in the prefrontal cortex. The CPT is a task for measuring sustained attention and involves watching letters that appear randomly on the computer screen while responding according to certain rules.

Intervention

The FEP is composed of cognitive flexibility, working memory, and planning modules; tasks are developed so that the complexity increases with successive sessions. Each module is composed of such as eye movement, perception, organization of information, and motor skill movement. During the session, the trainer encourages verbalization of problem-solving techniques and gives instruction to enable the patient to solve the task with effective strategies, helping them complete the task as correctly as possible.

In the cognitive flexibility module, the patient repeatedly practices engagement, disengagement, and re-engagement in a specific cognitive set. In the working memory module, patients proceed with trained with simultaneous processing tasks typified by a dual task. In the planning module, the trainer facilitates strategy formation and self-induced sequencing of actions through the solving of tasks. Specific examples of tasks are infinity symbol line drawing, sign copying, category formation, map explanation and finger tapping.

Statistical Analysis

Analysis was conducted on all participants after receiving their consent and dividing them into two groups. No participants withdrew from the study in either group, and evaluation was conducted on all participants before and after the intervention period or control six-month period. Chi-square tests were performed to assess intergroup differences in gender; Mann-Whitney U tests were performed to assess intergroup differences in age, years of education and other basic attributes, medication dose, and other background information. Mann-Whitney U tests were also performed to assess intergroup differences in pre-intervention IQ, cognitive function, social function and psychiatric symptoms, and also were performed to compare functional evaluations before and after the intervention. Statistical analysis was performed with SPSS version 20 with a 5% level of significance.

RESULTS

Participant Characteristics

All subjects 17 of who were randomly assigned to the control group to perform usual treatment and intervention

group to carry out the intervention by the FEP. The control group received treatment during the same period as the intervention group. They accepted regularly drug therapy and psychotherapy established by psychiatrist for approximately one regular time per month. They also accepted occupational therapy such as creative activities (*i.e.* handicraft, ceramics art or cooking), exercise, and group activities multiple times per week. The control group received no training related to cognitive function improvement. At the time of allocation, the patients were informed that FEP would be used, and intervention was performed in the patients who were aware that they had cognitive problems and expressed interest in the FEP.

The background information of patients in the two groups is shown in Table 1. Significant difference between the groups in the basic attributes such as age and years of education and all of the items including medication dose were not recognized.

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

	FEP group(n=8)	Control group(n=9)	P
	Mean(SD)	Mean(SD)	
Age	43.25(±14.50)	39.00(±11.09)	0.44
Years of education	13.63(±3.32)	13.11(±2.46)	0.81
Time since first contact with the psychiatric services	14.75(13.53)	11.78(±10.62)	0.73
Medication			
Antipsychotic medication (chlorpromazine equivalents)	940.56(±878.77)	876.67(±1006.36)	0.56
Anticholinergic agent (biperiden equivalents)	2.38(±2.56)	1.78(±1.79)	0.62
Gender(%male)	37.50	44.40	0.77

Baseline evaluation before the intervention is shown in Table 2. In the WCST, the control group had more errors (mean ± standard deviation (SD), 8.6 ± 4.8) than intervention group (3.6 ± 5.2) ($p < 0.048$). No other significant differences were observed between the intervention group and controls in IQ, BACS-J score, SCoRS-J score measuring social function, PANSS score accessing psychiatric symptoms, or any other measure.

Table 2. Neuropsychological, social and clinical characteristics at baseline.

	FEP group		Control group		P
	Mean	SD	Mean	SD	
IQ(WAIS-III)	88.4	21.9	70.9	15.6	0.53
BACS-J(Z-score) [†]					
Composite Score	-1.15	1.78	-2.34	1.76	0.18
Verbal Memory	-1.02	1.7	-2.64	1.41	0.08
Working Memory	-0.2	1.3	-1.63	1.41	0.07
Token Motor Task	-0.49	0.95	-0.75	1.27	0.63
Verbal Fluency	-0.47	1.31	-0.81	1.26	0.5
Symbol Coding	-0.49	1.52	-1.58	1.16	0.12
Tower of London	-1.52	1.87	-1.47	2.33	0.56
WCST					
Categories	4.1	2.1	1.4	2.1	0.09
Errors	3.6	5.2	8.6	4.8	0.048
CPT					
Reaction time	562	144.1	568.8	74.3	0.39
Errors	3.1	2.5	15	23	0.07
SCoRS-J					
Global Ratings(Patient)	4.9	1.6	4.9	2.3	0.84
Global Ratings(Informant)	3.6	1.8	4.8	2.1	0.49
Global Ratings(Interviewer)	5.1	1.1	5.6	1.5	0.31
LASMI					
Composite Score	10.1	2.1	9.6	2.6	0.39
GAF	48.9	10.8	44	7.9	0.24

(Table 2) contd....

	FEP group		Control group		p
	Mean	SD	Mean	SD	
PANSS					
Composite Score	79.9	7.9	77.4	6.2	0.77

†Values were normalized using the data of a healthy person

BACS-J; Brief Assessment of Cognition in Schizophrenia-Japanese version

WCST; Wisconsin card sorting test

CPT; Continuous Performance Test

SCoRS-J; Schizophrenia Cognition Rating Scale-Japanese version

LASMI; Life Assessment Scale for the Mentally Ill

GAF; Global Assessment of Functioning Scale

PANSS; Positive And Negative Syndrome Scale

Cognitive Function

Comparisons of functional measures before and after the intervention are shown in Table 3. Significant improvements were indicated to be seen by the intervention in composite score ($p < 0.02$) and the verbal memory ($p < 0.001$) and working memory ($p < 0.01$) subscales of the BACS-J. Although not significant, a tendency towards improvement was also observed in symbol coding in the BACS-J ($p < 0.054$).

Among the intervention group of eight, who z-score of BACS-J overall score has improved 1SD or more than the score of the baseline was 4 people. In other words, the improvement tendency in the intervention group was observed.

Psychiatric Symptoms

Overall PANSS score ($p < 0.03$) and GAF score ($p < 0.04$) differed significantly, with an improvement seen in the intervention group.

Social Function

A significant difference was observed in overall patient evaluation ($p < 0.01$), overall informant evaluation ($p < 0.03$), and overall interviewer evaluation ($p < 0.001$) in the SCoRS-J showing improvement from the intervention. A tendency towards improvement was also seen in total LASMI score ($p < 0.08$), although this difference was not significant.

Table 3. Results of Mann-Whitney U test.

			FEP group(n=8)		Control group(n=9)		p
			Baseline	Post-treatment	Baseline	Post-treatment	
BACS-J	Composite Score	Mean	-1.15	-0.19	-2.34	-2.18	0.02
		SD	1.78	1.6	1.76	1.5	
	Verbal Memory	Mean	-1.02	0.05	-2.64	-2.69	0.00
		SD	1.7	1.32	1.41	1.1	
	Working Memory	Mean	-0.2	-0.03	-1.63	-1.55	0.01
		SD	1.3	0.75	1.41	1.25	
	Token Motor Task	Mean	-0.49	0.04	-0.75	-0.7	0.16
		SD	0.95	1.06	1.27	1.25	
	Verbal Fluency	Mean	-0.47	0.28	-0.81	-0.84	0.15
		SD	1.31	1.34	1.26	1.08	
	Symbol Coding	Mean	-0.49	-0.45	-1.58	-1.67	0.54
		SD	1.52	1.45	1.16	1.24	
	Tower of London	Mean	-1.52	-0.61	-1.47	-0.82	0.39
		SD	1.87	1.96	2.33	1.39	
WCST	Categories	Mean	4.1	3.6	1.4	3.7	0.80
		SD	2.1	2.8	2.1	2.3	
	Errors	Mean	7.3	9.1	17.1	7.0	0.85
		SD	10.2	10.4	9.6	10.2	
CPT	Reaction time	Mean	562	587.5	568.8	603.2	0.63
		SD	144.1	158	74.3	108.5	
	Errors	Mean	3.1	4.5	15	11	0.24

(Table 3) *contd....*

			FEP group(n=8)		Control group(n=9)		p
			Baseline	Post-treatment	Baseline	Post-treatment	
		SD	2.5	2.6	23	12	
SCoRS-J	Global Ratings	Mean	4.9	2.3	4.9	5	0.01
	(Patient)	SD	1.6	0.7	2.3	2.4	
	Global Ratings	Mean	3.6	2.9	4.8	5.7	0.00
	(Informant)	SD	1.8	1.9	2.1	2.1	
	Global Ratings	Mean	5.1	2.8	5.6	5.2	0.01
	(Interviewer)	SD	1.1	0.5	1.5	1.3	
LASMI	Composite Score	Mean	10.1	8	9.6	9.8	0.08
		SD	2.1	2.2	2.6	2.6	
GAF		Mean	48.9	59.8	44	47.9	0.04
		SD	10.8	12	7.9	10.6	
PANSS	Composite Score	Mean	79.9	68	77.4	78.1	0.03
		SD	7.9	10.2	6.2	7.59	

DISCUSSION

The intervention group showed a significant effect in composite score and the verbal memory and working memory of the BACS-J, which evaluate cognitive function. Improvement of working memory in Wykes *et al.* [25] is shown, but a clear improvement was observed in working memory and verbal memory in this study. FEP, an intervention program in which patients are requested to simply and precisely verbalize the contents and solutions of tasks, is believed to improve cognitive impairment [26].

Moreover, having patients write out their thought process used to solve the task on paper required them to clearly express their own thoughts in words, which may have led to improvements. Moreover, internalization of learning strategies represented by the categorization of information may also be considered as a factor [27]. For WCST, significant difference was not observed in this study. This is the result of a different result of Wykes *et al.* [25] that significant improvement was observed in the intervention group.

With regard to psychiatric symptoms, improvement of the PANSS was significant tendency in Wykes *et al.* [25], but significant effect was observed in the total PANSS score and GAF score in this study.

Significant effects of intervention were observed in overall patient, informant and interviewer evaluations in the SCoRS-J that measures social function. This finding suggest that repeated training which requires patients to match their thoughts, words, and actions by verbalizing their problem solving approach leads to regulation with words and an increased sense of self-control. Moreover, FEP is a training method in which tasks are completed through the use of pencil and paper, and requires patients to actively and independently perform the exercises in order to achieve functional improvement. As a result, patients' initiative and intrinsic motivation increase, which in turn may lead to improvement in social function.

Using clinical psychologists and occupational therapists with many years' experience (mean of 16.3 ± 9.15 years) as trainers and having all trainers participate in a workshop before commencement of training may have been beneficial for ensuring improvement. This may increase intrinsic motivation in patients and may represent one reason why no participants withdrew from the study as well as why improvements were seen in evaluations of social function.

A benefit of the FEP is that it requires little financial expense, as training is based primarily on paper and pencil tasks and is therefore less expensive than other CRT approaches that use computers. This means that FEP can easily be implemented at numerous medical institutions and other facilities. The reported durations of the effects of CRT have varied, including from 6 months after implementation [25] to 3 months after the intervention [28], and there is still no consensus in this regard. Further research is clearly needed. We hereby demonstrated that intervention using the FEP improved cognitive function, social function, and psychiatric symptoms in patients with chronic schizophrenia with a longer mean disease duration than participants in the Wykes *et al.* [28] study (14 months *versus* 14.75 ± 13.53 years) and a larger dose of medication than those in Penadés *et al.* [9] and Wykes *et al.* [29].

LIMITATIONS

One limitation of the present study was the small sample size. Further studies examining more patients are needed.

Another limitation is that we did not examine the extent to which improvements from training were sustained over time. The effects of FEP need to be examined after a period of time has passed. Finally, as we did not investigate the length of disease duration, further studies are needed to determine whether or not efficacy differs with disease duration. We did not evaluate the cognitive function, social function or mental symptoms at 6 months after completion of the intervention, which is yet another limitation.

CONCLUSION

Intervention by Frontal/Executive Program (FEP) improved cognitive function and psychiatric symptoms in patients with chronic schizophrenia with long disease duration who require large doses of medication. Significant effects of intervention were observed in overall patient, informant and interviewer evaluations in the SCORS-J that measures social function. As FEP is a predominantly pencil-and-paper training method, it can be implemented at a lower cost than computer-based cognitive remediation therapy and thus has the advantage of imposing minimal financial burden.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

- [1] Saykin AJ, Shtasel DL, Gur RE, *et al.* Neuropsychological deficits in neuroleptic naive patients with first-episode schizophrenia. *Arch Gen Psychiatry* 1994; 51(2): 124-31. [<http://dx.doi.org/10.1001/archpsyc.1994.03950020048005>] [PMID: 7905258]
- [2] Wykes T, Reeder C. *Cognitive Remediation Therapy for Schizophrenia: Theory & Practice*. London: Routledge 2005.
- [3] Green MF. What are the functional consequences of neurocognitive deficits in schizophrenia? *Am J Psychiatry* 1996; 153(3): 321-30. [<http://dx.doi.org/10.1176/ajp.153.3.321>] [PMID: 8610818]
- [4] Evans JJ, Chua SE, McKenna PJ, Wilson BA. Assessment of the dysexecutive syndrome in schizophrenia. *Psychol Med* 1997; 27(3): 635-46. [<http://dx.doi.org/10.1017/S0033291797004790>] [PMID: 9153684]
- [5] Morice R, Delahunty A. Frontal/executive impairments in schizophrenia. *Schizophr Bull* 1996; 22(1): 125-37. [<http://dx.doi.org/10.1093/schbul/22.1.125>] [PMID: 8685655]
- [6] Reichenberg A, Harvey PD. Neuropsychological impairments in schizophrenia: Integration of performance-based and brain imaging findings. *Psychol Bull* 2007; 133(5): 833-58. [<http://dx.doi.org/10.1037/0033-2909.133.5.833>] [PMID: 17723032]
- [7] Green MF, Kern RS, Braff DL, Mintz J. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the right stuff? *Schizophr Bull* 2000; 26(1): 119-36. [<http://dx.doi.org/10.1093/oxfordjournals.schbul.a033430>] [PMID: 10755673]
- [8] Morice R. Cognitive inflexibility and pre-frontal dysfunction in schizophrenia and mania. *Br J Psychiatry* 1990; 157: 50-4. [<http://dx.doi.org/10.1192/bjpp.157.1.50>] [PMID: 2397362]
- [9] Penadés R, Catalán R, Salamero M, *et al.* Cognitive remediation therapy for outpatients with chronic schizophrenia: a controlled and randomized study. *Schizophr Res* 2006; 87(1-3): 323-31. [<http://dx.doi.org/10.1016/j.schres.2006.04.019>] [PMID: 16750611]
- [10] Vinogradov S, Fisher M, de Villiers-Sidani E. Cognitive training for impaired neural systems in neuropsychiatric illness. *Neuropsychopharmacology* 2012; 37(1): 43-76. [<http://dx.doi.org/10.1038/npp.2011.251>] [PMID: 22048465]
- [11] Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am J Psychiatry* 2011; 168(5): 472-85. [<http://dx.doi.org/10.1176/appi.ajp.2010.10060855>] [PMID: 21406461]
- [12] McGurk SR, Twamley EW, Sitzer DI, McHugo GJ, Mueser KT. A meta-analysis of cognitive remediation in schizophrenia. *Am J Psychiatry* 2007; 164(12): 1791-802. [<http://dx.doi.org/10.1176/appi.ajp.2007.07060906>] [PMID: 18056233]
- [13] dAmato T, Bation R, Cochet A, *et al.* A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *Schizophr Res* 2011; 125(2-3): 284-90. [<http://dx.doi.org/10.1016/j.schres.2010.10.023>] [PMID: 21094025]
- [14] Matsui M, Sibata T, Shosaku T. *Frontal/Executive Program-Japanese version(FEP-J): Cognitive Remediation Therapy program for schizophrenia*. Tokyo: Shinkoh-igaku 2015.

- [15] Diagnostic and statistical manual of mental disorders. 4th ed, text revision. Washington, DC: American Psychiatric Association 2000.
- [16] Delahunty A, Morice R. A Manual for Neurocognitive Rehabilitation for Patients with Chronic Schizophrenia: Frontal Executive Program. Albury New South Wales: Department of Health 1993.
- [17] Yamada H, Masui K, Kikumoto K. Positive and negative syndrome scale (PANSS). Tokyo: Seiwa-shoten 1991.
- [18] Kaneda Y, Ueoka Y, Sumiyoshi T, *et al.* Schizophrenia Cognition Rating Scale-Japanese version (SCoRS-J). *Seishin Igaku* 2010; 52: 1027-30.
- [19] Iwasaki S, Miyauchi M, Oshima I, *et al.* The Development of Life Assessment Scale for the Mentally Ill: an assessment of the reliability. *Seishin-Igaku* 1994; 36: 1139-51.
- [20] Keefe RS, Poe M, Walker TM, Kang JW, Harvey PD. The Schizophrenia Cognition Rating Scale: an interview-based assessment and its relationship to cognition, real-world functioning, and functional capacity. *Am J Psychiatry* 2006; 163(3): 426-32. [<http://dx.doi.org/10.1176/appi.ajp.163.3.426>] [PMID: 16513863]
- [21] Kaneda Y, Sumiyoshi T, Keefe R, Ishimoto Y, Numata S, Ohmori T. Brief assessment of cognition in schizophrenia: validation of the Japanese version. *Psychiatry Clin Neurosci* 2007; 61(6): 602-9. [<http://dx.doi.org/10.1111/j.1440-1819.2007.01725.x>] [PMID: 18081619]
- [22] Heaton R, Chelune G, Talley J, Kay G, Curtiss G. Wisconsin Card Sorting Test Manual, Revised and Expanded. Odessa, FL: Psychological Assessment Resources 1993.
- [23] Beck LH, Bransome ED Jr, Mirsky AF, Rosvold HE, Sarason I. A continuous performance test of brain damage. *J Consult Psychol* 1956; 20(5): 343-50. [<http://dx.doi.org/10.1037/h0043220>] [PMID: 13367264]
- [24] Keefe RS, Goldberg TE, Harvey PD, Gold JM, Poe MP, Coughenour L. The brief assessment of cognition in schizophrenia: reliability, sensitivity, and comparison with a standard neurocognitive battery. *Schizophr Res* 2004; 68(2-3): 283-97. [<http://dx.doi.org/10.1016/j.schres.2003.09.011>] [PMID: 15099610]
- [25] Wykes T, Reeder C, Landau S, *et al.* Cognitive remediation therapy in schizophrenia: randomised controlled trial. *Br J Psychiatry* 2007; 190: 421-7. [<http://dx.doi.org/10.1192/bjp.bp.106.026575>] [PMID: 17470957]
- [26] Wykes T, Reeder C, Williams C, Corner J, Rice C, Everitt B. Are the effects of cognitive remediation therapy (CRT) durable? Results from an exploratory trial in schizophrenia. *Schizophr Res* 2003; 61(2-3): 163-74. [[http://dx.doi.org/10.1016/S0920-9964\(02\)00239-6](http://dx.doi.org/10.1016/S0920-9964(02)00239-6)] [PMID: 12729868]
- [27] Wykes T, Spaulding WD. Thinking about the future cognitive remediation therapy what works and could we do better? *Schizophr Bull* 2011; 37(Suppl. 2): S80-90. [<http://dx.doi.org/10.1093/schbul/sbr064>] [PMID: 21860051]
- [28] Wykes T, Newton E, Landau S, Rice C, Thompson N, Frangou S. Cognitive remediation therapy (CRT) for young early onset patients with schizophrenia: an exploratory randomized controlled trial. *Schizophr Res* 2007; 94(1-3): 221-30. [<http://dx.doi.org/10.1016/j.schres.2007.03.030>] [PMID: 17524620]
- [29] Wykes T, Reeder C, Corner J, Williams C, Everitt B. The effects of neurocognitive remediation on executive processing in patients with schizophrenia. *Schizophr Bull* 1999; 25(2): 291-307. [<http://dx.doi.org/10.1093/oxfordjournals.schbul.a033379>] [PMID: 10416732]